112 年年會 海報論文展示：病例報告

目錄

病例報告　112_C 1

揭秘罕見：一例罕見胰腺胃腸間質瘤病例報告

Unveiling the Uncommon: a Case Report of Pancreas Gastrointestinal Stromal Tumor

曾弘鼎[1] 廖家毅[1] 霍德義[2,3]
[1]台北榮民總醫院內科部肝膽腸胃科 [2]台北榮民總醫院醫學研究部基礎研究科
[3]國立陽明交通大學藥理學研究所

Introduction

Around 90% of pancreatic tumors are adenocarcinomas, which are well-studied due to their prevalence and challenges. However, a smaller group of pancreatic neoplasms including islet cell tumors, papillary cystic neoplasms, lymphoma, acinar cell tumors, and metastatic tumors offer a different outlook, being rare and often non-malignant with better prognoses than pancreatic adenocarcinomas.

Case presentation

A 75 years old woman came to emergency department of this hospital with abdominal fullness sensation and fullness for 2 weeks. Abdominal computed tomography with contrast was conducted and a a 26.5cm mass was discovered in upper abdomen. The mass was suspicious arising from pancreas or central mesentery, pancreas cancer was firstly considered. Bilateral hydronephrosis, resulted from mass effect of abdominal tumor was also noted. Sono guide biopsy for the abdominal mass was conducted and the immunohistochemical studies for CD117, CD34, DOG-1, desmin (smooth muscle markers), and S-100 (nervefiber marker) are performed. The result of CD117, Dog1, CD34 was positive and Desmin and S-100 was negative. The patient was diagnosed gastro-intestinal stromal cell tumor(GIST). The chest CT was performed for complete staging and no metastasis was discovered. Surgical intervention in current status is not feasible due to large size. Imatinib was prescribed as neoadjuvant target therapy. The patient went home under stable condition. Tumor restaging would be conducted 3 months after treatment initiated.

Discussion

Gastrointestinal stromal tumors(GIST) is the most common gastrointestinal tract (GIT) tumor. It is believed that the tumors originate from interstitial cells of Cajal (ICCs). The most common locations that the tumors presented were stomach, small intestine and colon. The tumors arise from outside of the GIT are defined as extra-gastrointestinal stromal tumors (EGISTs). EGISTs represent about 5 to 10% of all GISTs. Among all EGIST, pancreatic EGISTs are extremely rare, which represent only 5% of all EGIST. The most common location of pancreatic EGIST was the pancreatic head, and most of the tumor exceeded 5cm. The clinical presentation of EGISTs was variant and non-specific. Most pancreatic EGISTs could be asymptomatic and are accidentally found during image study. The tumor could represent symptoms depending on the tumor's location and size. The most common symptoms include abdominal fullness, bowel habit change, weight loss, and jaundice.

Generally, the serum biomarker provided important clinical diagnostic value. Elevated carbohydrate antigen 19-9 and carcinoembryonic antigen (CEA) could be found in most pancreatic adenocarcinoma. However, the diagnosis value was limited in pancreatic GIST.

Radioevaluation including abdominal CT, US, and endoscopic US could be used to evaluate the tumor invasion.
The diagnosis of EGIST is based on histopathological, immunohistochemical, and molecular features. The most typical immunohistological staining features are CD117 and c-KIT. Approximately, 95% of tumors defined as GIST or EGIST stain CD117-positive. GISTs stain positive CD34 (60%-70%), heavy caldesmon (80%), SMA (30%-40%), S100 (5%), and desmin (<5%).
The curative treatment for EGISTs is surgical resection. The goal of tumor resection is to achieve clear margin and complete resection. Pancreaticoduodenectomy is the optimal treatment option for pancreatic head tumors and distal pancreatectomy could be considered in pancreatic tail tumors.
For those patients who are not suitable for operation, tyrosine kinase inhibitors, such as imatinib, can be used for neoadjuvant and adjuvant therapy with improved survival.
The prognosis of pancreatic EGISTs was worse than gastric GIST. The 5-year disease-free survival (DFS) and disease-specific survival rates are 66.1% and 95.8%. The tumor Mitotic index was the only risk factor for disease-specific survival of pancreatic GISTs.

Conclusion

Pancreatic extra-gastrointestinal stromal tumors are rare tumors which represent less than 1% of all gastrointestinal stromal tumors. It could be asymptomatic or presents symptoms according to the tumor location and size. The diagnosis is made according to histology, molecular and immunohistochemical features. The treatment of EGIST was similar to GIST, Curative surgical resection should be considered first. For those who are not suitable for surgical intervention, tyrosine kinase inhibitors, such as imatinib could be used.

病例報告　112_C 2

突發性雙腳非凹陷性水腫作為災難性腎臟腫瘤之初始表現症狀

Sudden Onset of Non-pitting Edema of Bilateral Legs as the Initial Presentation of Catastrophic Renal Cancer

林書聿[1] 林志慶[2]

[1]臺北榮民總醫院內科部 [2]臺北榮民總醫院內科部腎臟科

Introduction

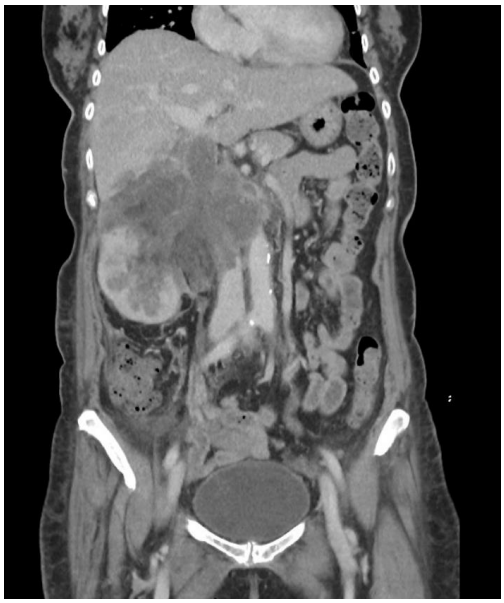
It is known that patients with malignant diseases have more thromboembolic events then general population. Previous studies showed a ninefold increased risk of venous thromboembolism(VTE)[1], and fivefold increased annual incidence of VTE in malignancy patients compared to the general population[2]. And 20-percents of first-time VTE was associated with cancer[3]. The mechanism of malignancy related thrombosis is not fully understood yet.

Case presentation

The patient is a 68-year-old female with a medical history of hypertension, type 2 diabetes mellitus, and hypothyroidism with regular thyroxine supplement use. Intermittent painless gross hematuria was noticed in August, 2022 and urine cytology was obtained, revealing atypical cells. Cystoscopy was performed and revealed no tumor growth, no urolithiasis in the urinary bladder. Renal magnetic resonance imaging (MRI) was done in September, 2022 and found no hydronephrosis, no hydroureter, no tumor growth at bilateral kidney.

The patient was then admitted to the nephrology ward for dysuria for 1 week in January, 2023. Urine analysis showed microscopic hematuria, pyuria, and bacteriuria. The patient was then treated with antibiotics for urinary tract infection. Due to right flank knocking pain noticed while admission, renal ultrasonography was arranged to rule out right acute pyelonephritis, which then revealed mild right hydronephrosis, heterogeneous echogenicity in right kidney, and hypoechoic nodule at right suprarenal region. Bilateral leg swelling was reported by the patient 1 day after renal ultrasonography. Physical examination showed bilateral lower leg non-tenderous, non-pitting edema, and we treated the leg edema with diuretics at first.

Figure 1. The coronal view of right renal tumor.
This is the post-contrast coronal view of abdominal computer tomography of our case. Lobulated tumor growth at right renal pelvis with infiltration to liver and right renal hilum. Compromised inferior vena cava(IVC) and abdominal aorta with IVC thrombosis. *IVC thrombosis.



Abdominal computed tomography was then arranged to rule out right renal abscess. However, a large tumor growth from the right kidney was found with renal hilum infiltration and encasing of right renal artery. Compromised inferior vena cava(IVC) and bilateral renal veins with thrombosis were found.(Figure 1.) The tumor had superiorly involvement of right adrenal

gland and liver, inferiorly extension to level of aortic bifurcation. Multiple lymph nodes are noticed at retrocaval, aortocaval and left retroperitoneum. There is also soft tissue nodules at both lower lungs, metastatic tumor was firstly considered. The patient then underwent a right kidney tumor and a lung tumor biopsy. Kidney biopsy pathology showed necrosis with atypical cells. Immunohistochemical stain showed positive for CK(cytokeratin), GATA3, and focally positive for EMA(Epithelial membrane antigen), while being negative for PAX8, and cathepsin K, suggesting a carcinoma. Lung biopsy pathology revealed squamous cell carcinoma. The patient was then referred to a medical oncologist for further malignancy treatment.
Due to tumor necrosis, biopsy result was not sufficient to determined which tumor type this current renal tumor is. However, the biopsy of metastatic lung lesion revealed squamous cell carcinoma. Oncological specialist favored renal squamous cell carcinoma with lung and liver metastasis, and the patient was then treated accordingly.

Discussion

In current understanding, malignancy cause thrombosis by direct and indirect mechanisms. Direct mechanisms were caused by cancer cell expression of procoagulant proteins. Indirect mechanisms include inflammatory cytokines and cancer-derived factors secretion and subsequential platelet activation, endothelial dysfunction, and release of neutrophil extracellular traps, which could further cause platelet aggregation and thromboembolic events[4-6]. Solid tumor could also cause extrinsic compression of vessels to increase the risk of thrombus formation[7,8].
The clinical presentation of IVC thrombosis varies significantly and may not correspond with the severity of IVC thrombosis. Nonspecific back, abdominal, or pelvic pain often precede leg symptoms[7]. Edemas of the lower body, the genitals, and the lower extremities may be found in these patients. Tortuous superficial veins on lower body parts may be found in more chronic courses[8]. As seen in our case, right side flank pain precedes bilateral leg edema.
Low-molecular-weight heparin(LMWH) has been the standard of care for treatment of acute cancer associated thrombosis for at least a decade. A meta-analysis of previous randomized controlled trials showed that, in compared with vitamin-K antagonist(VKA), LMWH reduced the risk of recurrent VTE by 40% with no difference in major bleeding[9].

Conclusion

We should be reminded that lower leg swelling could include severe differential diagnosis including malignancy, and in this current case, a catastrophic renal tumor. The possibility of IVC thrombosis should always be kept in mind when dealing with patients with nonspecific back, abdominal, or pelvic pain, with or without edemas of the lower limbs or the genitals.

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病例報告　112_C 3

常見誤診為惡性腫瘤引致膽管阻塞的免疫球蛋白 G4 相關性膽管炎
IgG4-Associated Cholangitis, A Great Mimicker of Malignant Biliary Obstruction – A Case Report and Review

朱純正 [1]　蔡弘正 [2]
臺北榮民總醫院 [1] 內科部 [2] 內科部過敏風濕免疫科

Introduction

Immunoglobulin G subclass 4 (IgG4)-related disease (IgG4-RD) stands as a nascent and emerging immune-mediated condition and is gaining more attention by clinicians in the past decades for its various clinical manifestations. With its multi-organs involving potency, apprehending IgG4-related disease poses a challenge, necessitating clinicians to possess a keen cognizance of this ailment. The hallmark of IgG4-RD is the infiltration of affected tissues by IgG4-positive plasma cells, resulting in characteristic histopathological findings including storiform fibrosis, increased eosinophils, obliterative phlebitis, and a lymphoplasmacytic infiltrate rich in IgG4-positive cells and could be presented as tumefactive lesions in those affected organs.

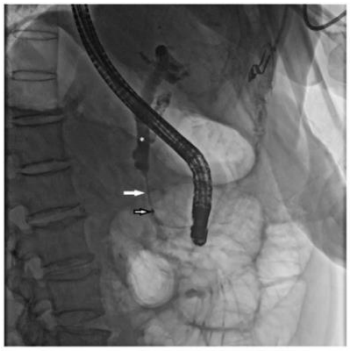
Concurrently, IgG4-associated cholangitis (IAC), as part of a larger spectrum of IgG4-RD, has surfaced as a unique and clinically consequential entity within the realm of hepatobiliary disorders and is one of the most common extra-pancreatic manifestations of IgG4-RD. It affects the biliary system which usually occurs along with autoimmune pancreatitis in about 90% of the cases but can occur at times in isolation[1]. IAC primarily involves the biliary tree, leading to a range of clinical presentations that often mimic other hepatobiliary disorders such as primary sclerosing cholangitis (PSC) and cholangiocarcinoma. Patients with IAC can present with obstructive jaundice, pruritus, abdominal pain, and constitutional symptoms. Accurate diagnosis hinges upon a multidisciplinary approach, integrating clinical, radiological, serological, and histopathological data. Elevated serum levels of IgG4 and characteristic radiological findings, such as biliary strictures with a "double ring" appearance on imaging, can provide crucial diagnostic clues.

Herein, we present a male patient who exhibited manifestations of obstructive jaundice, closely resembling cholangiocarcinoma, yet lacking the hallmarks of acute pancreatitis. Remarkably, this individual displayed a robust response to steroid therapy.

Case presentation

A 71-year-old Taiwanese male patient was hypertensive and was under medications was referred from Taipei City Hospital with painless obstructive jaundice and unintentional body weight loss for 9 kilograms within two weeks. He had clay-colored stool, dark-colored urine and pruritus and complained of anorexia upon his first visit. During his previous admission, abdominal computed tomography (CT) was carried out and revealed mild dilatation of biliary tract. Hence, he underwent endoscopic retrograde cholangiopancreatography (ERCP) which showed a 2.3 cm distal

Figure 1. ERCP showing stricture of distal common bile duct (white arrow) with subsequent dilation of upstream biliary tract (star). Tip of wire of ERCP (white arrow with black edge) was shown in the picture.



common bile duct (CBD) stricture with upstream biliary dilation (Figure 1). A biliary stent was inserted across the stenotic site and trans-ampullary biopsy was performed for suspicion of malignancy related obstruction. Magnetic resonance imaging (MRI) was performed after stent insertion and a tumefactive lesion was noted in peri-ampullary area with a mild swelling pancreas and a prominent wall-thickened CBD (Figure 2).

The patient was transferred to Taipei Veterans General Hospital due to suspected of distal cholangiocarcinoma. We reviewed his pathological slides and found no evidence of carcinoma but prominent lymphoplasmacytic infiltration in the lamina propria of the biopsy tissue with nearby storiform stromal fibrosis. The patient was further evaluated with serum levels of tumor markers, carcinoembryonic antigen (CEA: 1.6 ng/mL; range 0–5 ng/mL) and carbohydrate antigen 19–9 (CA 19–9: 11.8 U/mL; normal range 0–36 U/mL) which were within normal range. As a way out of this diagnostic riddle, the mass was suspected to be IAC and the serum level of IgG4 was tested which turned out 346.9 mg/dL (normal range 4-86 mg/dL).

An oral prednisolone 40mg was started and the patient took great stride in the following days, which further pointed the diagnosis toward IAC. The clinical improvement of the patient was accompanied by normalization of the liver functions (Table 1). The patient was followed up in our outpatient department of Rheumatology smoothly with a steroid tapering plan by 5 mg every two weeks.

Figure 2. Abdominal MRI (done after biliary stent insertion) showing a mass like lesion in peri-ampullary area. a: axial view showing a tumefactive lesion encasing the common bile duct with obvious wall-thickening appearance of the biliary structure (white arrow). b: coronal view showing mass like lesion in distal part of common bile duct (white arrow) and generally swelling appearance of the pancreatic head (star).

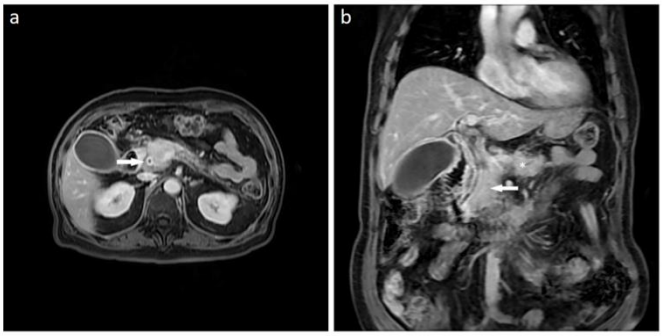


Table 1 Comparison of laboratory findings among the time of initial presentation, after stent insertion but before using steroid and one week after using prednisolone.

	Parameters	At the time of initial presentation	After stent insertion, but before using steroid	One week after using prednisolone	Reference range
1.	Total bilirubin	11.1	0.88	0.99	<1.2 g/dL
2.	Direct bilirubin	9.81	0.61	0.55	<0.5 mg/dL
3.	Alanine aminotransferase	195	11	10	<41 /L
4.	Aspartate aminotransferase	108	20	11	<40 /L
5.	Alkaline phosphatase	303	244	70~	40-129 /L
6.	Gamma-glutamyl transferase	637	264	54	8~61 U/L

Discussion

Our case underscores the diagnostic intricacies surrounding IAC, particularly when its clinical presentation mimics that of cholangiocarcinoma. It is vital to distinguish these two different diseases given the stark contrast in treatment approaches between IAC and cholangiocarcinoma.

Attaining an accurate diagnosis to cholangiocarcinoma is straightforward which often requires a direct biopsy to the lesion whereas diagnosing IAC presents a more nuanced

challenge. Because IAC lacks specific diagnostic features, a high index of suspicion in all patients with unexplainable biliary strictures leads to the most accurate diagnosis. The definitive diagnosis of IAC is based on the HISORt criteria (Histology, Imaging, Serology, Other organ involvement, and Response to therapy) which was firstly proposed by Ghazale et al. from the Mayo group. The histopathological (H) analysis of the tissue shows diagnostic hallmarks: lymphoplasmacytic infiltration, storiform fibrosis and obliterative phlebitis. MRI scan of the abdomen or cholangiogram (I) is used to identify any strictures in the biliary tree. Serological study (S) is positive when the levels of IgG4 in serum are greater than 135 mg/dL. Involvement of other organs (O) and response to steroid therapy (Rt), which shows the rapid resolution of hepatobiliary enzymes or the resolution of stricture, are the other components of the criteria. Either (H and Rt) or (S and I) are required for the definitive diagnosis. In our case, the biopsy tissue showed lymphoplasmacytic infiltration, serum IgG4 level was 346.9 mg/dL, MRI scan showed dilated left side IHDs with mild wall thickening of CBD/IHDs and the patient responded to steroid therapy, thus confirming the diagnosis of definitive IAC.

As for the treatment, surgical resection, notably encompassing extensive hepatic resection, continues to serve as the cornerstone of therapeutic intervention for perihilar cholangiocarcinoma[2]. While the therapeutic approach to IAC consists of immunosuppressive regimens, with corticosteroids serving as the primary treatment and prompt initiation of therapy can lead to significant clinical improvement and prevent disease progression. As an alternative, surgical resection or biliary drainage proved to be effective for symptom relief in IAC. Concerning the clinical courses after applying steroids, one study compares the rate of relapses by different way of treatment with 53% of cases relapse after withdrawing from steroids, whereas 44% relapse after surgery with following steroids[3]. The role of other immunomodulatory drugs such as rituximab or azathioprine harbors some ambiguity. One study showed improvement in biliary strictures after using rituximab while another study showed no difference in the relapse-free survival between patients of IAC treated with additional immunomodulatory drugs with steroids and steroids alone[4 5].

In our case, we soon applied steroids after confirming the diagnosis and lab data of his liver function test took great strides after using steroids. He is regularly followed up in our outpatient department and currently shows no signs of relapse.

Conclusion

The clinical and radiographic findings of IAC can resemble those of cholangiocarcinoma; however, the presence of low levels of tumor markers and elevated levels of serum IgG4 should lead to considering the possibility of IAC. As a highly steroid-sensitive immune-mediated disorder, both internal medicine physicians and surgeons should bear in mind this medical condition in patients with biliary strictures, in order to prevent patients from undergoing unnecessary surgical interventions or examinations.

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病例報告　112_C 4

Gallstone ileus : a case report An elderly patient presented with abdominal pain and vomiting for days

陳昱甫 [1] 謝秉翰 [1] 楊宗杰 [1,2] 羅景全 [1,2] 侯明志 [1,2]
[1] 台北榮民總醫院內科部胃腸肝膽科
[2] 國立陽明交通大學醫學院醫學系

Introduction

Gallstone ileus is a rare mechanical ileus caused by a gallstone impaction in the intestinal tract, which occurs in only 0.15% to 1.5% of cholelithiasis cases and less than 0.1% of overall cases of ileus[1]. The recurrence rate is between 5% and 8%[2].

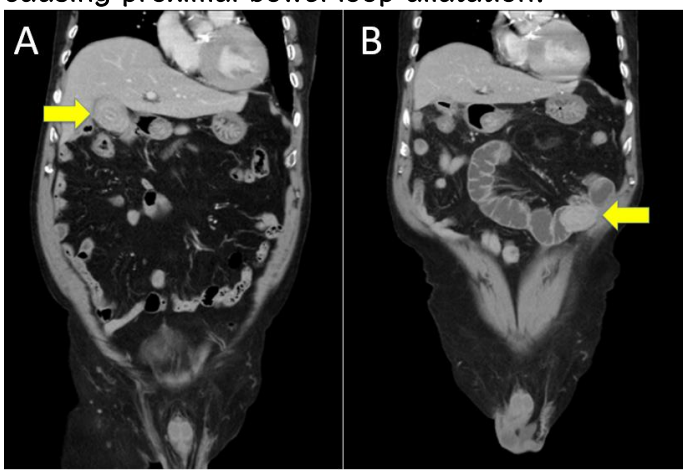
In most cases, gallstones are eliminated via an internal biliary fistula from the gallbladder to the duodenum, colon, or stomach. Internal biliary fistula are often caused by vascular insufficiency or chronic inflammation due to compression of the gallbladder wall during calculus formation, allowing for the expulsion of the calculus.

Gallstone ileus is a challenging condition to diagnose, and any delay in treatment may result in significant morbidity and mortality. In elderly patients presenting with abdominal pain, vomiting, and signs of small bowel obstruction, a heightened suspicion for gallstone ileus is warranted[3]. Abdominal radiography combined with CT scan is the most effective diagnostic tool[4]. The selection of treatment options should be made on a case-by-case basis. For elderly patients with significant comorbidities, enterolithotomy alone approach may be the most appropriate choice.

Case presentation

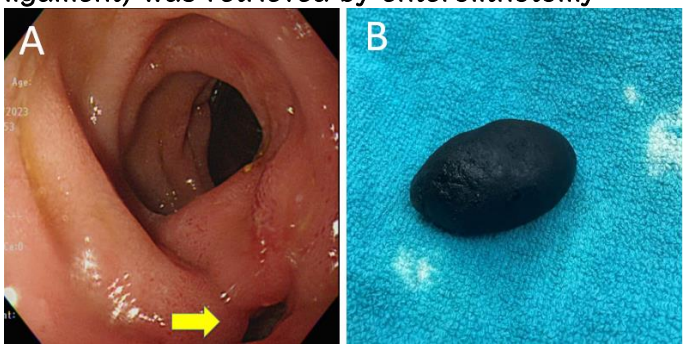
A 81-year-old male had the underlying diseases of right clear-cell renal cell carcinoma status post cryotherapy in stable condition, poorly differentiated gastric adenocarcinoma status post wedge resection with recent recurrence at anastomosis, old stroke, hyperlipidemia and hypertension. One 4.3 cm laminated gallstone had been documented on abdominal computed tomographic (CT) 5 months ago (Figure 1A). This time, he presented to the Emergency Department with intermittent vomiting for 4 days and periumbilical pain for 1 day. Physical examination revealed soft but distended abdomen with periumbilical tenderness. The bowel sounds were decreased on abdominal auscultation. Lab testing revealed an elevated white blood cell count (19800/μL) and an elevated C-reactive protein (1.66 mg/dL). The abdominal CT revealed wall thickening of gallbladder with internal air density, and a gallstone impaction in the small bowel with proximal bowel loop dilatation (Figure 1B).

Figure 1.
(A) Abdominal CT 5 months ago showed a laminated gallstone (arrow) with irregular wall thickening of gallbladder.
(B) Abdominal CT this time showed a 4.3 cm gallstone (arrow) impaction in the small bowel, causing proximal bowel loop dilatation.



Upper gastrointestinal endoscopy showed a small hole at duodenal bulb, suspected fistula formation (Figure 2A). Under the impression of cholecystoduodenal fistula related gallstone ileus, the patient underwent open enterolithotomy. A huge gallstone, 4*2.5 cm in size, locating at proximal jejunum (70 cm distal to the Treitz ligament) was retrieved by enterolithotomy (Figure 2B). He had an uneventful recovery thereafter.

Figure 2.
(A) Upper gastrointestinal endoscopy showed a small hole (arrow) at duodenal bulb, suspected cholecystoduodenal fistula formation
(B) A huge gallstone, 4*2.5 cm in size, locating at proximal jejunum (70 cm distal to the Treitz ligament) was retrieved by enterolithotomy



Discussion

Gallstone ileus presents with a incidence of 30-35 cases per 1,000,000 admissions over 45 years[5]. It is a rare complication of cholelithiasis, typically observed in elderly patients with multiple comorbidities. Gallstones cause ileal obstruction in 50-70% of cases, primarily affecting the narrowest segment of the intestine[6]. In this case, the patient's advanced age and multiple comorbidities resulted in his non-specific symptoms. This delayed the diagnosis and may have exacerbated the condition.

The clinical presentation of gallstone ileus includes abdominal pain, abdominal distension, vomiting, and fever. Abdominal CT is superior to plain abdominal film or ultrasound in diagnosing gallstone ileus, with up to 93% sensitivity[4]. In this case, we also performed UGI endoscopy, which revealed the presence of a duodenal fistula, suspected cholecystoduodenal fistula formation.

A history of gallstone, the presence of duodenal fistula, and the stone impaction in the small bowel shown on the present CT confirmed our diagnosis of gallstone ileus. Surgical treatment remains a subject of ongoing research and included[7]:

Enterolithotomy alone: less invasive, but may have more post-operation gallstone ileus recurrences.

Enterolithotomy with cholecystectomy performed later (two-stage surgery): maybe elective while patients had residual gallstones.

Enterolithotomy, cholecystectomy and fistula repair (one-stage surgery): more invasive, higher postoperative complications, higher mortality. Suitable for stable patients with less comorbidity.

Enterolithotomy alone was chosen for this patient considering his advanced age and multiple comorbidities. No recurrence of gallstone ileus was observed until now.

Conclusion

1. Gallstone ileus poses significant diagnostic and therapeutic challenges especially in elderly patients with multiple comorbidities. The use of CT scan can aid in accurate diagnosis.
2. A history of gallstone, the presence of duodenal fistula, and the stone impaction in the small bowel shown on the CT scan confirmed our diagnosis of gallstone ileus.
3. Treatment should be individualized. Enterolithotomy alone is a option for elderly patients with significant comorbidities. Prompt recognition and appropriate management are crucial in improving patient outcomes.

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病例報告　112_C 5

Recurrent intestinal Behçet's Disease complicated with cytomegalovirus colitis: a case report and review

Chin-Te Tseng[1] Ping-Han Hsieh[1] Tsung-Chieh Yang[1,2] Jiing-Chyuan Luo[1,2] Ming-Chih Hou[1,2]
[1]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital
[2]School of Medicine, College of Medicine, National Yang Ming Chiao Tung University

Introduction

Behçet's disease (BD) is a multi-systemic inflammatory disorder of an unknown etiology and shows a chronic recurrent clinical course. Among patients with BD, up to 5%~10% are diagnosed with intestinal BD[1].

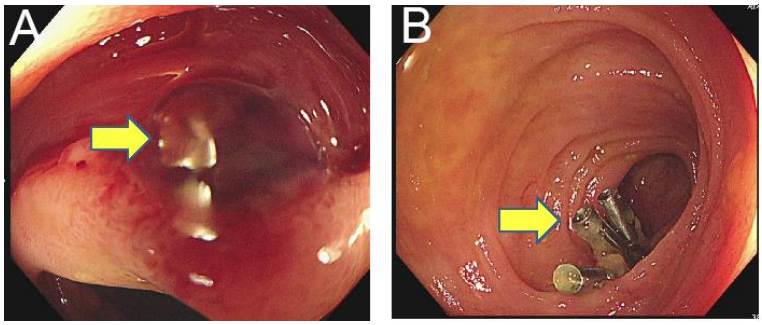
Intestinal BD is more frequently in East Asian countries than in Western or Middle Eastern countries. While any part of the gastrointestinal (GI) tract can be involved, the most common involved location is the ileocecal area. A few, large (>1cm), deep ulcerations with round/oval shape and discrete border are characteristic endoscopic findings of intestinal BD[2]. As intestinal BD shares some characteristics with inflammatory bowel disease, or cytomegalovirus (CMV) colitis, it is important to distinguish and treat these disease entities separately from the standpoint of precise medicine.

5-Aminosalicylic acids, corticosteroids, and immunomodulators are conventional therapies, but a considerable number of patients eventually become unresponsive to these pharmaceutical treatments. Recently, biologic agents, such as anti-tumor necrosis factor-alpha inhibitors, have also been suggested as a new treatment option for intestinal BD[3].

Case Presentation

A 57-year-old male had the underlying diseases of type 2 diabetes mellitus, hypertension, recurrent CMV viremia, and recurrent intestinal BD with history of perforated colon, peritonitis and septic shock status post ileostomy to bypass colon then closing ileostomy in 2012. He kept regular rheumatology outpatient clinic follow-up with Hydroxychloroquine and Prednisolone currently.

Figure 1.
(A) A deep ulcer (arrow) about 2x1 cm was noted at 15 cm proximal to the ICV
(B) APC and 4 endoclips (arrow) were applied for hemostasis



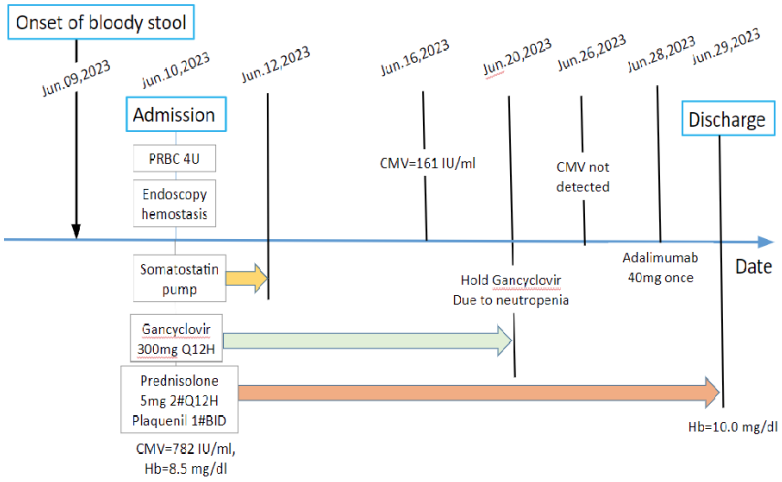
This time, he presented to the Emergency Department with right lower quadrant abdominal pain, massive bloody stool total 4 times in a day combined with dizziness. He also mentioned that progressed oral ulcer with intermittent low grade fever in the recent month even after up-titrating the steroid dose. Physical examination revealed soft abdomen with focal right lower tenderness. The bowel sounds were hyperactive on auscultation. Lab test revealed a decreased hemoglobin level (baseline: 10 mg/dl -> 8.5 mg/dl) and CRP elevation (3.43 mg/dl). Blood CMV PCR =782 IU/mL. Upper GI endoscopy showed only small mucosal breaks <5 mm above EC junction without gastric or duodenal ulcer. Colonoscopy disclosed a 1 cm round ulcer with a central brown protruding spot at 30 cm proximal to ileocecal valve (ICV), status post biopsy, argon plasma coagulation

(APC), and 2 endoclips application for hemostasis; another large deep ulcer about 2x1 cm was noted at 15 cm proximal to the ICV (Figure 1A), status post biopsy, APC, and 4 endoclips application for hemostasis (Figure 1B). Pathology of the biopsy specimen identified CMV by immunohistochemistry.

Under the impression of recurrent intestinal BD complicated with CMV colitis, the patient received packed red blood cells transfusion (total 4U), somatostatin pump (total 3 days), ganciclovir treatment (300mg Q12H for 10 days). And when CMV titer was undetectable, Adalimumab was prescribed after consulting with a rheumatologist.

After these treatment, his hemoglobin remained stable level without further bloody stool episode. Then he was arranged discharge with stable clinical condition.

Figure 2. Timeline of the patient's clinical course including clinical events, medication, and drug dosage



Discussion

Intestinal BD occurs in 5-10% of patients with BD. Although clinical manifestations of intestinal BD vary widely from mild abdominal pain to bowel perforation or massive hemorrhage, GI involvement of BD often predicts poor treatment response and unfavorable prognosis of the affected patients[4]. The pathogenesis of intestinal BD is related to an abnormal T-cell immune response and cytokines derived from T helper type 1 (Th1) lymphocytes, including TNF-α, IFN-γ, IL-12, and IL-18[5]. Hence, the novel anti-TNF-α agents were choice for intestinal BD who refractory to steroids.

CMV is prevalent among the general population with an overall seroprevalence of 30%-70% and GI CMV disease are one of the mostly encountered clinical manifestations. Esophagus and colon are the frequently involved sites. Patients with colonic CMV disease may present with diarrhea with or without blood, abdominal pain, urgency and tenesmus accompanied with systemic symptoms such as fever, malaise, anorexia and weight loss. Its presentation had some similarity with BD[6].

In this case, because histological examination of the biopsy specimen identified CMV and serological testing revealed a CMV real time PCR positive, we initiated induction therapy of CMV. In addition, colonoscopy showed deep ulcers, which was compatible with intestinal BD with recent bleeding, status post endoscopic hemostasis. Only when the blood CMV PCR was undetectable, the anti-TNF-α Adalimumab was prescribed. His hemoglobin level was kept in a stable level without further bloody stool episode.

Conclusions

1. GI manifestations of BD are of particular importance as they are associated with significant morbidity and mortality.
2. For those poor response to steroid, the novel monoclonal anti-TNF-α antibody might be a choice for recurrent BD.

3. CMV colitis might present with diarrhea with (or without) blood, abdominal pain, urgency and tenesmus accompanied with systemic symptoms such as fever, malaise, anorexia and weight loss. It is difficult for clinician to differentiate between BD. Some reports even revealed the CMV infections after experiencing the anti-TNF-α treatment[6].

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病例報告　112_C 6

右橫膈下動脈支配之肝癌繼栓塞及燒灼後併發右側膿胸

Hepatocellular carcinoma with extra-hepatic artery supply complicated with right side empyema after trans-arterial chemoembolization and radiofrequency ablation

賴信樺[1]　李癸汌[2]

[1]台北榮民總醫院內科部 [2]台北榮民總醫院內科部胃腸肝膽科

Introduction

Extrahepatic blood supply is seen in around 17–27% of hepatocellular carcinoma (HCC) lesions. Evidence suggests that the extrahepatic supplies commonly originate from the right inferior phrenic artery, cystic artery and omental artery. A previous history of trans-arterial chemoembolization (TACE) is an important predisposing factor for extrahepatic circulation in hepatocellular carcinoma. Additional extrahepatic collateral vessel chemoembolization is suggested to increase the efficacy of treatment. However, there is also evidence indicating that in some rare cases, pleural effusion and basal atelectasis were noted after chemoembolization of inferior phrenic artery or internal mammary artery. It is a much rare complication that empyema occurs after chemoembolization and radiofrequency ablation (RFA).

Case presentation

An 80-year-old male previously diagnosed with hepatocellular carcinoma in size of 5.1cm over liver 8th segment, BCLC stage B, presented to our hospital with shortness of breath and abdominal distension for one week. Tracing back while the patient received the first TACE, the angiography result revealed tumor stains at branches of the right hepatic artery with non-enhancing component at the center of the tumor. During the second TACE, the angiography result showed the blood supply of the tumor arised from right inferior phrenic artery and right posterior hepatic artery. His serum laboratory data revealed leukocytosis with high C-reactive protein (CRP) level. In this admission, chest x-ray image revealed right hemithorax white-out. Chest ultrasonography image showed large amount of right side pleural effusion. Patient underwent thoracocentesis and the pleural effusion analysis favored exudate with neutrophil predominance, indicating empyema. Hence, a chest tube was inserted for empyema drainage. Bacterial culture of peripheral blood and pleural effusion both yield Oxacillin-susceptible Staphylococcus aureus (OSSA). After intravenous antibiotics treatment, chest tube was removed successfully and the patient was discharged.

Discussion

For patients with nonmetastatic and unresectable HCC, there is evidence supported that the addition of ablative therapy was associated with improved freedom from local progression and overall survival. The most observed major complications after artery chemoembolization and ablation were gastrointestinal bleeding, abscess, liver failure and hepatic infarction. Empyema is a relatively rare complication. In one study, 55 patients underwent chemoembolization and only one case was complicated with liver abscess and empyema after combination of inferior phrenic artery and multiple intercostal artery chemoembolization. In this case, the patient developed right side empyema with bacteremia after chemoembolization

and ablation within one month. Chest tube placement is the least invasive and most common non-surgical modality for empyema and surgical intervention should be considered when drainage via tube thoracostomy fails or in multi-loculated empyema.

Conclusion

Extrahepatic circulation in hepatocellular carcinoma is mostly seen in patients with prior history of TACE. Right inferior phrenic artery is one of the common extrahepatic artery supplies for the HCC. It is suggested that combination of chemoembolization and ablation is suitable in patients with nonmetastatic and unresectable HCC. However, empyema after chemoembolization and ablation is a rare yet fatal complication.

病例報告　112_C 7

肺部蘭格罕細胞組織球增生症

Pulmonary Langerhans Cell Histiocytosis – A Case Report

林君豪[1]　劉嘉仁[2,3,4]
[1]臺北榮民總醫院內科部 [2]國立陽明大學內科學科副教授 [3]臺北榮民總醫院血友病整合治療中心主任
[4]臺北榮民總醫院內科部血液科主治醫師

Introduction

Histiocytosis is an uncommon hematological disorder derived from the monocyte and dendritic cell lineage. Histiocytosis can be categorized into five groups: Langerhans (L), Cutaneous and mucocutaneous (C), Rosai-Dorfman disease (R), Malignant histiocytosis (M), and Hemophagocytic lymphohistiocytosis (H) group.

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare cystic lung disease that usually involves the upper zone of the lung. Peak incidence is around 20-40 years of age. Diagnosis is mainly made by pathological proof of a lung biopsy. Histological features show peribronchial inflammatory lesions, with variably sized stellate nodules aggregates of Langerhans cells. Immunohistochemistry stains are positive for S-100, CD1a, Langerin, and BRAF. Treatment includes smoking cessation, *BRAF* inhibitors, MEK inhibitors, and other antimetabolites.

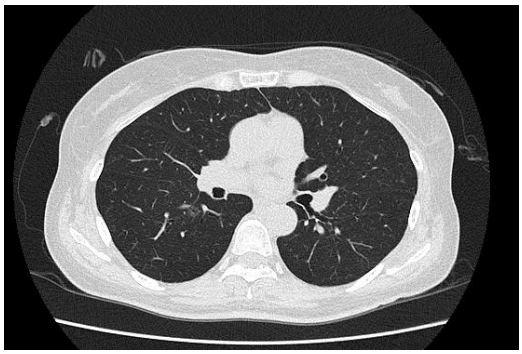
Here, we present an unusual case of a senior woman diagnosed with right lower lung PLCH.

Case presentation

This is a 65-year-old woman who had a history of dyslipidemia and active smoking for 60 pack-years. She initially underwent low-dose CT during a health check-up, which revealed two ground-glass opacity nodules at the periphery of right upper and lower lung, sized 3-5mm in diameter. During follow-up CT six months later, a solitary ground-glass opacity nodule with cystic content about 6mm in diameter at the B6 segment of the right lower lung was noticed (Fig. 1A). She denied symptoms of dyspnea, hemoptysis, cough, or constitutional symptoms. Blood tests including basic metabolic panels and blood counts were unremarkable. She underwent laparoscopic wedge resection of the right lower lung. A tentative pathological diagnosis of Langerhans cell histiocytosis was made. Thus, she was referred to our tertiary care center for further evaluation and management. During her first visit, a peripheral blood smear was done and no immature cells were found. A blood test also indicated no light chain restriction. Chest CT was arranged, and

Figure 1. Chest Images.
Preoperative chest CT (Panel A) showed a stationary 6 mm ground-glass opacity nodule with cystic content in the B6 segment of the right lower lung. Postoperative (Panel B) PET/CT showed a hypermetabolic lung nodule at the right hilum, which is compatible with PLCH residual tumor.

A



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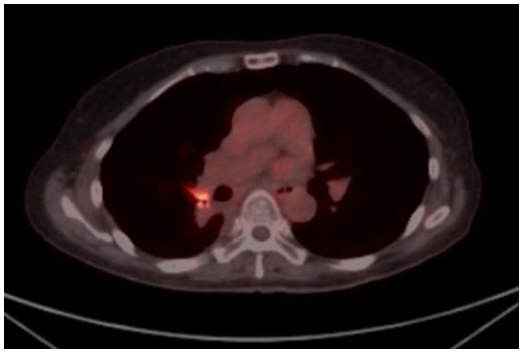


reported the presence of a 6mm sized nodule at the right upper lung, with enlarged lymph nodes over the paratracheal region, aortopulmonary window, subcarinal region, and right cardiogenic angle. Whole-body fluorodeoxyglucose (FDG)-PET/CT scan was also arranged and a hypermetabolic lung nodule at the right hilum was noticed, which may be correlated to a residual tumor; no abnormal bone marrow uptake was noticed (Fig. 1B).

We applied a pathology slide review for her lung specimen. Under microscopic inspection, sections of lung tissue show an aggregate of Langerhans cells with some eosinophils. Immunohistochemical staining of the Langerhans cells was positive for S-100, CD1a, Langerin, and BRAF; and negative for CD163 and TTF-1 stains (Fig. 2).

A final diagnosis of isolated pulmonary Langerhans cell histiocytosis was made. Cessation of cigarette smoking was suggested for initial management, and a follow-up appointment and chest radiography will be arranged (Fig. 3).

Figure 2. Biopsy Specimens.
Under high-power fields, sections of lung tissue showed an aggregate of Langerhans cells with some eosinophils (Panel A). The Langerhans cells are positive for S-100 (Panel B), CD1a (Panel C), Langerin, and weak positive BRAF (Panel D), and are negative for CD163 and TTF-1 on immunohistochemical stains.

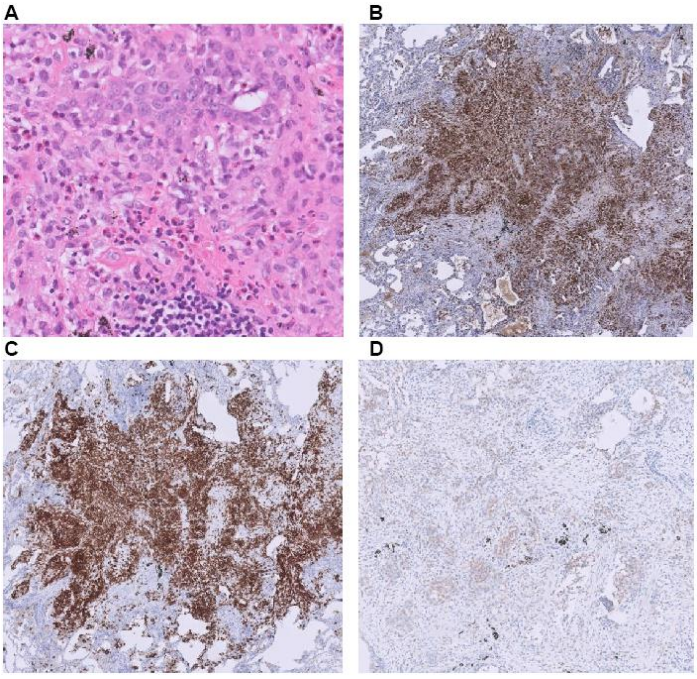


Figure 3. Timeline of the Patient's Disease Course.

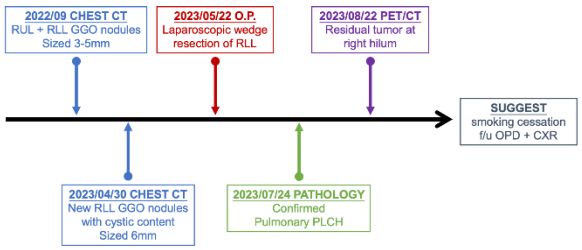
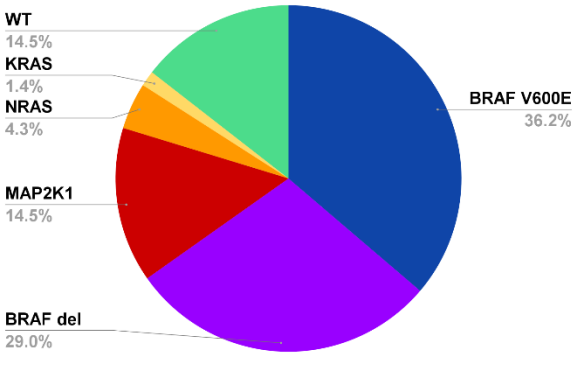


Figure 4. MAPK Alterations of LCH6. Adapted from Jouenne et al. (2020).
Notably, KRAS mutations were virtually absent from all PLCH lesions. BRAF V600E was not associated with clinical presentation or outcome.



Discussion

Histiocytosis is a rare neoplastic disorder derived from the monocyte, macrophage, and dendritic cell lineage. According to the Histiocytic Society classification[1], the disease can be categorized into five groups based on their clinical, histologic, immunophenotypic, and molecular features: Langerhans (L) group, Cutaneous and mucocutaneous (C) group, Rosai-Dorfman disease (R) group, Malignant histiocytosis (M) group, and Hemophagocytic lymphohistiocytosis (H) group. Commonly involved organs of Langerhans cell histiocytosis (LCH) include bone, skin, lungs, pituitary, central nervous system, and lymph nodes. Among

them, isolated pulmonary LCH accounts for 16% of all adult LCH[2].
PLCH occurs predominantly in young adults, with peak incidence at 20-40 years of age, and is known to be associated with cigarette smoking[3]. PLCH may be presented with incidental detection on chest radiographs or with symptoms, including respiratory symptoms, constitutional symptoms, or spontaneous pneumothorax[4].
Histological features of PLCH show peribronchial inflammatory lesions, with variably sized stellate nodule aggregates of Langerhans cells; also with eosinophils, lymphocytes, plasma cells, activated macrophages, and multinucleated giant cells. These Langerhans-like cells are positive for CD1a, S100, and langerin on immunostains[5]. Mitogen-activated protein kinase (MAPK) alterations are present in nearly 90% of LCH lesions[6] (Fig. 4).
Essential evaluation of PLCH includes laboratory testing, pulmonary function test, whole-body FDG-PET/CT scan including distal extremities, and lung biopsy, either via bronchoscopy or surgery. Highly specific image features of PLCH include small ill-defined or stellate nodules, reticular and nodular opacities, upper zone cysts or honeycombing, costophrenic angle sparing, and preservation of lung volume[7]. Differential diagnosis of similar HRCT image feature includes pulmonary lymphangioleiomyomatosis (LAM), tuberous sclerosis, lymphoid interstitial pneumonia, Birt-Hogg-Dubé syndrome, sarcoidosis, and idiopathic interstitial pneumonia.. Other evaluations may be useful under certain circumstances, including transthoracic echocardiography, bone marrow biopsy, endoscopic retrograde cholangiopancreatography, and endocrine evaluation.
Treatment of all PLCH patients requires smoking cessation and avoidance of smoke exposure. Many of the patients may have disease resolution with smoking cessation alone. For those with disease progression or who remain symptomatic, further treatments are required. Although the optimal therapy has not been determined, systemic glucocorticoid (e.g., prednisone 0.25 to 0.5 mg/kg per day initially with gradual tapering) might be a reasonable choice for first-line treatment. Subsequent systemic treatments, according to the National Comprehensive Cancer Network (NCCN) guidelines, include Vemurafenib and Dabrafenib for *BRAF* V600E mutated disease. Cobimetinib, an MEK inhibitor, is preferred for MAPK pathway mutation, or no other detectable mutation or testing is not available. Cytarabine and Cladribine may also be considered irrespective of mutation profile. For those refractory to systemic treatment, lung transplant, allogeneic hematopoietic cell transplant, and clinical trials should be considered (Fig. 5).
The prognosis of PLCH is usually favorable, with a 10-year overall survival rate exceeding 90 percent. However, the disease course of PLCH might be variable. Some may experience spontaneous remission over smoking cessation, and some might progress to pulmonary hypertension, chronic respiratory failure, and lung cancer[8].

Conclusion

PLCH is a rare hematological neoplastic disorder with variable presentation. Current treatment is largely based on expert opinion. Smoking cessation should be advised for all patients diagnosed with PLCH. For patients with symptomatic PLCH, systemic treatment such as glucocorticoid, BRAF inhibitor, MEK inhibitor, or antimetabolites should be considered.

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病例報告　112_C 8

服用 warfarin 的腹膜透析病人之鈣化尿毒血管病變

Calciphylaxis in peritoneal dialysis patient under warfarin therapy

何玉倩[1]　林志慶[2]

[1]臺北榮民總醫院內科部 [2]臺北榮民總醫院內科部腎臟內科 [3]國立陽明交通大學醫學院

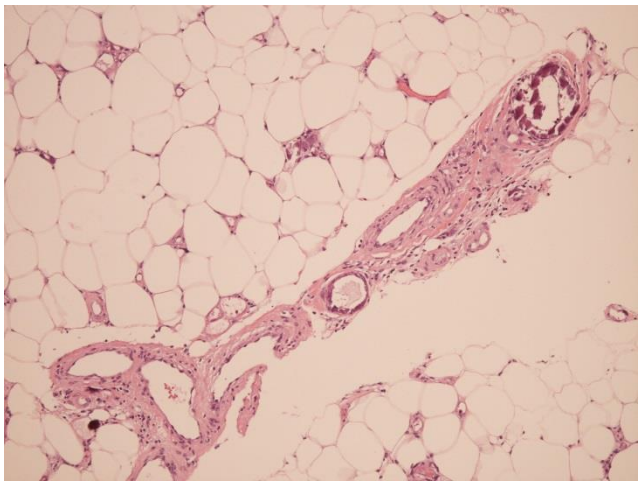
Introduction

Calciphylaxis, also called calcific uremic arteriolopathy, is a rare yet life-threatening disease due to vascular calcification and typically affects patients with end-stage renal disease (ESRD) [1,2,4]. The calcification of arterioles and capillaries in the dermis and subcutaneous adipose tissue results in skin ischemia and necrosis[1]. The mean age at diagnosis is 50 to 70 years old, 60 to 70% of which are mostly women[1]. The pathogenesis of calciphylaxis is unclear, but is proposed to be due to microvessel narrowing and calcification that may eventually lead to chronic ischemia[1,4]. Vascular occlusion induced by endothelial injury and microthrombosis can result in infarction. There is a higher incidence of calciphylaxis in patients undergoing peritoneal dialysis than in those undergoing hemodialysis[3]. The mortality rate is reported to be 45% to 80% at 1 year, with sepsis considered the most common cause of death[1,5,6].
Calciphylaxis causes painful, ischemic skin lesions due to microvessel occlusion in the subcutaneous adipose tissue and dermis. The initial skin presentations may include induration, plaques, nodules, livedo, or purpura[1,4]. Risk factors for calciphylaxis include obesity, diabetes mellitus, female sex, and dependence on dialysis for more than 2 years[1,2,3]. There are currently no approved therapies for calciphylaxis[1,2,6].

Case presentation

A 49-year-old female with a history of type 2 diabetes, ESRD on peritoneal dialysis for 4 years, infective endocarditis status post-mechanical mitral valve replacement in 2020, and under long-term use of warfarin, presented with poor wound healing over her left thigh for 2 weeks (Figure 2). She received an incisional biopsy and the biopsy results indicated calciphylaxis where there was calcification of small-sized vessels in the subcutaneous tissue. Fibrin thrombi were found in the vessels. Mild fat necrosis and focal widening of the fibrous bands in the subcutaneous tissue were also noted. A lipomembranous reaction was present (Figure 1). The management we gave included adequate pain control, infection control with empirical antibiotics, wound care with topical sulfasil after consultation with a plastic surgeon, hyperbaric oxygen therapy, and far-infrared therapy. Her initial intact parathyroid hormone level was at 374 pg/mL. Therefore, a subtotal parathyroidectomy was done for secondary hyperparathyroidism. In addition, due to long-term warfarin use, vitamin K2 was also given

Figure 1. Incisional biopsy over patient's left thigh indicated calciphylaxis with calcification of small-sized vessels in the subcutaneous tissue and fibrin thrombi in the vessels.



with the initial dose of 200 mcg twice daily and titrated to 400 mcg twice daily. The patient eventually died due to severe sepsis after one month of hospitalization.

Figure 2. Bilateral thigh skin lesions, poor wound healing after one month (February 2023 to March 2023) of wound care. No apparent infection sign but ischemic tissue bed often presented in patients with calciphylaxis.

Discussion

Our patient was supported by interdisciplinary management (including specialists in nephrology, nutrition, plastic surgery, and wound care) for calciphylaxis. However, pain control was still challenging in fear of opioid toxicity, and report showed resistance to high-dose opioids may develop[1]. Exudate and necrotic tissue removal and infection prevention are the major goals of wound care[1,6]. Our patient promptly received plastic surgeon consultation after admission. Due to no emergent surgical indication, she received topical sulfasil care, hyperbaric oxygen therapy[7], and far-infrared therapy.

To manage calciphylasix, risk factors should first be eliminated, including iatrogenic factors, such as treatment with warfarin[1,8]. The patient received more than two years of warfarin treatment for mechanical mitral valve replacement. Discontinuation of warfarin was considered inappropriate, yet study reported warfarin use was linked with increased mortality [1,6,8]. Vitamin K-dependent vascular factor matrix Gla protein (MGP) represents a powerful local calcification inhibitor in the arterial wall. Vitamin K antagonist (VKA) treatment interferes with the γ-carboxylation of MGP and hence impairs its activation[5]. Vitamin K2 supplementation activate MGP in patients on dialysis[5]. Under the use of a VKA, vitamin K2 instead of vitamin K1 was given to the patient, to prevent interfered with the effect of anticoagulation and promote MGP activation.

Hypercalcemia and hyperphosphatemia lead to calcium-phosphate deposits in arteries that compromise the vasculature[9]. Thus, hyperparathyroidism should be corrected in calciphylaxis patient. Our patient had secondary hyperparathyroidism, she received subtotal parathyroidectomy after admission.

Conclusion

Calciphylaxis is a lethal disorder of microvascular calcification that typically results in poor outcomes of painful cutaneous lesions and possible death from sepsis. Our patient received multidisciplinary team care; however, she eventually died after two month of diagnosis. Awareness of this disease in patient with risk factors and prompt evaluation were crucial to detect calciphylaxis.

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病例報告　112_C 9

腸道穿孔-一個酒精性肝硬化致頑固性腹水的案例回顧

A case of bowel perforation in a patient with alcoholic cirrhosis and refractory ascites

高士勛 [1]　李癸汌 [2,3]

[1] 臺北榮總內科部 [2] 臺北榮總肝膽腸胃科 [3] 國立陽明交通大學醫學系

Introduction

Ascites is a common complication of liver cirrhosis, occurring in 70% of patients with liver cirrhosis.[1] The first-line therapy for ascites control involves medical diuretics and sodium restriction.[2] However, in some cases, medical treatment is ineffective, which is known as refractory ascites. [2] Refractory ascites is associated with worse outcome in patients with liver cirrhosis with a 1-year mortality up to 50%.[3] Terminal ileum diverticulosis is a rare condition. [4] Here we report a case of liver cirrhosis with refractory ascites which prompted admission for ascites control. The patient also had history of terminal ileum diverticulosis. Bowel perforation and bacterial peritonitis occurred during admission for ascites control, and caused the death of the patient. Bowel perforation is an uncommon but fatal complication of terminal ileum diverticulosis, and it should be considered in physician's differential diagnosis.

Case presentation

This is a 67-year-old female with underlying disease including hypertension, type 2 diabetes mellitus and alcoholic liver cirrhosis with a Child-Pugh score 9(B). Additionally, she had been found to have diverticulosis during a routine colonoscopy examination in 2015, located at the terminal ileum and cecum. [Figure 1A] She underwent an abdominal Computed Tomography in September 2022, which also revealed the presence of diverticulosis near the ileocecal valve. [Figure 1B]

In February of year 2023, she was admitted to our hospital due to severe abdominal fullness. The blood test showed thrombocytopenia and direct-type hyperbilirubinemia. An abdominal sonography revealed massive amount of ascites. [Figure 2A, Figure 2B]

On March 4, 2023, a paracentesis was performed in the right lower quadrant of her abdomen, aspirating 2000 ml of ascites using a 20 gauge needle. The analysis revealed absence of peritonitis. Serum Ascites Albumin Gradient (SAAG) was 1.6 mg/dL, and the total protein level of ascites was 2.7 g/dL. However, one day after the paracentesis, she had a high fever up to 39°C, accompanied by diffuse abdominal pain. The physical examination revealed diffuse tenderness with rebounding tenderness, suggesting peritonitis. Blood culture collected on the same day yielded *Escherichia coli*.

Figure 1A diverticulosis noticed in colonoscopy in 2015

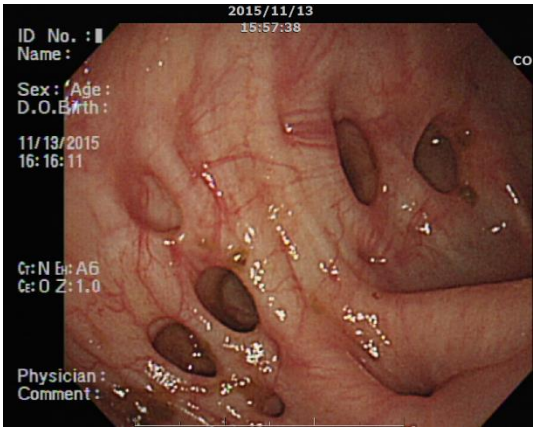
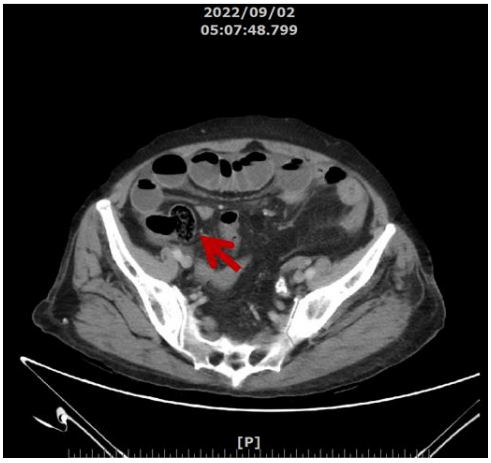


Figure 1B The red arrow shows the diverticulum near ileocecal valve



Empirical antibiotic with Cefoperazone-Sulbactam was prescribed. On March 6 of 2023, a follow-up paracentesis revealed 1338 Polymorphonuclear (PMN) granulocytes per microliter (Cells/uL) in ascites, which indicated a presumptive diagnosis of spontaneous bacterial peritonitis. However, the culture collected from ascites at that time did not revealed any possible pathogens, while the blood culture collected at this moment yielded *Eggerthella lenta* and *Clostridium clostridioforme*, which were all found as part of the human gut microbiota and are considered normal colonizers.[5-6] Her symptoms improved after the administration of antibiotics. A third follow-up paracentesis was performed on March 10 and showed improvement in her peritonitis with a PMN count 206 cells/uL. However, in the midnight of March 12, sepsis developed with severe abdominal pain and peritoneal sings. A lateral decubitus abdominal radiograph was taken, showing the presence of suspected abdominal free air. [Figure 3A]

Figure 2A, ascites at Morrison's pouch

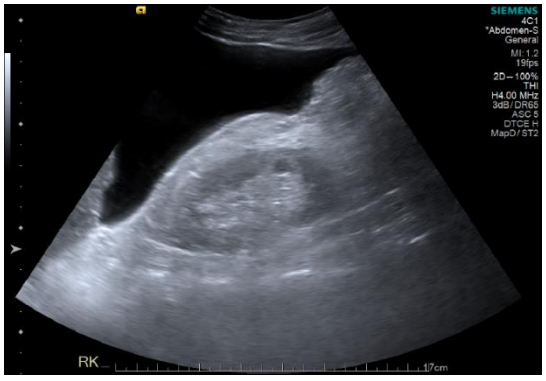


Figure 2B, ultrasonographic picture of mid-abdomen, revealing 6cm thickness of ascites

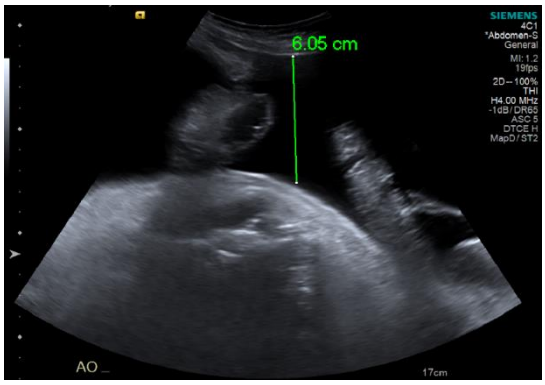
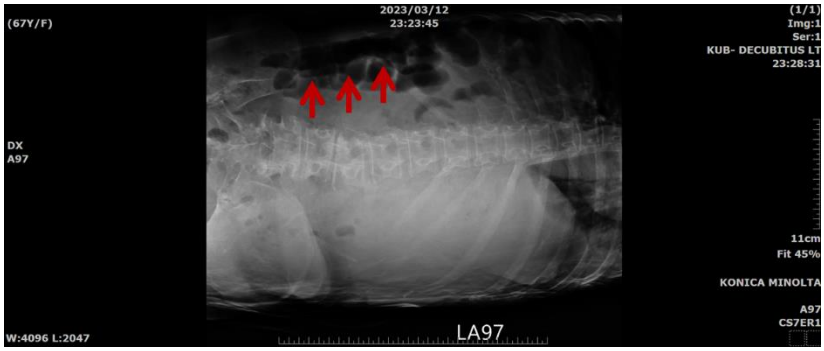


Figure 3A, lateral decubitus abdominal radiograph, arrowed shows the suspected free air



On March 13, a whole abdominal computed tomography scan was performed after stabilization of her vital signs and revealed pneumoperitoneum and mottled air densities at mesocolon on the right side, which was compatible with a hollow organ perforation. [Figure 3B, Figure 3C] Antibiotics were escalated from Cefoperazone -Sulbactam to Meropenem at this time. After a comprehensive discussion with the patient, she opted for conservative treatment over surgery, citing concerns about potential surgical complications. The paracentesis on March 13 revealed progression of peritonitis with the PMN count of 12346 cells/uL. The culture collected from the ascites yielded a mixture of Clostridium species, *Enterococcus avium*, *Enterococcus faeciumand*, *Bacteroides thetaiotaomicron* and Yeast. A pigtail was inserted for ascites drainage and Linezolid and Anidulafungin were added. On March 20, 2023, a follow-up methylene blue test still showed leakage from the drainage tube, indicating continued progression and poor healing of the bowel perforation. Following discussions again with the patient and her whole family, exploratory laparotomy was performed on March 20. During the operation, a 1cm x1cm perforation was found at the terminal ileum, located at 3 cm from ileocecal valve. Severe inflammatory changes over the surrounding tissue were also noticed. Ileocecal resection was then performed. [Figure 4A, Figure 4B]

Figure 3B, some free air (arrowed) noticed

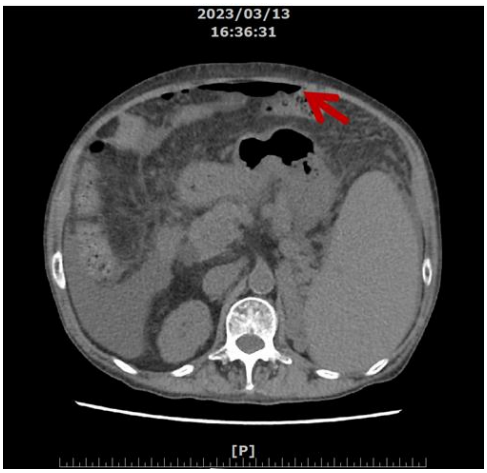


Figure 3C, the CT scan image showing fat stranding and some free air accumulation near ileocecal valve (arrowed)

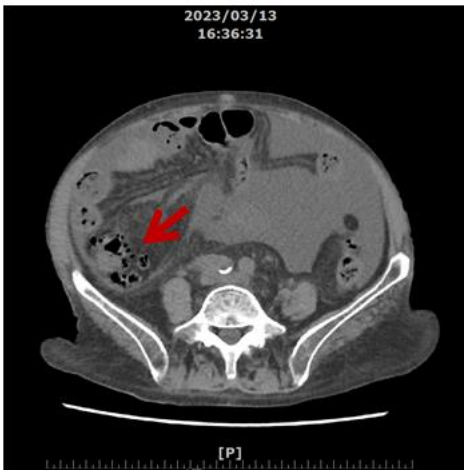


Figure 4A

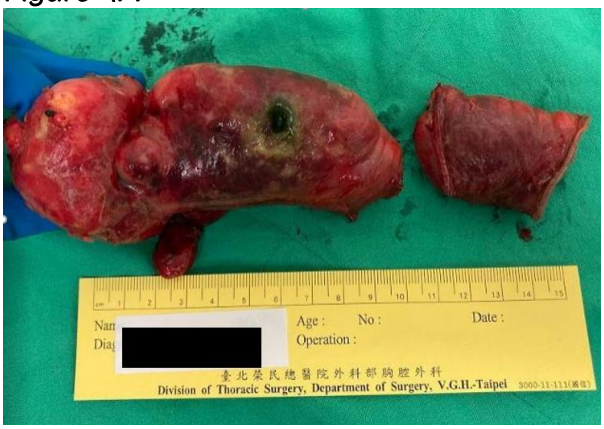
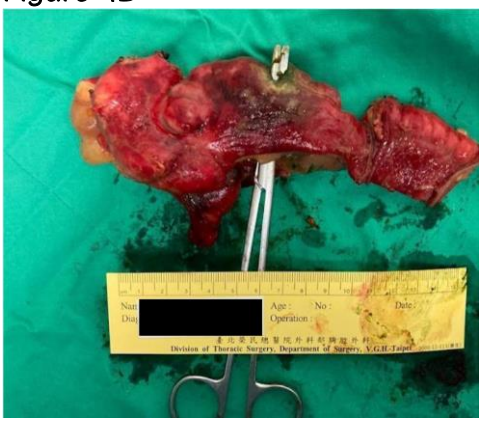


Figure 4B



Culture of ascites collected during the operation yielded the presence of *Trichosporon asahii*. Profound septic shock with multi-organ failure developed after the operation. *Trichosporon asahii* fungemia, *Candida fermentati* fungemia and *Enterobacter clocae* bacteremia was then developed. Unfortunately, her fungemia and bacteremia persisted and deteriorated despite parenteral antibiotics for months and she expired on June 13, 2023.

Discussion

In this case report, we presented a patient with refractory ascites who occurred bowel perforation. During the diagnostic process, we also considered other possible differential diagnoses, including spontaneous bacterial peritonitis and paracentesis-related bowel perforation. These were considered due to her clinical course and the fact that her perforation site was located in the terminal ileum, which was close to the tapping site. However, the diagnosis of paracentesis -related bowel perforation is less likely. First, the needle used for the paracentesis was an 20 gauge needle, whereas her perforation wound was measured 1cm x 1cm, which was significantly larger than the diameter of the needle. Second, the entire paracentesis was performed under ultrasonography guidance, ensuring the precise placement and a safe trajectory for the paracentesis needle. Third, unlike colon, which is anchored by mesentery, the ileum's position is not fixed, and it can be pushed aside even the needle contact closely. In addition, the rate of paracentesis perforation was

reported to have a low incidence rate; with only 6 cases in each 1000 paracentesis performed and was usually tolerated well with rare mortality according to previous study.[7,8]
Intestinal diverticulosis was also reported to be rare, compared with diverticulosis of colon and was predominantly observed in the jejunum.[9-11] Perforated diverticulosis is likewise an uncommon condition, with an overall incidence rate of 2.66 per 100,000 person-years. [12] Non-Merkel's ileal diverticulitis is an even rarer clinical condition that can lead to right lower quadrant abdominal pain, often mimicking other acute abdomen condition such as acute appendicitis.[13] Despite its low incidence rate reported, the complication can be fatal and usually need surgical intervention. [14] In this case, our surgeons suggested operation for the bowel perforation; however, the patient initially preferred conservative treatment over operation and eventually caused the mortality due to severe complication.

Conclusion

A 67-year-old female presented with alcoholic liver cirrhosis and refractory ascites. She also had a history of diverticulosis in the terminal ileum and cecum. Although terminal ileum diverticulitis is rarely reported, perforated ileum diverticulitis can result in fatal complications. Its early presentation can mimic other conditions such as acute appendicitis or spontaneous bacterial peritonitis. Therefore, early recognition of this diagnosis is crucial, and surgical intervention is recommended promptly upon diagnosis.

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病例報告　112_C 10

接受 B 細胞抑制療法之類風濕性關節炎病人得到 COVID-19 後發生不良預後：病例分享和見解
Worse Outcomes of COVID-19 in Rheumatoid Arthritis Patients undergoing B cell depletion therapy: Case Sharing and Insights

楊景涵[1] 蔡弘正[2,3] 陳明翰[2,3]
[1]臺北榮民總醫院內科部 [2]臺北榮民總醫院內科部過敏免疫風濕科 [3]國立陽明交通大學醫學院

Introduction

The severity and clinical vulnerability to Coronavirus Disease 2019 (COVID-19) variate among individuals with autoimmune conditions, comorbidities and those receiving immunosuppressants. Notably, patients who receive immunosuppressants have been documented to experience worse COVID-19 outcome.[1]

Generally, patients with rheumatoid arthritis (RA) initially receive conventional disease-modifying antirheumatic drugs (DMARDs) and anti-inflammatory drugs. Those refractory to conventional treatment may receive DMARDs combination or biologic agents. These biologic agents include tumor necrosis factor (TNF) inhibitors, Janus kinase (JAK) inhibitors, or rituximab. Rituximab, an anti-CD20 monoclonal antibody, leads to B lymphocytes depletion.[2] B lymphocytes contribute significantly in COVID-19 immune response. Its depletion may lead to impair immune response to COVID-19.[3]

Here, we present four RA patients who received long-term rituximab therapy and experienced poor outcomes following their contraction of COVID-19.

Table 1. Characteristic of 4 patients with rheumatoid arthritis undergoing rituximab treatment

Case	1	2	3	4
Age (years)	73	62	69	73
Gender	female	female	female	male
Rheumatic diseases	RA	RA	RA, Sjögren syndrome	RA
Concurrent diseases	Hypertension Dyslipidemia	Hypertension HBV carrier Type 2 DM Breast cancer, stable	Hypertension, Type 2 DM	Hypertension HBV carrier Hyperuricemia
Rituximab period	2012/7-2022/8	2012/8-2022/12	2010/8-2023/4	2012/3-2023/6
IgG/A/M (mg/dL)	542/48/12	693/112/13	641/78/21	785/85/28
CD4 count (/uL)	80	183	373	84
CD19 count (/uL)	0	0	0	0
Vaccination	Moderna*3	nil	nil	nil
IVIG days(1g/kg/day)	1	4	4	17
Outcome	Discharged	Intubated, tracheostomy discharged	Intubated, died	Intubated, died

Case presentation

Case 1

A 73-year-old female with RA and routinely received sulfasalazine, hydroxychloroquine and rituximab. She had received three shots of the Moderna COVID-19 vaccine before she had positive result for COVID-19 rapid antigen test in late November 2022. She visited our emergency department on December 23, 2022 due to progressive productive cough and

dyspnea. Chest CT revealed diffused ground glass opacity. Bronchoalveolar lavage fluid testing showed negative culture report but revealed lymphocyte-predominant pattern, suggesting pneumonitis. She was discharged after methylprednisolone and prophylactic antibiotics treatment. However, recurrent dyspnea was found and she was re-admitted to our hospital on February 3, 2023, on day 42 of her illness. The SARS-CoV-2 PCR Ct value was 20.1. Paxlovid and dexamethasone were given. IVIG was given for hypogammaglobulinemia. She was discharged in stable condition after two weeks.

Case 2

A 62-year-old female had been receiving rituximab regularly since 2012 for RA. She received Paxlovid for COVID-19 but symptoms such as fever, productive cough and dyspnea persisted for two weeks.

Her severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse-transcription polymerase chain reaction (RT-PCR) Ct value of 24.9 on February 4, 2023. Chest computed tomography (CT) scan revealed peripheral predominant ground glass infiltration over both lower lungs. Sputum culture result was negative. Empirical antibiotics, remdesivir and dexamethasone were administrated. Intravenous immunoglobulin (IVIG) was given for hypogammaglobulinemia. However, acute respiratory distress syndrome and respiratory acidosis developed that led to intrahospital cardiac arrest. She was intubated for 1 month, and underwent tracheostomy due to difficult weaning from ventilation. Nintedanib was given for chest consolidation and fibrosis change. She exhibited prolonged viral carriage, with SARS-CoV-2 Ct value 27.7 on July 23, day 169, and she received repeated remdesivir before discharged.

Case 3

A 69-year-old female with rheumatological history of RA with interstitial lung disease, and she had been receiving rituximab regularly since 2010. Initial testing of SARS-CoV-2 RT-PCR Ct value was 25.4 on May 2, 2023. She had recurrent dyspnea 1 week after treated with remdesivir, dexamethasone and tocilizumab. IVIG was given for hypogammaglobulinemia. Subsequent chest CT scan showed no pulmonary embolism but revealed ill-defined patchy ground glass opacities over bilateral lungs. She had progressive hypoxemia, deteriorated chest CT with consolidation and reticulation despite receiving repeated course of remdesivir, tocilizumab, nintedanib, baricitinib and even after Evusheld. On June 20, day 49 of her illness, repeated PCR test showed Ct value of 16.7. She was intubated on June 24 and died on June 30 due to profound hypoxemia, accompanied by hypotension and bradycardia.

Case 4

A 73-year-old male has rheumatological history of RA for more than 20 years. He had been receiving methotrexate, hydroxychloroquine and rituximab regularly. He presented with fever and productive cough for 2 weeks, and was diagnosed with COVID-19 on July 9, 2023. SARS-CoV-2 RT-PCR Ct value was 20.5. Despite a treatment course with dexamethasone, remdesivir, and baricitinib, the patient experienced recurrent fever, and the SARS-CoV-2 Ct value measured 13.1 on August 30, 2023, day 52. He received fourth course of remdesivir on September 1, 2023. He was intubated on September 2. The patient died on September 14 with coinfection with COVID-19 associated pulmonary aspergillosis and cytomegalovirus pneumonitis

Discussion

Rituximab is a chimeric monoclonal antibody targeted against B cell marker CD20. The

mechanism of rituximab include B cell signaling inhibition, calcium flux, complement-mediated lysis, apoptosis and antibody-dependent cytotoxicity.

Various immunosuppressive agents exert different effects on COVID-19 severity. A statistical data from the global rheumatology alliance (GRA) reported that RA patients treated with rituximab and JAK inhibitors tended to experience worse disease severity compared to those receiving TNF inhibitors.[4] A cohort study indicated that rituximab users had higher mortality compared to matched comparators irrespective of rheumatic or neurologic diseases.[5] A retrospective cohort study specifically focused on RA patient with rituximab exposure found an increased risks of COVID-19 related invasive ventilation and intensive care unit admission.[6]

The abovementioned patients shared common characteristics of low CD19 count and hypogammaglobulinemia, which led to IVIG administration. Still, persistent positive SARS-CoV-2 PCR results was noted for weeks. Delayed B cells recovery at about 6 months after rituximab administration may contribute to prolonged viral shedding and persistent SARS-CoV-2 infection.[7,8] Prolonged immunosuppression effect leads to sustained innate immune response impairment and fail to build immunological memory. A retrospective study reported that 26% patient had IgG hypogammaglobulinemia after rituximab initiation, 56% patient during median 42 months follow up period, and 4.2% patient required IgG replacement due to recurrent infections.[9]

These patients also had low CD4 count. Indeed, rituximab also induces T cell depletion. The cytokines and chemokines produced by B cell affect the cell migration, and B cell plays a role in stimulating CD4 cell proliferative. Therefore, rituximab exposure affects both the innate and adaptive immune systems.[10]

Only one patient had received COVID-19 vaccination, and this patient did not required intubation. Although patient who have received rituximab may exhibit impaired immunoglobulin response following vaccination, T cell reactivity with interferon-gamma secretion was observed in some cases.[11] There is necessity that these patients receive vaccination.

Conclusion

Rituximab causes prolonged B cell depletion and hypogammaglobulinemia, which may lead to prolonged viral shedding and infection courses. This impaired immune response can result in detrimental COVID-19 outcomes in RA patients receiving rituximab. Vaccination should be encouraged and serum level immunoglobulin should be monitored regularly.

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病例報告　112_C 11

一位洗腎病人以過敏反應表現之肝素引起之血小板低下症：病歷報告

Heparin-induced thrombocytopenia in a hemodialysis patient presented with anaphylactoid reactions

李欣恬 楊智宇 唐德成
臺北榮民總醫院

Introduction

Heparin-induced thrombocytopenia (HIT) is a severe immune-mediated adverse drug reaction after exposure to heparin. The generation of heparin-PF4 antibodies (HIT antibodies) activates platelets via their FcγIIa receptors and causes thrombocytopenia and thromboembolic complications. HIT was first described in the 1970s. However, despite the wide use of heparin in hemodialysis patients, the prevalence of HIT in hemodialysis patients is not well defined. We present the diagnosis and treatment of HIT in a fresh hemodialysis patient.

Case presentation

A 64-year-old man suffered from general weakness for one month. He had underlying hypertension and chronic kidney disease without regular control and follow-up; aortic dissection with conservation treatment and regular follow-up. After admission, end-stage kidney disease with occult infection was diagnosed, and the patient started antibiotic treatment and hemodialysis on the second day of admission. On the first day of hemodialysis, the patient complained of dyspnea around 20 minutes after initiating hemodialysis, and desaturation from to spO2 70% under ambient air was noticed. After hemodialysis ceased, the patient desaturation resolved. The same scenario happens over time whenever the patient receives hemodialysis. Further on, isolated thrombocytopenia was noticed on Day 8 after starting hemodialysis, and the nadir platelet (30,000 /uL) occurred on Day 12. The peripheral blood smear was unrevealing. The infection marker showed improvement, and no active inflammatory process was found by the inflammation scan. Disseminated intravascular coagulation was less likely. Since the patient was freshly exposed to heparin, thrombocytopenia developed on Day 8 after heparin use. The patient's heparin-induced thrombocytopenia was suspected, 4T score was 6. Heparin during hemodialysis has been held since Day 16.

We shifted to Clexane 1000U SC on Day 23. Anti-platelet factor 4 antibody revealed positive (OD value > 3) on Day 26 and D32 (Figure 1). A diagnosis of HIT was made. The patient received anticoagulation-free hemodialysis. Thrombocytopenia improved (platelet 85000 /uL) within two weeks after cessation of heparin and resolved (platelet 179000/ uL) during outpatient clinic follow-up.

Discussion

Heparin was first discovered in 1916 and had facilitated hemodialysis by preventing circuit clotting since the 1940s. Until now, heparin is still considered to be the best option of anticoagulation during hemodialysis due to its very short half-life, safety, low cost, and long experience of using.

HIT is a life-threatening condition. Ceasing all forms of heparin and prescribing alternative anticoagulation are the key management in patients with HIT. There are three main strategy

of anticoagulation during hemodialysis in patient with HIT, including anticoagulant-free dialysis, regional anticoagulation, and alternative anticoagulants.
Anticoagulant-free dialysis lead to premature termination of hemodialysis due to high clotting risk. HepZero study demonstrated higher success rate by using a heparin-grafted membrane rather than regular saline flushes or pre-dilution method. However, heparin-grafted membrane is considered inappropriate to patient with HIT.
Regional anticoagulation including prostacyclin and citrate have been reported but rarely provided because of its side effects and inconvenience. Prostacyclin has vasodilatory effect that cause hypotension and headache while citrate has metabolic derangements. Furthermore, citrate block the coagulation cascade by chelating calcium, which requires frequent monitoring of serum calcium level.
Wafarin is contraindicated in the early stage of HIT due to its paradoxical effect on coagulation. Wafarin inhibits vitamin K as well as protein C and protein S, our body natural anticoagulant, which may precipitate thrombosis or skin necrosis if initiating without other concurrent anticoagulation. It should not be given until the platelet count has fully recovered.
Non–vitamin K oral anticoagulants (NOAC), either direct thrombin inhibitor or direct factor Xa inhibitor were reported to be used off-label in HIT patients. However, its safety and efficacy use in hemodialysis patients is not well established.
The most extensively used newer anticoagulant, Argatroban and Danaparoid, were suggested according to European and British guideline. However, only Argatroban was approved by the Food and Drug administration (FDA). Argatroban directly inhibits thrombin and is metabolized in liver; thus consider safe in hemodialysis patient. Danaparoid carries a predominant anti-Xa activity but require dose adjustment in hemodialysis patient due to its kidney elimination property. Bivalirudin, a reversible direct thrombin inhibitor, has been used during percutaneous interventions but not approved for HIT treatment. Fondaparinux, a factor Xa inhibitor, is contraindicated in severe renal insufficiency but has been used off-label in hemodialysis patient. Lepirudin, a direct thrombin inhibitor, was the first medication approved by FDA for HIT treatment. However, it was out of production since 2012 due to its antibodies formation in half of recipients. Clearance of lepirudin antibodies is decreased with impaired renal function while risk of bleeding increases by prolong half life.
Newer anticoagulant have emerged and under rigorous attempts to treat patient with HIT. Nevertheless, the currently available alternative anticoagulants, including Argatroban, Danaparoid, Bivalirudin and Fondaparinux were not accessible in most hospitals and hemodialysis centers in Taiwan.
Although there is cross-reactivity between unfractionated heparin (UFH) and Low-Molecular-Weight Heparin (LMWH) antibodies, the LMWH was reported to have a 10-fold lesser risk of HIT than UFH. We demonstrated a patient treated successfully with LMWH at first and further anticoagulant-free hemodialysis after HIT diagnoses were established.

Conclusions

HIT is not uncommon in European or American literature. However, the prevalence of HIT in the Taiwan population is unknown. Further, thrombocytopenia in hemodialysis patients is common, which makes the diagnosis of HIT in hemodialysis patients more challenging. This case reminds us of the differential diagnosis of HIT in hemodialysis patients with unexplained acute thrombocytopenia. There is evolving evidence of alternative anticoagulants under investigation in the hemodialysis patient population.

病例報告　112_C 12

人類免疫缺乏病毒造成的免疫性血小板低下紫斑症

Immune thrombocytopenic purpura caused by human immunodeficiency virus: A case report

宣怡天　巫炳峰
台北榮民總醫院內科部感染科

Introduction

Immune thrombocytopenic purpura (ITP) is an acquired disease. The etiology of ITP is immune-mediated destruction of platelets and possibly inhibition of platelet release from the megakaryocyte. Primary ITP is a diagnosis of exclusion after ruled out all possible causes. Common secondary causes of ITP are autoimmune disorders, particularly systemic lupus erythematosus, and infections, such as Human Immunodeficiency Virus (HIV), Helicobacter pylori and hepatitis C.

ITP is defined by mucocutaneous bleeding and a low, frequently extremely low, platelet count, while the peripheral blood cells and smear are typically normal. Patients typically manifest as either ecchymoses and petechiae or as incidental thrombocytopenia discovered during a routine blood draw. Mucocutaneous bleeding, such as oral mucosa, gastrointestinal, or heavy menstrual bleeding, may be present.

Case presentation

This 72-year-old male has the underlying disease of hypertension. Low platelet count was noted last year during routine health check-up. Due to this condition, he went to other hospital for help. Platelet count of 120,000/microL and 60,000/microL was recorded but fluctuated over time. He received no medication for thrombocytopenia last year. Easy fatigue and multiple petechiae persisted with occasional sub-conjunctival hemorrhage has been noted for 3 months. The patient denied symptoms of oral bloody blister, melena, hematochezia, ecchymosis. He received folk therapy including acupuncture and bloodletting a year ago. Whether the therapy instrument was sterilized was known. He denied any medication except anti-hypertensives and contact to contagious people or animal. Due to personal reason, he came to our hospital for help.

Upon arrival, his consciousness was clear and vital sign was stable. Physical examination showed subconjunctival hemorrhage, petechiae over four limbs. Blood tests revealed a normal coagulation screen, liver and renal function tests, but a platelet count of 4000/microL without hemolytic anemia. A blood film confirmed the thrombocytopenia, with normal red and white cell morphology. Antinuclear antibody showed: 1:80 Polar/Anti-Golgi pattern. Anti-beta2-Glycoprotein-I IgG/IgM, Anti-dsDNA, IgG, IgA, IgM, C3, C4 were normal. Protein electrophoresis showed: no monoclonal gammopathy. Bone marrow biopsy was also performed and revealed cellularity about 35%, no clonal chromosomal abnormalities. Helicobacter pylori stool antigen, hepatitis B surface antigen, anti-hepatitis C antibody were all negative. However, HIV antibody and antigen combination assay showed positive. And then HIV-I Confirmatory Test was performed which was also positive. Serum HIV viral load was 64100 copies/mL. CD4+ lymphocyte was 396.2 cell/microL. Thus, we screen opportunistic infection. Blood cryptococcal antigen test, blood cytomegalovirus polymerase chain reaction test, interferon-gamma release assays for tuberculosis screening were not

detected. Under the impression of immune thrombocytopenic purpura caused by HIV infection, he received antiretroviral therapy (ART) with doravirine/lamivudine/tenofovir disoproxil fumarate and methylprednisolone 62.5mg/day followed by a taper. His thrombocytopenia gradually improved.

Discussion

HIV is a retrovirus and causes the infection of humans through exposure to body fluid, such as blood, semen, and vaginal fluids. Over time without treatment, HIV-infected patients progress to acquired immunodeficiency syndrome (AIDS) and become susceptible to life-threatening opportunistic infections and cancers.

The etiologies that contribute to HIV induced ITP are multifactorial. In individuals with early HIV infection, autoimmunity appears to be a crucial factor. This is manifested by ineffective thrombopoiesis, attributed to cross-reactivity between HIV envelope glycoproteins 160/120 and platelet glycoprotein IIb/IIIa. Furthermore, the direct infection of megakaryocytes by HIV might play a significant role in reducing platelet counts in those with AIDS. Moreover, individuals in advanced stages of AIDS exhibit heightened serum markers of immune activation, including C-reactive protein (CRP). Functionally, CRP plays a key role in enhancing IgG-mediated platelet destruction[1].

In the United States, the one-year incidence of significant thrombocytopenia, defined as a platelet count of ≤30,000/microL, varies. It had been reported to be as low as 1.7% in individuals with asymptomatic HIV infection, increases to 3.1% when the CD4+ count is below 200 cells/microL, and reaches as high as 8.7% in cases with AIDS-defining illnesses.[1]

For individuals who have not yet initiated ART and are experiencing mild to moderate thrombocytopenia (platelet count >40,000/microL), starting ART alone, without the need for additional ITP therapies, is deemed appropriate. In many cases, this approach is often adequate to elevate the platelet count[2].

In cases of severe thrombocytopenia, where the platelet count is below 20,000 to 30,000/microL, initiating an ITP-specific treatment (glucocorticoids or intravenous immune globulin) should be considered. If thrombocytopenia causes clinically significant bleeding, platelet transfusions should be used[3].

Conclusion

This is a case of ITP caused by HIV infection. The initial presentation was thrombocytopenia without symptoms noted by routine health check-up. This case indicates the importance of thorough examination and further investigations when presented with unexplained thrombocytopenia. ITP caused by HIV infection can be treated and improved with the use of ART.

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病例報告　112_C 13

以動眼神經麻痺為表現之巨細胞動脈炎
Giant Cell Arteritis Presenting with Third Cranial Nerve Palsy

張彥安 孫易暄 賴建志
台北榮民總醫院內科部過敏免疫風濕科

Introduction

Giant cells arteritis (GCA), also known as temporal arteritis, cranial arteritis, and granulomatous arteritis, is a disease of distinct clinical manifestation and pathophysiology. The incidence of GCA differs in different regions and races. The highest incidence is found in Scandinavians of 21.6 per 100,000 people[1]. In Taiwan, the incidence of GCA is unknown, with only a few case reports being published[2,3].

Most cases of GCA are presented with temporal headache, blurred vision, and jaw claudication. Only 3 previously reported cases presented a third cranial nerve palsy with ptosis and ophthalmoplegia [4]. Herein, we presented an unusual case of GCA presenting with diplopia and ptosis.

Case presentation

A 69-year-old man was admitted to Taipei Veteran General Hospital's neurology ward due to left side headache for 2 months, and diplopia and ptosis for 4 days. His pain was in linear pattern along anterior part of his ear, with throbbing, and 12-hour duration. He also addressed intermittent jaw claudication in the past few months. Then, he developed diplopia and ptosis 4 days prior to his admission.

On bedside examination, he's afebrile, hemodynamically stable with clear consciousness. His left temporal artery was tender when palpated. Neurological examination revealed left ptosis (Fig. 1) with neutral position as down-and-out, and EOM limitation at left eye when adduction. His hemogram showed mild decreased white blood cell count (WBC: 2430 /ul), and microcytic anemia (Hb: 8.5 g/dl). Acute phase reactants revealed elevated ESR (120 mm/hr), and elevated CRP (6.54 mg/dl). Brain CT with contrast showed aneurysmal dilatation of left paraclinoid ICA. Brain MRI with contrast showed left paraclinoid ICA aneurysmal formation about 0.2cm in diameter. Carotid angiography of bilateral internal carotid artery revealed a small vascular pouch about 2mm in the left parasellar internal carotid artery. Regarding that the above-mentioned images couldn't explain his symptoms. Rheumatologist was consulted for further evaluation.

Temporal artery ultrasound was arranged by rheumatologist, which revealed thickened and hypoechoic left common superficial temporal artery wall, left parietal temporal artery wall, and left frontal temporal wall appearance, with positive halo sign (Fig. 2). We thus arranged MR vessel wall imaging and temporal artery biopsy. MR vessel wall image showed prominent bilateral superficial temporal artery and left middle meningeal artery with thicken enhancement in the arterial wall (Fig. 3).

The patient's condition was compatible with giant cell arteritis according to 2022 American College of Rheumatology/EULAR classification criteria for giant cell arteritis[5], with jaw claudication (+2), new temporal headache (+2), abnormal examination of temporal artery (+2), elevated ESR (+3), halo sign on ultrasound (+5).

Thus, the patient started on prednisolone 1mg/kg/day. His symptoms improved after 2 days of prednisolone treatment. Temporal artery biopsy was conducted after 5 days of prednisolone treatment, which only showed arteriosclerosis.

After 14 days of steroid treatment, his left side headache, diplopia, and ptosis subsided dramatically (Fig. 4). Lab data also revealed normalized hemogram and decreased ESR level (10mm/hr).

Figure 1. Patient on admission, presented with left ptosis.

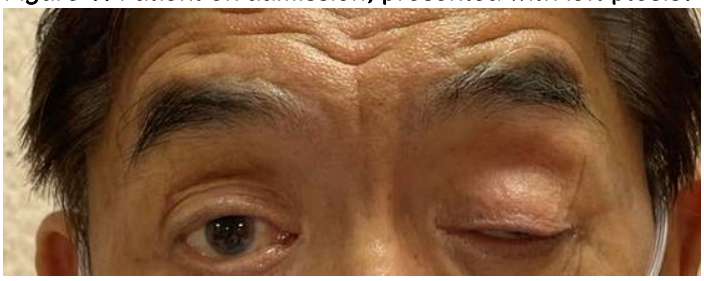

Figure 2. Halo sign of left parietal temporal artery (A) transverse, D1=0.6mm, D2=0.73mm, D3=0.51mm (B) longitudinal, D1=0.64mm, D2=0.66mm

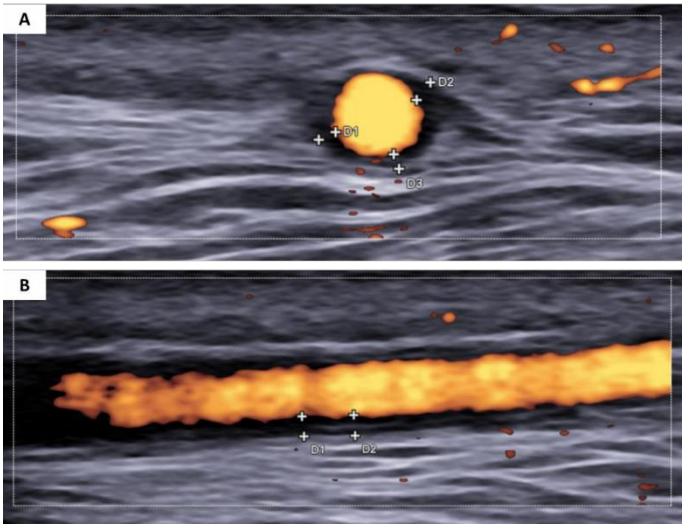

Figure 3. MR vessel wall image shows prominent bilateral temporal artery and left middle meningeal artery.

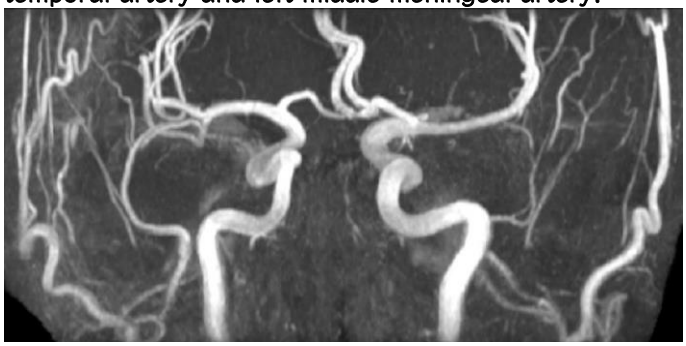

Figure 4. Patient after 14 days of treatment, shows improved left ptosis.

Discussion

GCA involves inflammation in medium-sized muscular arteries from the aortic arch. Commonly affected arteries include the temporal, vertebral, ophthalmic, and posterior ciliary arteries. In mild cases, inflammation is limited, but it can become transmural with granulomas containing giant cells, histiocytes, lymphocytes, and plasma cells[1].

Typical GCA symptoms include headache (76%), weight loss (43%), fever (42%), visual symptoms (37%), jaw claudication (34%), and polymyalgia rheumatica (34%). Headaches vary from mild to severe, often requiring immediate IV pain relief[1]. Temporal arteries may enlarge, become nodular, tender, and lose their pulse. Vision loss is common, often due to anterior ischemic optic neuropathy from ciliary artery occlusion. Ophthalmoplegia occurs in 5-10%, while ptosis is rarer, usually sparing the pupil[1].

Lab tests reveal anemia, thrombocytosis, and elevated ESR and CRP levels. ESR elevation up to 100mm/hr yields a positive likelihood ratio of 1.9 and a negative likelihood ratio of 0.8. Temporal artery biopsy (TAB) is the gold standard, but sensitivity may decrease due to inadequate samples or prior steroid use.

2022 EULAR/ACR recommendations[5] favor temporal ultrasound as the primary GCA

investigation. Ultrasound features include the halo sign, compression sign, stenosis, and vessel occlusion, with an "ultrasound halo scoring" to improve diagnosis[6]. High-resolution MRI shows contrast-enhanced cranial arteries, aiding detection, and long-term monitoring. PET-CT detects large vessel involvement, especially in patients with pelvic girdle involvement and limb claudication.

Initial GCA treatment is glucocorticoids. For patients with cranial ischemia and threatened vision loss, IV pulse steroid therapy is recommended according to the 2021 ACR Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis[7]. Other newly diagnosed patients receive high-dose oral glucocorticoids (1mg/kg/day). Tocilizumab offers steroid-sparing effects but lacks long-term data and may have economic challenges due to its cost.

Conclusion

GCA is an important differential diagnosis for headaches in elderly. However, it is rarely recognized due to its low incidence in Taiwan. We presented a rare case of GCA with third nerve ophthalmoplegia, and the use of different image modality to reach final diagnosis. Therefore, patients presented with ptosis and diplopia should be assessed thoroughly for vasculitis.

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病例報告　112_C 14

以咳血表現的 ANCA 相關血管炎

ANCA-associated vasculitis presenting with hemoptysis

何治廷[1]　蔡弘正[2]
[1]臺北榮民總醫院內科部　[2]臺北榮民總醫院過敏免疫風濕科

Introduction

ANCA-associated small-vessel vasculitis. Typical clinical features include constitutional symptoms, such as weight loss, fever, chills, night sweats, changes in appetite, changes in sleep, chronic pain, fatigue, and malaise, and localized manifestations in renal, lungs, gastrointestinal symptom, and neurological symptoms. Testing modalities include laboratory studies, imaging, and biopsy. Emergent management may be required.

Case presentation

This 56-year-old woman has an underlying disease of invasive ductal carcinoma. According to the patient's statement, she presented with a productive cough with whitish sputum initially. Blood-tinged sputum then developed, followed by hemoptysis in the last 2 weeks. She denied epistaxis, acid regurgitation, arthralgia, body weight loss, skin rash, ecchymosis, petechiae, or arthralgia. There was no recent contact history or anticoagulant/antiplatelet medication use. There was no history of foreign body choking.

She first went to LMD and took doxycycline, then azithromycin. She also underwent nasal endoscopy but showed no bleeding in the nasal mucosa. However, due to non-resolving symptoms, she went to our hospital's emergency room for help on 8/10. At triage, the vital signs and oxygenation were fair. Lab data showed acute kidney injury, elevated CRP level, anemia, and neutrophil-predominant leukocytosis. Chest x-ray showed patchy infiltration, especially in the right lower lung, and scattered in the left lung. Chest CT showed bilateral diffuse ill-defined patchy infiltration with lower lung predominance and left pleural effusion. A chest medicine physician was consulted, and admission for further survey was suggested. After admission, hemoptysis was still noted, and the patient looked weak and pale. Critical status was informed. We discussed with Rheumatologist and Nephrologist, autoimmune-related lung and kidney disease was suspected.

After being well informed about the clinical condition and plan of treatment, the patient and her husband understood and agreed with it. Methylprednisolone 16mg BID was given. Plasmapheresis was also arranged. No significant discomfort was noted during and after plasmapheresis. IV immunoglobulin was given on 2023/8/12 and 2023/8/13.

Chest X-ray on 2023/8/16 revealed improving lung infiltrates, but lab data showed worsening kidney function. The 5th plasmapheresis was done on 2023/8/18, followed by self- paid rituximab administration. No significant discomfort was noted. We tried to taper her oxygen demand from HFNC to N/C. Sono-guide renal biopsy was performed smoothly on 8/23. The result showed diffuse necrotizing and crescentic glomerulonephritis without an immune complex deposition process, compatible with an ANCA-associated glomerulonephritis.

We gradually tapered oxygen demand, and she could keep saturation around 95% under room air under kept current plan of treatment. The amount of urine output was around 2 liters each day without using diuretics. Prednisolone 5 mg BID, colchicine 0.5mg BID, and

methotrexate 2.5 mg TIW were given for maintenance treatment. Under relatively stable conditions, she may be discharged on 2023/8/30 and OPD follow-up was arranged.

Discussion

The case presented with hemoptysis and desaturation. Therefore, steroid, plasmapheresis, IV immunoglobulin, and rituximab were prescribed due to critical illness. Cyclophosphamide was not given due to a rapid decline in renal function. ANCA-associated glomerulonephritis was proved with renal pathology. After a series of management, the patient's renal function had partially recovered and no hemoptysis was noted anymore. Maintenance treatment was required. Further management with steroid pulse therapy or further dosage of rituximab may be taken into consideration.

Conclusion

Microscopic polyangiitis is an ANCA-associated small-vessel vasculitis. ANCAs (mostcommonly MPO-ANCAs) are present in up to 75% of patients with MPA. Typical clinical features include pauci-immune glomerulonephritis with hypertension, pulmonary vasculitis, palpable purpura, nodules, abdominal pain, mononeuritis multiplex, and distal symmetric polyneuropathy. Laboratory tests show a sudden rise in serum BUN and creatinine as well as RBC casts and dysmorphic red blood cells on urinalysis. Diagnosis is confirmed by biopsy. CT chest is indicated in all patients with pulmonary symptoms and often reveals ground-glass opacifications or nodular lesions. Management involves immunosuppressive agents, typically glucocorticoids combined with methotrexate, cyclophosphamide, or rituximab. Plasmapheresis may be considered for patients with severe disease. Relapses are common.

病例報告　112_C 15

以感染性直腸炎為表現的猴痘病毒感染

Infectious proctitis as the clinical manifestation of Mpox

謝尚融[1] 陳伯亮[2] 黃鈴茹[3]
[1]臺北榮民總醫院內科部 [2]臺北榮民總醫院重症醫學部 [3]臺北榮民總醫院內科部一般內科

Introduction

Mpox, formerly Monkeypox, has been known as a zoonoses and was first isolated from monkey in laboratory in 1958; except the outbreak in the U.S. in 2003, most cases were limited in Africa before 2022.[1,2] Since 2022, Mpox has transmitted outside Africa and the World Health Organization (WHO) designated the Mpox outbreak since 2022 as a global public health emergency on Jul 23, 2022.[3] Most Mpox cases during this epidemic were immunocompromised host, such as people living with HIV (PLHIV) or men who have sex with men. The first imported case was identified in Taiwan on Jun 24, 2022 and 328 cases confirmed on Sep 11, 2023. Most Mpox- infected individual presented fever and skin rash, but not proctitis.[3,4] Here we present a case of infectious proctitis secondary to Mpox virus in a patient with rectal pain.

Case presentation

A 34-year-old man, a well-controlled HIV patient with regularly bictegravir/ emtricitabine/ tenofovir alafenamide use (HIV RNA: 28 copies/mL, CD4 count: 644/uL), presented to the emergency department with initial symptoms of fever, watery diarrhea, general weakness, rhinorrhea, and cough. He was independent in all activities of daily living. He was sexually active with male partners and has inconsistent condom usage.

Initially diagnosed with influenza at a local medical clinic, symptoms of fever resolved with Oseltamivir and Relenza; however, anal pain with discharge and intermittent blood-tinged stool was still noted after the anti-influenza treatment.

The initial vital signs were stable. Physical examination revealed multiple blister around buttock, perineum, inguinal, face, and hands. There was no painful sensation on blister. Anorectal examination revealed a 3cm open wound with pus discharge at posterior midline. Lab findings showed mild leukocytosis (WBC: 11400/uL), mildly elevated CRP (2.14 mg/dL), without anemia, hepatic or renal dysfunction, or electrolyte imbalance. Abdominal CT demonstrated rectal wall thickening, indicative of proctitis.

After admission to the general ward, initial treatment included empiric antibiotics with ampicillin/sulbactam. Warm sitz-bath and pain control with Traceton (Tramadol/ acetaminophen) were administered. Since multiple blisters on various parts of the body raised concerns of Mpox or HSV infection, contact isolation measurement was initiated on day 1 of hospitalization. Anal swabs for Mpox virus PCR, HSV-1 PCR, HSV-2 PCR, CT/NG panel were collected. Blood tests for syphilis, hepatitis B, and hepatitis C serology were also taken. The patient was isolated due to potential airborne transmission. On day 5 of hospitalization, Taiwan Centers for Disease Control (Taiwan CDC) replied that Mpox virus PCR test revealed positive, while all other pathogen tests revealed negative. Antiviral therapy with Tecovirimat was not initiated based on current Taiwan CDC's treatment recommendations[5]. On day 6, sigmoidoscopy was performed and revealed mucosal edema and erythema in the lower rectum,

with healing scars suggestive of previous ulcers. One biopsy was obtained and the pathology revealed an ulcer. Aerobic culture revealed mixed GPC in group and GNBs, while anaerobic culture revealed Prevotella bivia. Mpox virus PCR from rectal specimen revealed positive. On day 5, he was discharged to self-isolate at home due to relieved pain and stable clinical condition. Self-health monitoring instructions and out-patient clinic follow-up was informed.

Discussion

This case exemplifies the diverse of clinical manifestations of Mpox in an immunocompromised host. Rectal discomfort is a prevalent manifestation of Mpox, with numerous reports indicating proctitis as a recurring complication. In a study across 16 nations, proctitis or anorectal pain was observed in 14% of individuals, while 73% of individuals exhibited anogenital skin lesions[6].

A multidisciplinary approach, timely diagnostics, and a high index of clinical suspicion are important to outbreak containment.

Conclusion

Infectious proctitis could be a clinical manifestation of Mpox infection. Rectal pain with anogenital skin lesions should prompt clinical suspicion of Mpox, especially for PLHIV.

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病例報告　112_C 16

硬皮症腎危機合併原發性血栓性微血管病之案例報告

Scleroderma renal crisis complicated with thrombotic microangiopathy: a case report

黃子綝[1] 牛志遠[2] 何揚[3]

[1]台北榮民總醫院內科部 [2]國立陽明交通大學附設醫院內科部腎臟科 [3]台北榮民總醫院職業醫學及臨床毒物部

Introduction

Scleroderma, as known as systemic sclerosis (SSc), is a connective tissue disease (CTD), which affects skin, blood vessels, heart, lungs, kidneys, gastrointestinal (GI) tract and musculoskeletal system. Severe cases can lead to interstitial lung disease, pulmonary hypertension, and acute kidney failure crises. It may overlap with other connective tissue diseases, which is named overlap syndrome. Life-threatening renal involvement called scleroderma renal crisis (SRC). Thrombotic microangiopathy (TMA) is defined by impaired organ function resulting from the formation of platelet thrombi in the microvasculature, accompanied by microangiopathic hemolytic anemia and severe thrombocytopenia, and it may, at times, complicated with SRC.

Case presentation

A 67 year-old male presented to emergency department with shortness of breath and was diagnosed with anemia and acute kidney injury. Renal biopsy showed glomeruli with ischemic change, endothelial cell swelling, and concentric myointimal thickening (onion-skin change) of the interlobular arteries. The features were compatible with thrombotic microangiopathy (TMA) and accelerated hypertension. ANA titer was 1:1280, anti-Scl-70 positive. Nailfold capillary examination results were compatible with chronic stage of sclerodermic microangiopath. SSc-TMA overlap syndrome was diagnosed. ADAMTS-13 were normal, therefore excluding thrombotic thrombocytopenic purpura (TTP). Atypical hemolytic uremic syndrome (aHUS) gene test showed a pathogenic gene, MTP (CD46), variant. Thus, this case was diagnosed as TMA associated with SSc. The patient was treated with ramipril, hydroxychloroquine, therapeutic plasma exchange (TPE) for 5 times and hemodialysis.

Discussion

Scleroderma renal crisis (SRC), could lead to abrupt malignant hypertension and acute kidney failure. In Taiwan, it is estimated to occur in approximately 2.5% of all systemic sclerosis patients. Despite its relatively low occurrence rate, SRC represents the most unfavorable prognosis and fastest progressing complication of systemic sclerosis. It is rarely associated with atypical haemolytic uraemic syndrome. The current literature does not contain any relevant case reports.

Conslusion

We herein described a SSc patient with biopsy proven SRC complicated with thrombotic microangiopathy which aHUS gene (CD46) test showed positive result.

病例報告　112_C 17

周邊動脈阻塞疾病經皮血管成型術後併用高強度 statin 及 trimethoprim/sulfamethoxazole 致橫紋肌溶解症：個案報告與文獻回顧

Rhabdomyolysis by High-Intensity Statin and Trimethoprim/sulfamethoxazole after Percutaneous Transluminal Angioplasty for peripheral arterial occlusion disease

高定瑋[1] 羅皓允[1,2] 張勤斌[3]
[1]國立台灣大學醫學院附設醫院 [2]國立臺灣大學醫學院附設醫院新竹臺大分院
[3]國立臺灣大學醫學院附設醫院新竹臺大分院生醫醫院竹東院區

Introduction

Statin related myopathy has been well established, but progression to rhabdomyolysis is seldom encountered. According to epidemiological statistics, the overall incidence of statin-related rhabdomyolysis was less than 0.1%. Progressive skeletal muscle injury is nevertheless associated with a high risk of renal replacement therapy and all-cause mortality. As the prevalent use of statin and adjuvant medications against comorbidities, recognition of such complications and prompted corresponding managements are pivotal to improve outcomes.

Case presentation

An 82-year-old man presented with chronic wound over bilateral legs caused by chronic limb ischemia. Vascular duplex illustrated critical stenosis over bilateral lower extremities. Two-staged percutaneous transluminal angiography by local ballooning was performed to achieve adequate reperfusion. High dose atorvastatin was added after the procedure, conjunctionally with trimethoprim/sulfamethoxazole (TMP/SMX) against Stenotrophomonas strain over gangrene. Nevertheless, acute kidney injury complicating metabolic acidosis and imbalanced electrolytes developed. Comprehensive workup rendered critical rhabdomyolysis with a high McMahon score of 13. Drug-related was favored after excluding other etiologies. Statin was halted, and TMP/SMX was substituted with quinolone. The serum level of creatinine kinase was eventually normalized one week later, and kidney function was restored.

Discussion

We herein reported a case of drug-related severe rhabdomyolysis, which was considered a culprit to atorvastatin. According to anecdotal case reports and corresponding drug labeling, most of the patients with statin-related rhabdomyolysis were notable for predisposing conditions, including advanced age, untreated hypothyroidism, and chronic kidney disease. Aside from comorbidities, drug-drug interactions have been identified as contributors to muscle injury associated with statins. The Drug-Induced Rhabdomyolysis Atlas specifically identifies parallel medications that affect the metabolism by cytochrome P450, which significantly increases the risk of muscle injury. In our case, the patient has been concurrently initiated atorvastatin and TMP/SMX. However, TMP and SMX are recognized as antagonists specifically against CYP2C8 and CYP2C9, respectively. The effect of attenuating CYP3A4 becomes significant only when the steady-state plasma concentrations of TMP/SMX reach 250/500 μM. It is therefore less likely that TMP/SMX exaggerated the effect of statins leading to rhabdomyolysis in this individual. Anecdotal reports have described TMP/SMX as a culprit in drug-related rhabdomyolysis, mostly associated with prophylactic use against

Pneumocystis jirovecii pneumonia or *Toxoplasma gondii* in immunocompromised patients. However, in this case, only regular doses of TMP/SMX has been initiated for several days before the onset of myopathy. TMP/SMX is therefore less likely as the culprit medication as well.

Acute kidney injury is the most prominent complication of rhabdomyolysis. Direct injury of *myoglobin* and oxidative injury bring about acute tubular necrosis. Fluid resuscitation to facilitate *myoglobin* clearance remained the mainstay treatment. A cohort study suggested early and vigorous crystalloid supplementation was associated with a more favorable prognosis. Additional mannitol to augment urine output and urine alkalinization with sodium bicarbonate nevertheless failed to decrease the rates of kidney failure, dialysis, and all-cause mortality. However, the evidence was primarily established on populations with traumatic causes. Generalization to patients with drug-related rhabdomyolysis warranted further investigations. Hemodialysis serves as the ultimate measure to rescue acute kidney injury. Specific high-flux hemofiltration was demonstrated to remove *myoglobin* more effectively, whilst randomized control trial revealed pronouncedly higher mortality. Generally, continuous renal replacement therapy was associated with no disease-specific benefit, including statin-related etiology. For prognostication, the McMahon score was established to predict the risk of acute kidney injury and dialysis. Our case presented with high score but hemodialysis was not mandated, potentially due to early recognition and prompt elimination of triggering factors.

Effective management of lipid burden remained crucial in individuals with high cardiovascular events but experienced statin-related adverse events. A recent retrospective study demonstrated no significant increase in statin discontinuation when a drug-drug interaction is present. Nevertheless, determining whether to resume statin treatment in this population poses a clinical conundrum. Current guidelines still recommended resuming statin therapy to protect against future cardiovascular events. Skeletal muscle injury is still possible to develop after reinitiation of statin if in the absence of clinical parameters that could be modified. Therefore, either decreasing the dose or shifting to another statin are viable alternatives to prevent the recurrence of rhabdomyolysis and promote patient adherence. For statin-intolerant individuals confirmed by rechallenge, GAUSS-3 (Goal Achievement after Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects-3) study proposed switching statins to proprotein convertase subtilisin/kexin type 9 inhibitors is a safe and effective approach to orchestrate serum cholesterol level.

Conclusion

Statin-related rhabdomyolysis is a rare yet catastrophic complication. Very elderly patients with predisposing factors are particularly susceptible to drug-induced skeletal muscle injury. Introducing statin in these individuals hence involves a personalized and cautious assessment of the potential benefits and risks. Fluid replenishment to augment urine output and management of complications secondary to acute kidney insufficiency are key aspects of treatments. Once rhabdomyolysis is ameliorated, re-evaluation of cardiovascular risk and resuming lipid-lowering agents are endorsed to improve overall prognosis.

病例報告　112_C 18

新冠肺炎併發變性血紅素血症之個案報告

Dapsone-related Methemoglobinemia complicating SARS-CoV-2 infection: A case report

鄧書帆[1] 黃立恒[2] 鄭喬峯[2]
[1]臺大醫院內科部 [2]臺大醫院內科部風濕免疫科

Introduction

Methemoglobinemia is characterized by impaired oxygen-carrying ability of hemoglobin, leading to tissue hypoxia. We presented a patient in whom methemoglobinemia complicated SARS-CoV-2 infection and discussed a few special considerations in diagnosis and treatment.

Case presentation

This is a 72-year-old man with medical history of autoimmune hemolytic anemia and idiopathic pulmonary fibrosis. Trimethoprim/Sulfamethoxazole was given for PJP prophylaxis during intensive immunotherapy. One month before admission, it was switched to Dapsone due to elevated liver enzymes. This time, he came to emergency room for acute fever and dyspnea. SARS-CoV-2 infection was diagnosed via PCR testing. Remdesivir, glucocorticoid and empirical Piperacillin/Tazobactam were given. Oxygenation was tapered from facial mask to nasal cannula on admission.

Meanwhile, abrupt desaturation occurred in the evening of admission day. High-flow nasal cannula 80%/60L was required to maintain his oxygen saturation above 90%. Despite the event, he looked easy on physical exam and arterial blood sampling revealed a Chocolate-color appearance. Serum c-reactive protein, ferritin and d-dimer level remained stationary while lactate dehydrogenase rose up. Hemoglobin level lowered from 9 to 7 (g/dL) without overt bleeding. Ct value of SARS-CoV-2 PCR test was higher and chest plain film was stationary. Methemoglobinemia was confirmed later with a MetHb level of 10.4%.

High-dose Ascorbic acid (6000 mg per day), in addition to a dose of Tocilizumab for severe SARS-CoV-2 infection, was given with gradual tapering. His oxygenation and hemoglobin level improved dramatically on the next day. Serum methemoglobin level lowered to 1.7% on the 4th day of treatment. 3 weeks later, he was discharged from the hospital without oxygen support.

Discussion

There are several reports of methemoglobinemia causing or mimicking “happy hypoxia” during SARS-CoV-2 infection[1]. But to our knowledge, this patient provided one of the first few domestic experience. Some of the reported patients are linked to oxidative medications, such as Dapsone[2], but some are not. Accordingly, it is postulated that infections (including SARS-CoV-2) and acute illness, serve as excessive oxidative stress and result in Methemoglobinemia[3].

Secondly, the Methemoglobin level in this case was not as high as previously reported to cause such severe symptom or change of oxygenation saturation (usually required MetHb around 20%). Looking back, we speculated that the underlying interstitial lung disease and chronic anemia also make him more vulnerable.

Lastly, symptomatic Methemoglobinemia was mostly treated with Methylene blue. However, it may paradoxically aggravate the condition in patients with chronic hemolysis, especially G6PD deficiency. Ascorbic acid, due its anti-oxidative property, have been suggested as an alternative but the dosing regimen is still variable. Our patient provided a successful reference.

Conclusion

Methemoglobinemia can develop during SARS-CoV-2 infection. Clinician should list it in the differential of dyspnea, especially when there is relevant medication history or when the degree of respiratory distress was disproportionate to oxygen saturation. In patients with hemolysis, Ascorbic acid is an alternative to methylene blue.

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病例報告　112_C 19

以免疫調節藥物及血漿置換術成功治療抗-MDA5-抗體陽性之皮肌炎 併呼吸衰竭

Anti-MDA5 dermatomyositis with rapidly-progressive interstitial lung disease successfully-treated with immunotherapy and plasmapheresis: a case report

蕭竣仁[1] 黃立恒[2] 張庭暐[3] 呂政勳[2]

[1]台灣大學附設醫院內科部 [2]台灣大學附設醫院內科部風濕免疫科 [3]台灣大學附設醫院新竹分院整合醫學科

Introduction

Anti-melanoma differentiation-associated gene 5 (MDA5) dermatomyositis is notorious of rapid-progressive interstitial lung disease (RP-ILD) and severe skin manifestation while muscular involvement may be minimal. Mortality rate was high. We presented one such patient successfully managed with intensive immunosuppression therapy and plasmapheresis.

Case presentation

This is a 51-year-old woman with obesity (Body mass index: 34) but no other established medical condition. 1 month before admission, her exercise capacity gradually decreased but there was no difficulty to climb up stairs or raise up her arms. In outpatient department, computed tomography of chest revealed bilateral diffuse ground-glass opacities and pulmonary function test showed restrictive ventilatory defect (FVC: 1.4L, 58% predicted).
3 days before admission, she came to emergency room for fever and worsening dyspnea. Physical exam revealed violaceous skin eruptions at her forehead, posterior neck and dorsal hands. Dermatologist confirmed Heliotrope sign, Shawl sign and Gottron sign. C-reactive protein and white blood cell count elevated while creatine kinase level was not. Under the impression of amyopathic dermatomyositis with interstitial lung disease, we started methylprednisolone at a dose of 0.5-0.6mg/kg/day. However, her oxygen requirement further rose to non-rebreathing mask and intubation was performed. Upon intensive care unit admission, anti-MDA5 antibody returned strongly positive (3+).
Intravenous Cyclophosphamide (400mg, on day 3 then cycle 2 on day 32), Double- filtration plasmapheresis (DFPP, day 2–day 11, 5 sessions), Rituximab (500mg, D12) and oral Leflunomide (20mg once daily) were applied. She was extubated on day 4. High-flow nasal cannula was gradually weaned off in the floor and she was discharged on day 40. After discharge, seven cycles of monthly cyclophosphamide pulse therapy were given. At 1 year, her glucocorticoid was reduced to 5mg every other day and pulmonary function test showed improvement (FVC: 1.75L, 72% predicted).

Discussion

Rapidly progressive interstitial lung disease is a frequent and severe manifestation of anti-MDA5 dermatomyositis. Currently, a multicenter prospective study from Japan[1] favored initial combination of high-dose glucocorticoids, tacrolimus, and intravenous cyclophosphamide) over step-up therapies (6-month survival rates: 89% versus 33%).
In another retrospective study of refractory anti-MDA5-RP-ILD patients[2], adding plasmapheresis to standard immunosuppressive therapy resulted in a better survival (5 of 8 patients versus 0 of 5 patients). This was in line with our experience, which additional plasmapheresis allowed for a rapid reduction of glucocorticoid to 0.2-0.3 mg/kg/day in 2

weeks, minimizing potential infections.

Conclusion

RP-ILD is a hallmark of anti-MDA5 dermatomyositis. Combination of immunosuppressive therapy is essential. In severe or refractory patients, plasmapheresis may be considered.

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病例報告　112_C 20

肝細胞癌皮膚轉移: 一個罕見的臍周腫瘤個案報告

Cutaneous Metastasis from Hepatocellular Carcinoma: A Rare Cause of Periumbilical Bulging Tumor

徐善維[1] 高偉育[1,2,3,4] 黃昱閔[5,6]

[1]臺北醫學大學附設醫院消化內科 [2]臺北醫學大學醫學院醫學系消化內科學科 [3]臺北醫學大學消化醫學研究中心, [4]臺北醫學大學臺北癌症中心 [5]臺北醫學大學醫學院醫學系外科學科 [6]臺北醫學大學附設醫院一般外科

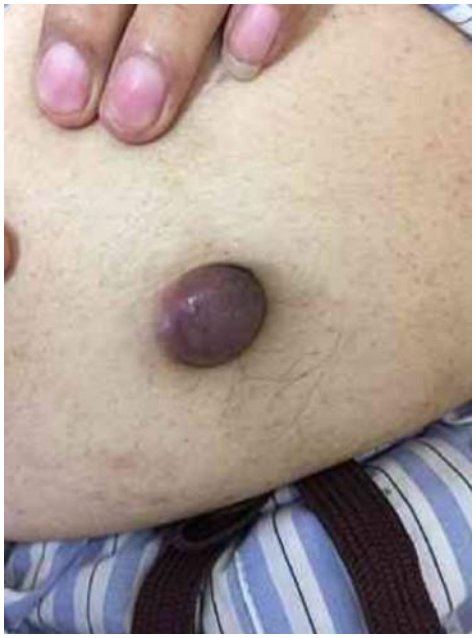
Introduction

Hepatocellular carcinoma (HCC) accounts for approximately 90% of primary liver cancers[1]. It is notorious for being one of the most common cancers and the fourth most frequent cause of cancer-related deaths worldwide[2]. The annual recurrence rate of HCC after surgical resection exceeds 10%, reaching up to about 80% within 5 years after surgery. Although the likelihood is low, HCC can develop extrahepatic metastasis. The most common site for HCC metastasis is the lung, followed by abdominal lymph nodes, bones, and adrenal glands[3]. Cutaneous and muscle metastasis from HCC, however, are extremely rare, with only a few case reports existing. In this report, we present a case with rare cutaneous HCC metastases in the periumbilical area.

Case Presentation

A 64-year-old man presented with a slow-growing, firm, non-painful, bulging mass adjacent to the umbilicus (Figure 1). The mass measured up to 3 cm in diameter and was dark purplish in color. The patient has a history of hepatitis C viral-related cirrhosis, Child-Pugh score B7, complicated by esophageal varices. He had been diagnosed with HCC four years ago, initially at Barcelona Clinic Liver Cancer stage B. He received several rounds of trans-arterial chemo-embolization and radio-frequency ablation (RFA). However, recurrent HCC occurred a few months later, and he subsequently underwent laparoscopic partial hepatectomy. The patient was otherwise well until the appearance of the periumbilical protruding mass. Laboratory data in the outpatient clinic showed slightly elevated aminotransferase levels (AST 59 U/L, ALT 26 U/L), without total bilirubin elevation (Bilirubin T 0.5 mg/dL). The alpha-fetoprotein level was 8524 ng/mL. Abdominal computed tomography revealed portal venous thrombosis and a periumbilical tumor with hypervascularity and subcutaneous extension (Figure 2). The patient underwent en bloc resection of the tumor. The excisional biopsy specimen confirmed metastatic HCC, with free section margins (Figure 3). After the surgical removal of the subcutaneous metastatic tumor, the patient received radiotherapy for portal venous thrombosis.

Figure 1. Picture of the periumbilical lesion presented in admission



Discussion

Cutaneous metastases of HCC are exceedingly rare, with only a handful of reported cases. Some of them were reported to be caused by tumor seeding during diagnostic procedures or locoregional treatments, such as liver biopsy, percutaneous ethanol injection and RFA. The main route of this type of metastases is supposed to be along the tract of the needle used in these procedures[4]. This case, however, is among a small minority of reported cases of cutaneous metastatic HCC that are associated with abdominal surgical intervention, and is considered to be a consequence of port-site metastasis (PSM). PSM is recognized as a notable complication of laparoscopic surgeries, and is characterized by direct malignant cells implantation at a trocar insertion site after a laparoscopic resection of an intra-abdominal tumor. Although not fully understood, some possible pathogenesis of PSM have been proposed. Curet et al. raised two feasible leading factors resulting in PSM, namely pneumoperitoneum and direct tumor contamination. During the abdominal laparoscopic surgery with carbon dioxide (CO2) insufflation, iatrogenic pneumoperitoneum may shuck some malignant cells off the tumor surface, spreading them into the gaseous peritoneal cavity via aerosolization[5,6]. Several methods have been proposed to prevent PSM, including stricter modifications to surgical techniques and intraperitoneal irrigation with chemotherapy agents. Other promising approaches involve hyperthermic CO2 insufflation and humidified CO2 insufflation, both of which have shown efficacy in preventing peritoneal tumor spreading in some animal experiments[7]. The potential use of these methods in preventing PSM in the future is promising.

Figure 2 Abdominal computed tomography revealed: A) portal venous thrombosis (arrow), B) a solid heterogenous and hypervascular tumor (arrow) adjacent to umbilicus and extending into the subcutaneous adipose tissue.

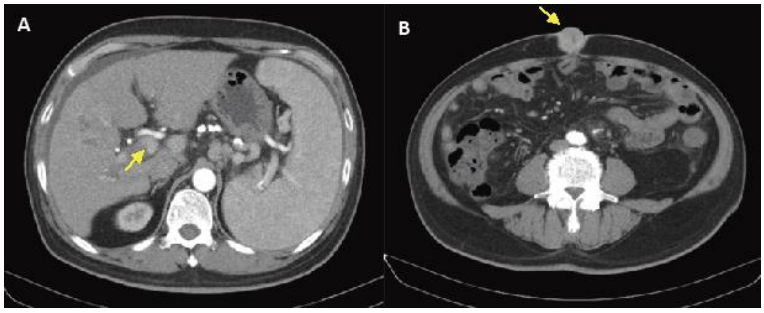
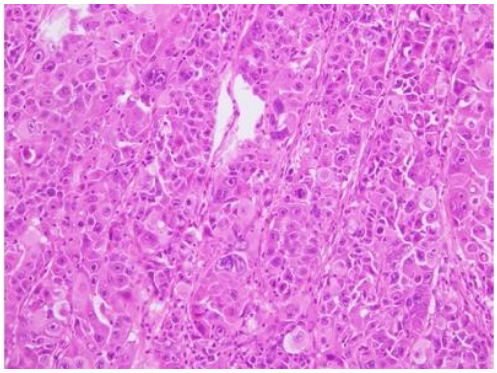


Figure 3 Histology revealed metastatic carcinoma with trabecular and nested patterns, characterized by abundant eosinophilic cells with marked nuclear pleomorphism.



Conclusion

This case emphasizes the possibility of PSM following laparoscopic resection of HCC. Although rare, the dissemination of tumor cells into the subcutaneous abdominal wall via an iatrogenic route is not impossible, and diligent attention to surgical technique plays an important role in avoiding this complication. Further studies are required to explore other methods of preventing PSM.

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病例報告　112_C 21

一位 COVID-19 感染患者出現肺栓塞之個案報告

a case of pulmonary embolism in a patient after COVID-19 infection

羅紹齊[1] 陳錫賢[2,3]

[1]臺北醫學大學附設醫院內科部 [2]臺北醫學大學附設醫院內科部腎臟內科 [3]臺北醫學大學醫學系腎臟內科

Introduction

Introduction: There is a significant association between COVID-19 infection and pulmonary embolism. In previous systematic reviews, up to 21% of infected individuals experienced this complication. However, it is often overlooked in clinical practice as symptoms may not always be apparent. Its pathophysiological mechanism is attributed to microvascular in situ immunothrombosis, leading to endothelial cell dysfunction and tissue factor expression.

Case presentation

A 81-year-old woman with underlying disease of atrial fibrillation and right breast invasive ductal carcinoma (pT2N3aM0 stage IIIC, status post right simple mastectomy and axillary lymph node dissection) was found to have COVID-19 one month ago. She had no fever, chills, short of breath, and headache and then she was treated with Molnupiravir at that time. However, after 1 month, she was admitted to our hospital with fever (39.4℃), chills, mild cough, dizziness, and sudden onset of incontinence.

Discussion

A total 2.5% incidence of both arterial and venous thrombosis at day 30 following discharge and venous thromboembolism alone is 0.6–0.48%. In a 52 reported cases, the minimum reported days after diagnosis is 7 days and the maximum is 180 days (mean 35.1 days) with documented hypercoagulability up to 62 days. The cutting point of D-dimer for prognosis varied in many studies. Patients with D-dimer >1mg/L present a 20-fold mortality risk, and the other study showed The D-dimer value of 2.025 mg/L was the optimal probability cutoff for judging an outcome of death.

Conclusion

COVID-19 has now officially entered the stage of coexistence with humans. Individuals of any medical condition may potentially experience such an infection and seek treatment under the care of various specialized medical professionals. Even if patients have mild symptoms at the onset of infection, COVID-19 still poses numerous potential complications and long-term effects, warranting heightened vigilance from healthcare professionals.

病例報告　112_C 22

慢性上腹痛一個罕見的原因－全身性肥大細胞增生症

A Rare Cause of Chronic Abdominal Pain - Systemic Mastocytosis

呂建宏 [1,4]　蔡嘉晉 [3]　張甄 [1,2,4]

[1] 台北醫學大學附設醫院消化內科 [2] 台北醫學大學醫學院內科學科 [3] 台北醫學大學附設醫院病理科

[4] 台北醫學大學消化醫學研究中心

Introduction

Mastocytosis is a rare disease characterized by pathologic proliferation of mast cells. It is classified into cutaneous mastocytosis (CM) with skin-limited disease, systemic mastocytosis (SM) with the presence of extracutaneous organ involvement, and mast cell sarcoma (MCS), a very rare disease with solid tumor presentation[1]. SM as a cause of chronic abdominal pain is rare and should not be neglected. Here, we presented a case with presentation of chronic abdominal pain and associated gastrointestinal symptoms and diagnosed with systemic mastocytosis.

Case presentation

This 49-year-old woman presented with epigastric dull pain intermittently for 1 year. The pain aggravated and was more frequent after meals. Abdominal fullness, nausea, vomiting, and frequent diarrhea without blood or mucus components were also reported. She sought medical attention at the outpatient clinic at this hospital. She had received a diagnosis of chronic hepatitis B, two hepatic hemangiomas and benign multinodular goiter, for which she had been followed up at the outpatient clinic setting regularly. The physical examination revealed mild abdominal distension without abdominal tenderness. Basic laboratory tests were only significant for mild dyslipidemia. She reported no use of cigarettes or alcohol. There were no known allergies. Her father had a medical history of esophageal cancer and her brother had thyroid cancer. Oral proton-pump inhibitors and anticholinergics were prescribed but the symptoms persisted.

Figure 1. (A) Esophagogastroduodenoscopy image of second portion of duodenum revealing multiple friable nodular lesions in white light. (B) Nodular lesions in narrow-band image.

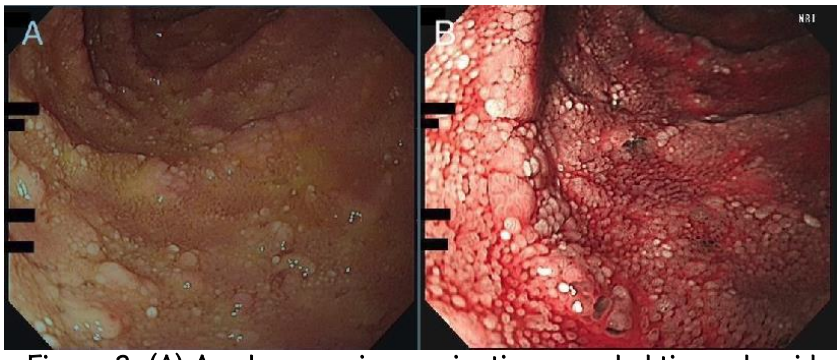
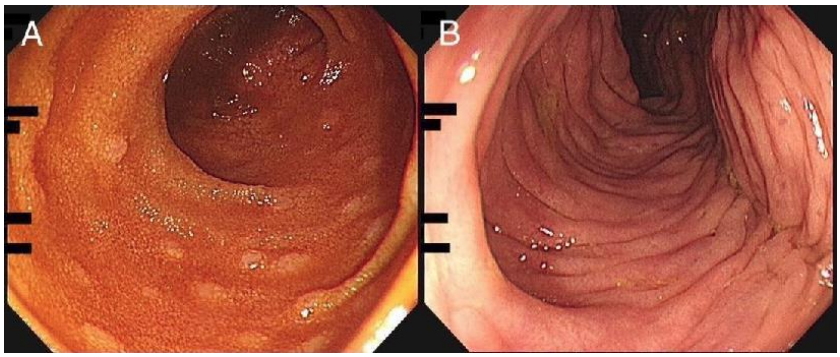


Figure 2. (A) A colonoscopic examination revealed tiny polypoid lesions and nodular lesions at the terminal ileum. (B) Swelling mucosa with pits at the proximal colon.



She received upper and lower gastrointestinal endoscopies for further evaluation. An esophagogastroduodenoscopy revealed multiple nodular friable lesions around 3 millimeter in size located at the second portion of duodenum (Figure 1). A colonoscopic examination revealed tiny polypoid lesions and nodular lesions at the terminal ileum (Figure 2A), and swelling mucosa with pits at the proximal colon (Figure 2B). The pathology report of the nodular lesions at duodenum showed compact intramucosal infiltrates of mast cells admixed with some eosinophils in sheet pattern in the lamina propria (Figure 3). The pathology report of the terminal ileum and proximal colon revealed aggregates of mast cells admixed with some eosinophils infiltrates in the superficial lamina propria (Figure 4A). Immunohistochemically, the mast cells were positive for CD117, CD30 and CD25, and negative for S-100 and CD1a. A bone marrow biopsy showed normocellular marrow with scattered mast cells (Figure 4B). The genetic study was a wild type of KITD816V with normal karyotypes (46,XX). The genetic study, pathology reports and elevation of serum tryptase were compatible with systemic mastocytosis. A computed tomography of the abdomen and pelvis revealed mesenteric panniculitis without space-occupying lesions. A hemato-oncologist was consulted for further management. A histamine H1-receptor antagonist was given for long-term control. Her symptoms improved. She remained generally well and followed up at an out-patient clinic setting until now.

Figure 3. (A) The histopathological examination (H&E stain, original magnification x400) of the duodenum revealed compact intramucosal infiltrates of mast cells admixed with some eosinophils in sheet pattern in the lamina propria. (B) By immunohistochemistry, the mast cells are positive for CD117

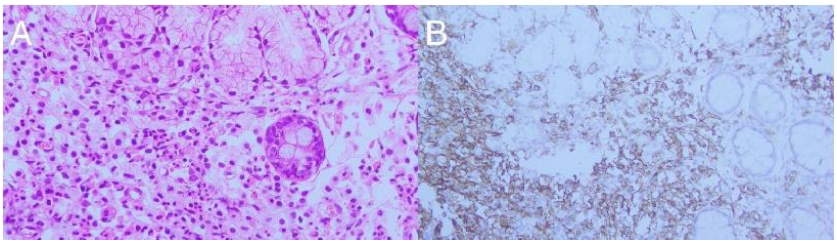
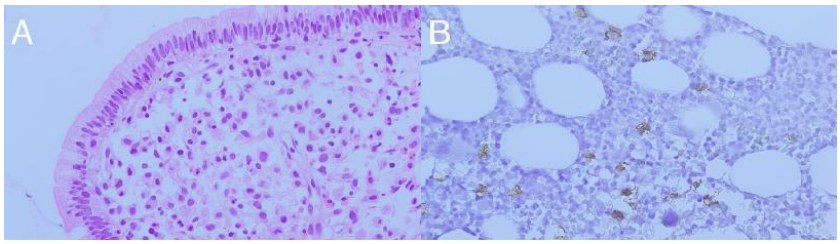


Figure 4. (A) The histopathological examination (H&E stain, original magnification x400) of the terminal ileum revealed aggregates of mast cells admixed with some eosinophils infiltrates in the superficial lamina propria and (B) the bone marrow biopsy showed normocellular marrow with immunohistochemically CD117-positive scattered mast cells.



Discussion

System mastocytosis (SM) is a rare disorder with aberrant proliferation of mast cells in organs other than the skin, including liver, spleen, gastrointestinal tract, and bone marrow[1,2]. SM accounts for 10% of mastocytosis and is predominant in adults[2]. Most cases revealed KITD816V mutation resulting in dysregulation of c-Kit receptor tyrosine kinase and subsequent abnormal growth and differentiation of mast cells[2,3]. The mediators released from mast cells caused the diversity of clinical symptoms, including flush, pruritus, diarrhea, nausea, vomiting, myalgia, and anaphylactoid reaction. The diagnosis according to WHO classification is made based on the histologic evidence of abnormal infiltrates of mast cells, KITD816V mutation and elevated serum tryptase[3]. The natural history of disease ranges from indolent disease to advanced disease, which needs aggressive treatment such as cytoreductive therapy or allogenic hematopoietic stem cell transplant[3].

Gastrointestinal symptoms are frequently reported in systemic mastocytosis with a

prevalence of 60-80%[2,4]. The most frequent GI symptom is diarrhea and bloating, followed by abdominal pain in a study of 83 cases[5]. In addition, risk of peptic ulcer is also elevated with systemic mastocytosis possibly due to increased histamine production[5]. The diagnosis of systemic mastocytosis is difficult if no cutaneous manifestation is present, and thus non-specific GI symptoms can be misdiagnosed as inflammatory bowel disease. The endoscopic findings include mucosal nodularity, erosions, or loss of mucosal folds[2]. Although GI symptoms are not life-threatening, patients are likely to have decreased life quality and chronic and severe symptoms. Therefore, a prompt diagnosis of systemic mastocytosis with GI symptoms is warranted, which depends on physicians' alertness.

Conclusion

Our case demonstrated that although not a common cause, chronic abdominal pain with associated GI symptoms can be the presentations of systemic mastocytosis. Due to its non-specific GI symptoms, SM can be misdiagnosed as inflammatory bowel disease or irritable bowel disease. A timely diagnosis and appropriate treatment can improve patients' outcome significantly, which depends on clinicians' awareness and alertness to the disease.

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病例報告　112_C 23

李斯特菌腹膜炎之案例報告

Bacterial Peritonitis Induced by Listeria monocytogenes: A Case Report

林庭右[1] 陳錫賢[1,2]
[1]台北醫學大學附設醫院內科部 [2]台北醫學大學附設醫院內科部腎臟內科

Introduction

Listeria monocytogenes, a Gram-positive bacterium characterized by catalase-positive and beta-hemolytic attributes, is associated with a heightened risk of infection in specific patient cohorts, encompassing immunocompromised individuals, pregnant women, infants, the elderly, and those with diabetes. Within the spectrum of Listeria monocytogenes-related infections, peritonitis remains a relatively infrequent manifestation, although it exhibits a more substantial incidence among patients with cirrhosis and those undergoing peritoneal dialysis. Instances of Listeria monocytogenes-induced sepsis is exceptionally rare. In this report, we present a distinctive case involving a patient afflicted with end-stage renal disease, who underwent two months of peritoneal dialysis and subsequently expired due to Listeria peritonitis and septicemia.

Case presentation

We present a case involving a 70-year-old male afflicted with end-stage renal disease, who had initiated peritoneal dialysis for a duration of two months. The patient sought medical attention at our emergency department, reporting a one-week history of general malaise, nausea, and diminished appetite. Laboratory investigations revealed thrombocytopenia, anemia, hyponatremia, and elevated serum BUN/creatinine levels. Upon physical examination, the patient exhibited vital signs within the following ranges: temperature 36.7°C, pulse 91, respiratory rate 16, and blood pressure 137/90. Consequently, he was promptly admitted to our facility, initially receiving management for suspected inadequate dialysis and electrolyte imbalances.

On the second day of hospitalization, the patient's clinical condition deteriorated, manifesting hypotension. Suspecting peritonitis, intraperitoneal Cefazolin and Ceftazidime were administered. Subsequently, the peritoneal dialysate culture revealed the presence of gram-positive bacilli (GPB), prompting a treatment regimen adjustment to Vancomycin and Ceftazidime. Despite these interventions, the patient's condition continued to decline, characterized by persistent hypotension, hypothermia and pancytopenia.

Two days following the initial culture results, the GPB was identified as Listeria monocytogenes, leading to an immediate prescription of intravenous ampicillin therapy. Regrettably, despite these efforts, the patient succumbed to the infection a few hours after the administration of intravenous ampicillin. Postmortem blood cultures also confirmed the presence of Listeria monocytogenes.

Discussion

Listeria monocytogenes, a motile Gram-positive bacilli, is renowned for its association with foodborne illnesses, owing to its capacity to thrive across a broad temperature spectrum and endure high salinity conditions. Sporadic instances of listeriosis are commonly linked to

contaminated food items, encompassing undercooked meats and soft cheeses.
Listeria monocytogenes-induced peritonitis represents a rare subset within bacterial peritonitis cases, predominantly characterized by abdominal pain and the presence of cloudy dialysate. Remarkably, relapse cases remain notably infrequent.
This case report highlights a unique occurrence of Listeria peritonitis in an Asian patient, distinguished by positive peritoneal dialysate and blood culture results, coupled with the development of severe sepsis resulting in mortality. The challenge posed by the ineffectiveness of intraperitoneal Vancomycin therapy, as observed in previous cases, highlights the intricacies involved in managing Listeria-induced peritonitis among peritoneal dialysis patients.

Conclusion

Listeria monocytogenes-induced peritonitis is uncommon in occurrence, with limited documented cases in the medical literature. Defining the optimal antibiotic regimen and treatment duration poses challenges, although Ampicillin therapy is gaining prominence.
Healthcare providers should exercise heightened vigilance when patients do not respond promptly to standard antibiotic therapies, especially among immunocompromised individuals.

病例報告　112_C 24

Case series - Gastric heterotopia beyond esophagus in the gastrointestinal tract

胡彥佶 [1,2]　陳和美 [1]
[1] 博仁綜合醫院胃腸肝膽科　[2] 陽明交大醫學院

Introduction

Heterotopic gastric mucosa (HGM) is histologically similar to the gastric mucosa, which consists of oxyntic mucosa with mucus-secreting columnar cells, chief cells, and parietal cells. According to histology, HGM can be classified into three types. 1. fundic-type (parietal cells predominated); 2. antral-type (chief cells predominated); and 3. transitional-type (chief and parietal cells mixed)[1]. Also, Helicobacter infection, inflammation, intestinal metaplasia, and dysplasia could be reported within the HGM patch. It was reported that the incidence rate of HGM in the general population was about 1-2% and it was mostly found in the distal esophagus and duodenal bulb, and rarely found in the colon[2-6].

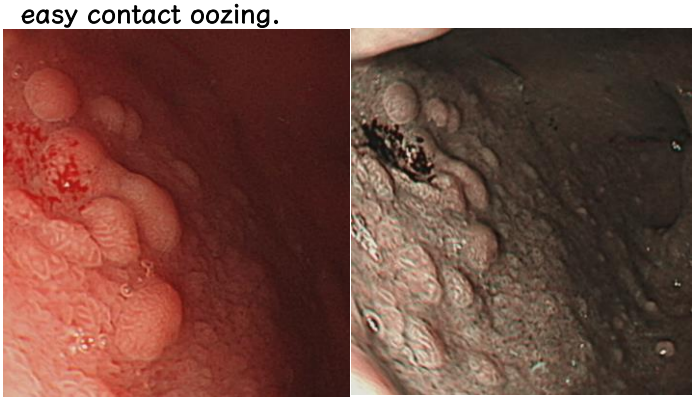
Since 1st description of gastric heterotopia in 1939[7], HGM has been reported in many case reports. The symptoms of HGM varied in a wide range, and they were related to the site of HGM involvement. A retrospective cohort study in China for esophageal HGM showed 9% of the patients had heartburn and dysphagia, 5.7% of the patients had throat discomfort, and 62% of the patient had epigastric discomfort[1]. For rectal HGM, the symptoms could range from asymptomatic to painless bleeding[3]. Alco, HGM in Meckel diverticulum can induce symptoms similar to acute appendicitis.[5] In some case-reports, HGM can even lead to bowel obstruction. It is hard to tell the serrate polypoid lesions from HGM to other etiologies endoscopically. Here we share two cases of HGM in small and large intestine.

Case Report

Case 1

A 51 years old healthy Taiwanese man received a panendoscopy as a health examination. Granulating mucosal change was seen at the duodenal bulb, and the involved foci was about 1cm. Histopathologic examination of the biopsy samples taken from the polypoidal formations showed duodenal type mucosa and gastric type glands, with no sign of dysplasia. Heterotopic duodenal gastric mucosa was reported. (Figure 1.) Colonoscopy was performed, too. And two polyps reported tubular adenoma in size of 0.3cm in the transverse colon and 0.5cm in the rectum, respectively, were resected.

Figure 1. Endoscopic images (A) Endoscopy view under normal light, (B) Endoscopic views under NBI. The heterotopic gastric mucosa (HGM) in bulb of duodenum showed granulating mucosal change and easy contact oozing.



Case 2

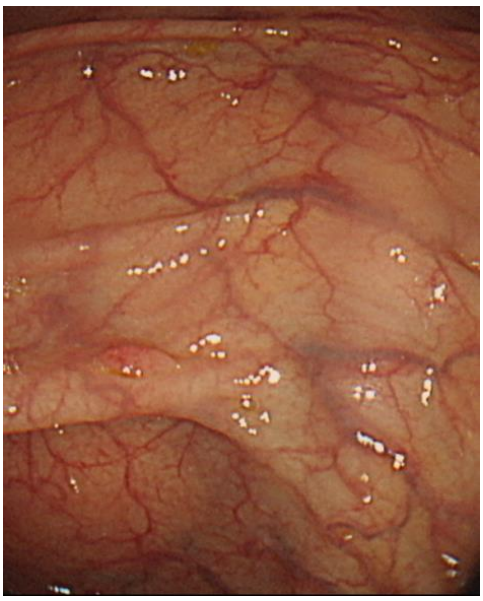
A 52 years old Taiwanese man with no underlying disease received a colonoscopy as a health examination. A 0.3cm polyp was seen at ascending colon, NICE type 2, JNET type 1.

Polypectomy with cold snare was performed. The histopathological report of the biopsy sample was colonic mucosa with gastric-type glands. Gastric heterotopia was reported. (Figure 2.) Panendoscopy was performed, and more than 5 polyps were noted and biopsied. Histological reports were fundic gland polyps.

Discussion

Gastric heterotopia has been reported in various locations along the GI tract, and the endoscopic presentation of the lesions could also be different. Diverticulum, ulcer, polyp, or flat/depressed lesion were reported in colonic HGM; diminutive polyps, elevated patches, and flat erythematous areas were reported in duodenal HGM[3,8]. The most common presentation and location was salmon-colored patch (inlet patch) in the upper third of the esophagus[9]. The polypoid like HGM in the ascending colon in our case was a very rare condition, instead.

Figure 2. Serrate polyp-like heterotopic gastric mucosa (HGM) in ascending colon



The origin and formation of HGM is not very clear, and 3 hypotheses had been proposed. (1)Developmental remnant of stomach tissue. However, this could only explain the HGM at distal esophagus, while HGM at other distal intestines or gallbladder could hardly explain[6,10]. (2)Abnormal mucosal regeneration following the destruction of normal intestinal mucosa. Nevertheless, there is insufficient evidence of HGM formation following gastroenteritis or inflammatory disease[11]. (3)An error of differentiation causing HGM formation is a reasonable hypothesis which can elucidate why HGM can be found within the whole gastrointestinal tract. From the "stem cell theory", HGM is a result of an error in either the positioning of endodermal stem cells during organogenesis or a result of the erroneous differentiation of pluripotent endodermal stem cells in the GI tract[9,11].

HGM was considered part of a spectrum of metaplastic change related to peptic disorders[5] and it was also considered an origin of GI malignancy, including esophageal adenocarcinoma, despite the malignant progression of HGM is rare. The malignant progression within HGM in the esophagus was considered a stepwise pattern. It starts at heterotopic, but otherwise "normal" epithelium, and may change to low- and then high-grade dysplasia, and at last advance to carcinoma[10]. Similar potential of malignant transformation was also suspected in the gallbladder and colon HGM[6]. When HGM was found with pyloric gland adenoma, surface dysplasia, and adenocarcinoma, it suggests that HGM is undergoing neoplastic transformation[9].

Resection by either surgical or endoscopic methods is the main treatment to the HGM in the GI tract other than esophagus since the HGM usually presents as polypoid lesions and sometimes causes bleeding and bowel obstruction[3,9]. HGM related colorectal bleeding can be controlled by using histamine-2 receptor blockers[7].

Conclusion

Heterotopic gastric mucosa is a predominantly benign lesion in the gastrointestinal tract, but the association with malignant neoplasm still emphasizes us to recognize the entity. Standard

management of the HGM depends on the symptom and morphology of each case.

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病例報告　112_C 25

類似大腸癌的結核性腸炎

Mimicking colon cancer tuberculosis colitis

陳宗蔚[1]　張雅媛[2]
[1]台北市立聯合醫院仁愛院區內科部　[2]臺北市立聯合醫院仁愛院區內科部感染科

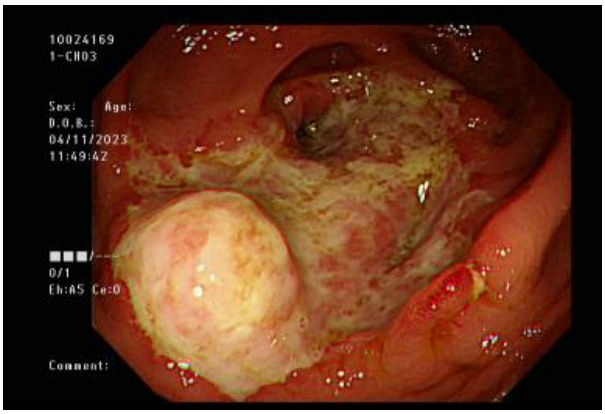
Introduction

Extrapulmonary tuberculosis (TB) accounted for 10.3% of registered tuberculosis cases in Taiwan[1]. Gastrointestinal TB accounts for 5% of all extrapulmonary tuberculosis cases[2]. Here we reported an immunocompetent case of cecal TB initially presented with positive stool occult blood and mimicking colon cancer.

Case presentation

This is a 65-year-old man without significant past medical history. During regular health checkup, stool occult blood test was positive. He denied weight change, bowel habits change, black or bloody stools, poor intake, and abdominal pain but he found slender-shape stool these weeks. He visited hospital first, where colonoscopy and abdominal computed tomography (CT) were performed. Cecal cancer was suspected but the biopsy showed no malignancy. He visited our hospital for second opinion. Colonoscopy revealed one over 4cm ulcerative lesion at cecum, covered with yellow-whitish mucus, with ileocecal valve invasion status post biopsy (Fig. 1). The pathological report of biopsy disclosed granulomatous inflammation with ulceration and the presence of acid-fast positive bacilli. Therefore, we checked human immunodeficiency virus (HIV), CEA, amoebic hemagglutination, blood cytomegalovirus *polymerase chain reaction* (PCR), serum hepatitis A, B and C markers, chest X-ray, and three sets of sputum/stool acid fast stain and tuberculosis culture, which were all within normal limits except for one set *Mycobacterium kansasii in* sputum sample and one set *M. tuberculosis complex* in stool sample (fully drug sensitive). Two months of HERZ (isoniazid, ethambutol, rifampin, pyrazinamide) and four months rifampin and isoniazid therapy were prescribed.

Fig.1 The picture of colonoscopy, one over 4cm ulcerative lesion at cecum, covered with yellow-whitish mucus, with ileocecal valve invasion.



Discussion

The diagnosis of extrapulmonary TB can be challenging. The most common site of intestinal TB was terminal ileum and cecum.[3] Biopsy was often required to establish the diagnosis. Stool tuberculosis culture can also identify mycobacterium TB. This intestinal tuberculosis case is hypertrophic presentation and presents as mass and atypical infection but without pulmonary TB.

Conclusion

Intestinal TB can mimic malignant tumor clinically. Biopsy specimens should be sent for acid-fast stain smear, mycobacterial culture and/or PCR to establish the diagnosis. Diagnosing intestinal TB is a challenge for clinicians in patients with normal immunity who do not have respiratory symptoms, pulmonary manifestations, gastrointestinal symptoms, or pulmonary manifestations.

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病例報告　112_C 26

中藥導致的藥物所引起之肝臟損傷

Traditional chinese medication related drug induced liver injury

陳弘恩[1]　林柏任[2]
[1]臺北市立聯合醫院仁愛院區內科部　[2]聯合醫院仁愛院區消化內科

Introduction

The definition of drug-induced liver injury is impaired liver function caused by drugs, herbs, traditional Chinese medicine, or other toxic substances. It is a common cause of acute liver failure. The clinical diagnosis of DILI is a significant challenge due to the wide variety of drugs or toxins that can potentially cause it, and the fact that common drugs or toxins may vary in different regions. Therefore, there are many studies and case reports documenting the drugs or toxins that may commonly cause DILI in specific countries or regions. This is beneficial for early detection and diagnosis of DILI in patients. Early diagnosis of DILI and discontinuation of the potentially offending drug is associated with better prognosis for patients.

Case presentation

A 47-year-old male with the underlying disease of HBV carriear, HIV infection and allergic rhinitis. According to the patient's statememt, He was just came back from Philipines on 112/1/21. At Philpines on about first week, he was found he had fever with chillness and poor appetite, general weakness since then. The patient said may contact to dirty water but refused contact to animal or "drugs". After back to Taiwan, the symptoms peresist and progressive poor appetite, tea color urine, itch for 2 months. There was no fever, no obvious epigastric pain(dyspepsia only), Upper respiratory symptoms, TOCC of COVID-19, skin rashes, ulcer, mouth ulcer, dry mouth. Due to the symptoms mentioned above, he was went to our hospital. At there, CT were arranged and showed > Mild transient hepatic attenuation difference in the liver. > Gallstones. ERCP also done and showed no dilated or stricture of bile duct. Lab data also obtain found HBV viral load undective, ANA(-), anti-mitochonrdia (-), anti-smooth muscle (-), Ferritin were low. However, the symtoms did not improved. Under the impression of direct type hyperbillirubinemia, cause to be determined, the patient was admitted for further evaluation and treatment. After admitted to our ward, we keep empirical ceftriaxone + doxycycline + Famciclovir treatment. We also give Urso and silymarin for hyperbilirubinemia. We will follow lab data afterward but only found ANA (+), HAV-IgM negative. Other were unremarkable. MRCP were done on 3/6 and showed 1. Fatty liver 2. Collapsed gallbladder with thickening wall. Suspect chronic cholecystitis. Hence, we arrange Liver biopsy on 3/7 and showed chronic hepatitis with marked cholestasis, bridging fibrosis and mild inflammatory activity. Due to billirubin slowly decrease, after discussed with patient, he preferred follow at OPD.

Discussion

Diagnosing DILI is difficult as there are no specific biomarkers or histologic features that identify a drug as the cause of hepatic injury.[2] There have been suggestions to use biomarkers in high-risk patients, including microRNA 122, which is a specific marker of DILI.[1,32] In our cases, biomarkers were not used; instead, the causality was objectively

defined through the RUCAM/CIOMS score and Naranjo algorithm.

Conclusion

The drugs and toxins responsible for DILI can vary significantly based on the common medications used by the population in different regions. Familiarity with commonly used drugs in various regions is of great help in diagnosis and treatment. In Asian regions, the use of traditional Chinese medicine is an important consideration when assessing potential causes of DILI. This case report highlights a traditional Chinese medicine that may be a potential cause of DILI, providing valuable reference for future clinical diagnosis by physicians.

病例報告　112_C 27

壞疽性膿皰發生於愛滋病感染者正接受瀰漫性大 B 細胞淋巴瘤化學治療中

Ecthyma gangrenosum in a patient with human immunodeficiency virus infection and undergoing chemotherapy for diffuse large B cell lymphoma

陳映歡[1] 鄭企峰[2] 張雅媛[3]
台北市立聯合醫院仁愛院區 [1]一般內科 [2]內科部血液腫瘤科 [3]內科部感染科

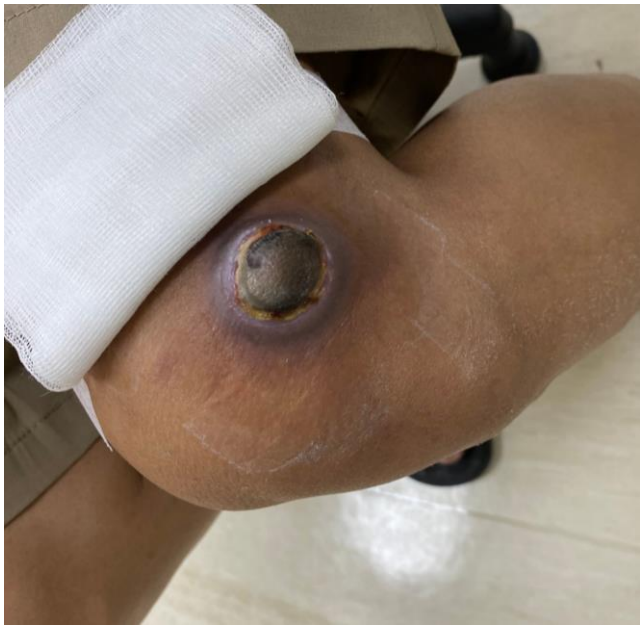
Introduction

Ecthyma gangrenosum (EG) is a rare skin lesion which commonly caused by fulminant *Pseudomonas aeruginosa* related bacteremia and occurs in immunocompromised patients. *P. aeruginosa* can be involved in general skin and soft tissue infections, and the general treatment should aggressive surgical debridement of necrotic tissue. We reported a patient with human immunodeficiency virus (HIV) infection with acquired immunodeficiency syndrome (AIDS) status who developed atypical skin manifestations while undergoing chemotherapy for diffuse large B cell lymphoma (DLBCL).

Case presentation

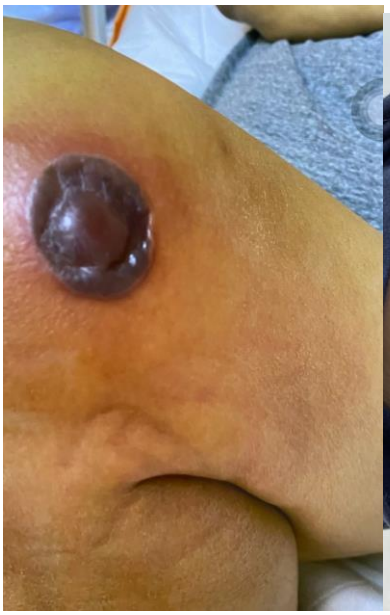
A 44-year-old male had the medical history of ankylosing spondylitis but loss follow-up. This time, he was admitted due to one bulky tumor mass up to 14cm over left axillary for two months. DLBCL (Lugano stage IV, with dural involvement) and HIV were newly diagnosed with AIDS status (HIV viral load 426,000 copies/ml, CD4 count 27.0/uL). He received combination antiretroviral therapy (Bictegravir + Emtricitabine + Tenofovir Alafenamide) for HIV treatment and chemotherapy with EPOCH-R 2 cycles and had adverse effects grade 4 of neutropenia. Then, multiple protruding dark color granulation tissue were noted over left lateral knee (3.0x2.5cm, picture 1), lower abdomen (4.0x1.5cm), right flank (5.0c2.0cm), and right hip (2.5x2.0cm). We arranged wound debridement and the wound culture report revealed *P. aeruginosa* (all sensitive to anti-pseudomonas antibiotics). The lesions pathology showed all necrotizing inflammation (soft tissue with extensive necrosis, dense neutrophilic and lymphoplasmocytic infiltrate). We tracked back about his skin manifestation at home before admission, and the lesion of EC was typical finding with painless red bullae by previous photos (picture 2). Antibiotic treatment with ceftazidime was given for 7 days. After discharge 3 days later, one eschar in the center surrounded by rapid progressed erythema was noted over his left scapular (picture 3) with neutropenic fever, and the wound pus culture isolated *Pseudomonas aeruginosa* again and *Serratia marcescens*. Heart echo showed no infective vegetation. Treatment with antibiotics of cefepime for 5 days and oral form ciprofloxacin for 4 days were prescribed.

Picture 1

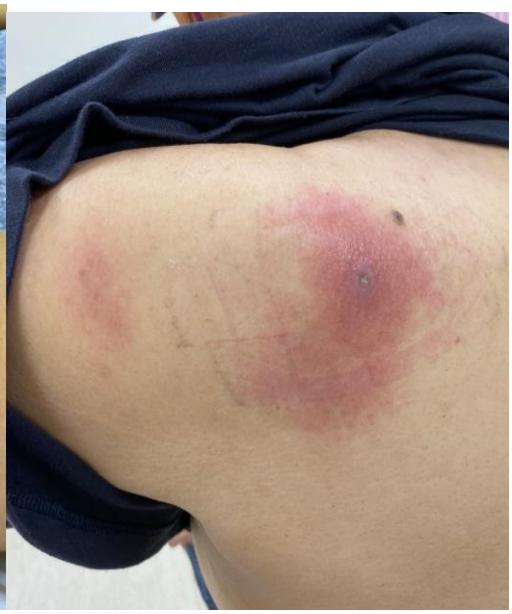


Discussion

Picture 2



Picture 3



The EC results from bacterial invasion of the media and adventitia of blood vessels with secondary ischemic necrosis. It is characterized by initial red macules or bullae which progresses to gangrenous ulcers in the center surrounded with erythematous borders. It is usually caused by *P. aeruginosa*, however, it can also be caused by systemic infection with bacterial pathogens (*Aeromonas* spp, *Citrobacter* spp, *Escherichia coli, methicillin-resistant S. aureus, Streptococcus pyogenes*) as well as fungi (*Candida* spp, *Fusarium* spp). Antipseudomonal antibiotics should be considered when treat EC, and surgery for necrotic lesions or abscesses is often need. Culture of wound exudates/tissue and blood is important given for specific microbial diagnosis. Soft tissue infection due to *P. aeruginosa* will be often fulminant and rapid progression and also associated with poor outcomes than other pathogens.

Conclusion

We reported one patient who conformed *P. aeruginosa* related EC, and he had severe immunocompromised status due *naïve* HIV under AIDS and chemotherapy for treat of DLBLC. We require attention not only to *P. aeruginosa* bacteremia during neutropenic fever, but also to atypical EC skin manifestations.

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病例報告　112_C 28

地舒單抗相關低血鈣發生在肺癌病患之案例報告

Severe hypocalcemia after denosumab administration in two patients with lung cancer

解弘宇[1] 董睿哲[1] 王喬弘[2] 楊文萍[3]
台北市立聯合醫院仁愛院區 [1]一般內科 [2]胸腔內科 [3]新陳代謝科

Introduction

Lung cancer is the second most common cancer worldwide in 2020. Skeletal-related events (SREs) like pathologic fracture or spinal cord compression are commonly seen in metastatic lung cancer. Denosumab, a monoclonal antibody, which binds to RANKL and hinders it from activating osteoclasts, inhibited bone resorption in bone metastasis from solid tumors and reduced bone turnover and destruction. However, there is an increased risk of life-threatening denosumab-induced hypocalcemia. Here we present 2 cases with severe hypocalcemia, which was induced by denosumab.

Cases presentation

Case 1

A 72-year-old man with bone metastasis in spine, sternum, and bilateral ribs from stage IV lung cancer, who was referred to our hospital for hoarseness, general weakness, and poor appetite. Due to severe low back pain secondary to osteolytic lesions, the patient received denosumab 120mg on 8th February and 22thMarch, 2021 respectively. On presentation on 26thMarch, serum calcium was found to be severely low at 5.8mg/dL(normal range 8.1~10.4 mg/dl) . His initial serum calcium level prior to denosumab was normal but 25-OH-D was 9.9 ng/ml (normal range >30 ng/ml). He received an infusion of calcium carbonate followed by the continuous intravenous administration of calcium, and oral vitamin D supplement after which his hypocalcemia persisted for at least 8 weeks. Additional laboratory workup was significant for hyperparathyroidism, hypothyroidism and high alkaline phosphatase. We hypothesize that the patients' history of low vitamin D, low activity and long half- life of denosumab were responsible for the duration and severity of hypocalcemia.

Case 2

A 73-year-old man with bone metastasis over left rib and T-spine from stage IV lung cancer, who was hospitalized to be evaluated and treated for dyspnea and left sided sharp chest pain when cough. Denosumab 120mg was prescribed on 8th June, 2021 for left rib metastasis.
On presentation on 25thJune, serum calcium was found to be severely low at 5.8mg/dL(serum calcium level prior to denosumab was 9.4mg/dL). No muscle cramp, no Chvostek sign was noted. QTc interval mildly prolonged to 488ms. Intravenous infusion of calcium gluconate, oral calcitriol and vitamin D3 were administered. Calcium level recovered to normal range after one week supplement.

Discussion

Bone metastases are common in lung cancer and should be treated with bone-targeted agents before debilitating complications. Denosumab was showed to be benefit on overall survival in those patients. However studies have showed denosumab has a higher risk of severe life-threatening hypocalcemia. The maximum serum drug level of denosumab reaches 7-21 days

after administration. In our cases, the first patient received two doses of denosumab with the latter one only 3 days before hypocalcemia was noted, therefore caused prolonged hypocalcemia to 8 weeks despite supplement. In the other hand, the second patient received only one dose three weeks before hypocalcemia was detected, so his duration of hypocalcemia just lasted for one week.
High bone turnover markers, hyperparathyroidism, low vitamin D and low body weight and decrease activity may be risk factors for severe hypocalcemia.

Conclusion

SREs like pathologic fractures, spinal cord compression, and bone pain are common in metastatic lung cancer. Denosumab is a bone-protective agent used for prevention of SREs in lung cancer. Denosumab can cause hypocalcemia within one week to one month of its administration and may require hospital admission. Patients receiving denosumab should be on calcium and vitamin D supplementation with dosing adjustments based on laboratory parameters.

病例報告　112_C 29

IgG4 相關性甲狀腺疾病

IgG4-related disease of the thyroid gland: a rare case report

林泰宇[1] 江泰平[2] 張廷安[3] 許智堯[4] 楊文萍[4]
台北市立聯合醫院仁愛院區 [1]一般內科 [2]一般外科 [3]病理科 [4]內分泌與新陳代謝科

Introduction

Immunoglobulin G4 (IgG4)-related disease is a new spectrum of diseases involving multiple organ systems, including pancreas, liver, salivary gland and thyroid. IgG4-related thyroid disease had four subcategories, IgG4-related Hashimoto's thyroiditis, fibrosing variant of Hashimoto's thyroiditis (HT), Riedel's thyroiditis and Graves disease with elevated IgG4 levels. Due to characterized as rapidly enlarged nodule, IgG4-related thyroid disease might be diagnosis as malignancy or infection at first.
We present a case with IgG4-related Hashimoto's thyroiditis.

Case presentation

A 65-year-old woman was referred to our facility because of exponential increase of the thyroid gland. Her thyroid function was under euthyroid status, with serum TSH level 3.63 uIU/ml (normal range 0.27~4.2 uIU/ml) and free T4 1.28 ng/dl(normal range 0.93~1.7 ng/dl). However serum autoantibody were high with anti-TPO 3730 U/ml (normal range <115 U/ml) and thyroglobulin antibody >4000 U/ml (normal range <34 U/ml). Because her thyroid gland constantly increase in size and hardness, we performed thyroid echo for her. Thyroid echo showed bilateral hypoechoic and hypovascular lesions. Fine-needle aspiration was performed, and the smear consisted of lymphocytes infiltration. The Bethesda category was III: Atypia of undetermined significance.
The patient received right total and left subtotal thyroidectomy. Histology showed dense lymphoplasmocytic infiltration, accompanying with predominantly interfollicular fibrosis. Immunostain revealed predominance of IgG4-secreting plasma cells. IgG4-related Hashimoto thyroiditis was diagnosis. Primary hypothyroidism was found after surgery, and the patient received Eltroxin(L-Thyroxine) 100mcg per day since then.

Discussion

IgG4-related disease(IgG4-RD) was a rare immune-mediated fibroinflammatory condition affecting multiple organ systems, including the pancreas, salivary gland, lacrimal gland, lung, kidney, pituitary, thyroid, bile duct, peritoneum, and aorta. In Japan, the estimated prevalence is about 0.28 to 1.08 per 100,000 of population. Common manifestations were subacute development of a mass in the affected organ, lymphadenopathy and weight loss.
IgG4-related thyroid disease(IgG4-RTD) is a distinct subtype of IgG4-RD characterized by positive circulating thyroid antibodies and a high rate of hypothyroidism. Classification of IgG4-RTD had four groups: IgG4-related Hashimoto's thyroiditis, fibrosing variant of Hashimoto's thyroiditis, Riedel's thyroiditis and Graves disease with elevated IgG4 levels. Overlapping among these groups has been observed. Diagnostic criteria for IgG4-RTD are comprised of the following five items: I) enlargement of the thyroid, II) hypoechoic lesions in the thyroid by ultrasonography, III) elevated serum IgG4 levels, IV) histopathological findings

in the thyroid lesion (IgG4+ plasma cells >20/HPF and IgG4+/IgG+ plasma cell ratio >30%) and V) involvement of other organs. There is no standard treatment for IgG4-RTD. Glucocorticoid could be first line treatment choice, and tamoxifen or rituximab could be used in patients who fail to respond to glucocorticoid. Total thyroidectomy could provide quickly relieving the symptoms and avoid long-term adverse drug effect of immunotherapy.
In our case, only neck mass was found without significant other organ involvement. Fine-needle aspiration exam only provided limited results. Due to malignancy risk was about 5% to 15%, surgical intervention was arranged to rule out malignancy. IgG4-related Hashimoto's thyroiditis was diagnosis afterwards.

Conclusion

IgG4-related thyroid disease was a rare disease and could be easily treated as malignancy at first.
Only a small portion of patients with HT with high titers of anti-thyroid anti-bodies may overlap the IgG4-related thyroiditis. Diagnosis often was made after surgical resection and biopsy .

病例報告　112_C 30

一位思覺失調症合併嚴重低血鈉患者案例報告

A schizophrenia patient with psychogenic polydipsia complicated to severe hyponatremia

許峻維[1] 徐永勳[2]
台北市立聯合醫院仁愛院區 [1]一般內科 [2]腎臟科

Introduction

Hyponatremia was defined as serum sodium concentration lower than 135 mEq/L. It was a common electrolytes imbalance and may cause serious and even life-threating conditions. The causes of hyponatremia was variable and pose a great challenge in diagnosis and management.

Case presentation

A 49-year-old man had medical diseases as hypertension, type 2 diabetes mellitus, and schizophrenia. He presented to our emergency department due to a falling down episode at home with head contusion to a table corner without initial loss of consciousness. At ED, there was a 4cm scalp laceration wound with active bleeding, and then suture for wound closure was performed. However, a sudden onset of generalized tonic-clonic seizure attacked during the procedure and followed by apnea with cardiac arrest. Cardiopulmonary resuscitation was initiated immediately and then ROSC in 5 minutes later. On physical examination, there was pitting edema over bilateral lower extremities. The laboratory study revealed mild leukocytosis , severe hyponatremia (Na=102 mEq/L) and normal renal function (serum creatinine level = 0.8 mg/dL). The whole body computed tomography scan without contrast media showed no obvious intracerebral hemorrhage or brain edema. There were some focal consolidations at right middle and lower lobe which was suggestive of pneumonia. Detailed history taking from his brother, the patient had uncontrolled urge to drink a large amount of bottled tea beverage which might exceed 10 liters of per day. Besides, he also took Escitalopram which was a kind of selective serotonin reuptake inhibitors due to schizophrenia. 3% saline infusion was administered due to symptomatic hyponatremia, and we also gave 5% dextrose water as well as desmopressin for prevention of osmotic demyelination syndrome. Meanwhile, his urine chemistry data showed Osmolarity= 115 Osm/L, Na =6 mEq/L and K = 38.1 mEq/L while serum sodium level increased from 102 to 107 mEq/day in one day. Under close monitor, his serum sodium level was increased to normal range with clear consciousness.

Discussion

An accurate diagnosis of the etiology of hyponatremia is the key point because it determines how we manage this disorder. Intially, we should exclude the pseudohyponatremia such as hyperglycemia or hyperlipidemia. The ECF volume status should be evaluated clinically and obtained urine electrolytes excretion data could allow physician to initiate the treatment. Review of the drug history is also important. There are some common medication which may induce hyponatremia such as thiazide diuretics, SSRIs, NSAIDs and etc. Once the patient had symptomatic hyponatremia which often developed once serum sodium concentration was below 120 mEq/L, we should use 3% saline for rapid correction. The diagnosis could not always be accurate intially, and hence we should closely monitor the patient's serum sodium

level and beware of excessively rapid correction which may cause severe neurological complication due to osmotic demyelination. In our case, the patient had compulsive water drinking due to underlying schizophrenia. This history strongly implied that his hyponatremia was attributed to psychogenic polydipsia. He also had polyuria and the appearance of urine seemed just like water. The urine chemistry data showed osmolarity = 115 Osm/L. Typically urine osmolarity should be below 100 Osm/L in primary polydipsia, hence this data suggested his hyponatremia may be partially due to Escitalopram (SSRIs) which may induce ADH secretion.

Conclusion

Hyponatremia is a common eletrolyte disorder but could lead to morbidity and mortality. There are various causes of hyponatremia and thus the therapy should be based mainly on possible underlying etiology. Closely monitoring serum sodium level is very important because too rapid correction or wrong direction of treatment may induce severe neurological complications and even death.

病例報告　112_C 31

新冠肺炎誘發急性呼吸窘迫症候群併頑固性高碳酸血症經恩慈間質幹細胞治療後康復個案

Recovery of a Case with COVID-19 from Severe Acute Respiratory Disease Syndrome with Refractory Hypercapnia Following Compassionate Mesenchymal Stem Cell Therapy

汪揚[1] 林賢君[1,2] 王婕妤[1] 李枝新[1,2] 歐聰億[1,3]

[1]臺北市立萬芳醫院醫院內科部 [2]臺北市立萬芳醫院醫院內科部胸腔內科 [3]臺北市立萬芳醫院醫院內科部感染科

Introduction

COVID-19 is a pandemic caused by the infection of acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clinical presentations of patients with COVID-19 varied widely from minimal upper respiratory symptoms to ARDS and multiple organ failures[1]. Although the Omicron variants are considered less virulent than the Delta and other ancestor variants, the cumulative deaths in the Omicron pandemic exceeded the Delta wave[2]. For vulnerable populations confronting the virus tsunami, the threat of lethal cytokine-releasing syndrome due to severe COVID-19 never wanes. Herein, we share our experience of a patient with COVID-19-associated ARDS who successfully weaned from prolonged mechanical ventilatory support due to refractory hypercapnia after the treatment of compassionate mesenchymal stem cell (MSC) therapy.

Case presentation

A 72-year-old man visited the emergency department due to diarrhea, general malaise, anorexia, and a persistent fever for four days. He had the underlying diseases of hypertension, diabetes mellitus, and obstructive sleep apnea with regular medical treatment. A positive severe acute respiratory syndrome coronavirus 2 reverse transcription-polymerase chain reaction test and low saturation of peripheral oxygen (SpO2 92%) were recorded, and he was hospitalized. D-dimer (1.1 mg/L fibrinogen equivalent unit) and fibrinogen (653 mg/dL) were slightly increased, while the fibrin degradation products were undetectable (<4 ug/mL). He developed hypoxemic respiratory failure and was supported with mechanical ventilation on the first day of admission. Dexamethasone, Remdesivir, tocilizumab, levofloxacin, enoxaparin, and ertapenem were administered. He deliberately removed the endotracheal tube himself on the fourth day and was re-intubated two days later as the ARDS deteriorated. His oxygenation improved partially with a lung protective strategy using a high positive end-expiratory pressure of 12 cmH2O. Still, he remained ventilator-dependent due to progressive hypercapnia despite excessively large minute ventilation applied (Table 1). An episode of Candida glabrata septicemia ensued on the 28th day of admission and was successfully treated with anidulafungin. Decreased fibrinogen (145 mg/dL) was accompanied by elevated FDP (52.7 ug/mL) and D-dimer (14.5 mg/L fibrinogen equivalent unit), indicating a dysregulated coagulation activation. Due to refractory hypercapnia, compassionate MSC therapy, which consisted of 10^6 cells/kg of allogeneic umbilical cord blood-derived MSC for each intravenous infusion, was administered on the 30th, 33rd, 40th, 43rd, 50th, and 53rd days of hospitalization. Hypercapnia resolved gradually, along with improved fibrinogen, fibrin degradation products, and D-dimer levels. He was successfully weaned from mechanical ventilation on the 60th day. After being discharged, he underwent rehabilitation, and no

residual exercise limitation was observed after a year.

Table 1. Respiratory parameters of a 71-year-old man with COVID-19-associated acute respiratory distress syndrome who suffered from difficult-to-wean due to refractory hypercapnia.

Time (day)	7	21	35	49	60
VT (mL/kg)	8.8	6.46	5.1	5.5	7.7
MV (L/min)	7.8	12.2	10.3	8.7	6.5
$PaCO_2$ (mmHg)	41.6	105.0	84.5	49.1	36.6
PaO_2 (mmHg)	64.0	119.4	91.9	67.3	109.2
PEEP (cmH_2O)	12	10	10	8	8
FiO_2 (%)	85	65	40	30	30
Fibrinogen (mg/dL)	206	145	284	268	465
FDP (ug/mL)	29.2	52.7	11.6	<4.0	<4.0
D-dimer (mg/L FEU)	8.7	14.5	3.42	1.6	0.9

MSC, mesenchymal stem cell; VT, tidal volume; MV, minute ventilation; PaCO2, arterial partial pressure of carbon-dioxide; PaO2, arterial partial pressure of oxygen; PEEP, positive end-expiratory pressure; FiO2, inspired fraction of oxygen; FDP, fibrin degradation products; FEU, fibrinogen equivalent unit.

Discussion

A growing body of preclinical evidence suggested that MSC holds substantial therapeutic promise for various inflammatory disorders. The MSC had been considered a potential therapeutic method for ARDS before and during the COVID-19 pandemic. In acute lung injury, the MSC modifies critical pathobiological pathways in ARDS through paracrine and physical interactions to improve alveolar fluid clearance, enhance the phagocytotic activity of phagocytic cells, suppress platelet hyperactivity, and exert anti-apoptotic effects on host cells[3]. The MSC therapy was noted to improve survival and shorten the time to recovery in some published randomized controlled trials and meta-analyses[4,5]. On the contrary, there were few studies limited to MSC treatment in patients with hypercapnic respiratory failure.

Hypercapnia was not uncommon in patients with COVID-19-associated ARDS. Tsonas and colleagues reported that over half of the COVID-19 patients requiring invasive ventilatory support had $PaCO_2$ over 45mmHg[6]. The possible mechanisms for hypercapnia included the widely accepted ventilator protective strategy using low tidal volume, which inevitably increases the fraction of dead space ventilation for patients with ARDS[6]. Patients with higher body mass index, a history of chronic obstructive pulmonary disease, extensive lung injury, and thromboembolism of pulmonary vasculature may aggravate the risk of hypercapnia[6]. Patients with hypercapnia tended to require longer mechanical ventilation, intensive care unit stay, and length of hospitalization[6]. With augmented platelet hyperactivity, ARDS in patients with COVID-19 is characterized by micro-thromboembolism in the pulmonary vascular bed, which leads to increased dead-space ventilation more than in non-COVID-19 ARDS[7]. As manifested in our case, the inhibitory effect of MSC on platelet activation and aggregation may counteract the dysregulation of the coagulation cascade and accelerate the repairment of pulmonary microvasculature to ameliorate the refractory hypercapnia[8].

Conclusion

Although the mechanisms of MSC treatment in patients with hypercapnic respiratory failure

are yet to be disclosed, growing evidence has shown promising therapeutic effects of MSC therapy in COVID-19-associated ARDS.

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病例報告　112_C 32

神經性梅毒併發縱向廣泛橫貫性脊髓炎

Neurosyphilis with longitudinally extensive transverse myelitis

陳建良[1,4] 洪東源[2] 何宗翰[3] 汪靖勛[1]

[1]三軍總醫院內科部感染科 [2]三軍總醫院神經外科部 [3]三軍總醫院神經科部 [4]國軍高雄總醫院左營分院內科部

Introduction

Longitudinally Extensive Transverse Myelitis (LETM) is a rare but severe neurological disorder characterized by inflammation spanning three or more vertebral segments of the spinal cord. While LETM is commonly associated with autoimmune conditions such as neuromyelitis optica and multiple sclerosis, infectious etiologies are less frequently considered. Neurosyphilis, could be presented at any stage of syphilis infection[1] affecting the central nervous system, has been implicated in a variety of neurological complications but is seldom reported as a cause of LETM. The intersection of neurosyphilis and LETM presents a unique diagnostic and therapeutic challenge, given the rarity of this association and the potential for irreversible neurological damage if not promptly identified and treated. Here we present a case with initial diagnosis of LETM and further found to be infected with syphilis.

Case presentation

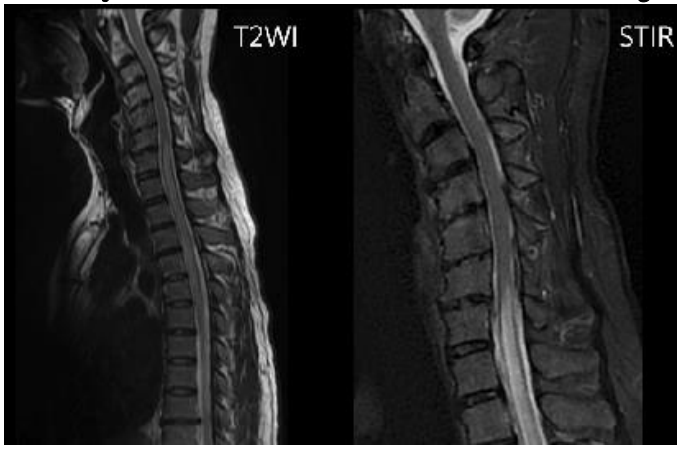
A 56-year-old male with no history of systemic disease was referred to our institution for surgical evaluation of lower extremity weakness persisting for one week. He had previously been diagnosed with L5-S1 spondylolisthesis and cauda equina syndrome at another hospital three days prior. Upon admission, his vital signs were as follows: body temperature 36.8°C, blood pressure 145/90 mmHg, respiratory rate 18/min, and pulse rate 92/min.

Neurological examination revealed intact consciousness, muscle strength graded as 5/5 in both arms and 4/5 in both legs. Deep tendon reflexes were normal in the upper extremities but hyperactive in the knees and ankles. Decreased anal tone and paresthesia with a sensory level at T1 were noted. Laboratory tests showed normal white blood cell count and C-reactive protein levels. Cervical spine MRI demonstrated long-segment high signal intensity at C6-T7 levels on T2WI and STIR images[figure 1], suggestive of demyelination or transverse myelitis.

The patient was initiated on intravenous methylprednisolone for a presumptive diagnosis of longitudinally extensive transverse myelitis. Lumbar puncture revealed a CSF glucose level of 77 mg/dL, total protein 66 mg/dL, and white blood cell count of 85/uL with 86% lymphocyte predominance. Microbiological stains were negative. Subsequent CSF RPR and VDRL tests yielded titers of 1:4096 and 1:1, respectively.

The patient was then treated with intravenous ceftriaxone (2g/day) for 14 days. Serum RPR titer was 1:128, confirmed by a treponemal chemiluminescence immunoassay

Figure 1 Cervical spine MRI in the emergent department demonstrated long-segment high signal intensity at C6-T7 levels on T2WI and STIR images



with an index of 62.3 (normal < 0.9). Adjunctive therapies included 10 sessions of hyperbaric oxygen therapy and five sessions of plasma exchange. A second lumbar puncture was conducted on the 20th day, revealing a non-reactive CSF VDRL. The patient was discharged on the 42nd day, showing improved muscle strength in the lower extremities and resolved paresthesia.

Discussion

The patient's initial presentation was complicated by a prior diagnosis of L5-S1 spondylolisthesis and cauda equina syndrome, which could have potentially masked the underlying etiology. However, the absence of systemic symptoms, normal inflammatory markers, and specific MRI findings prompted further investigation.

The CSF VDRL has been considered the gold standard for diagnosing neurosyphilis. Compared to VDRL, the CSF RPR assay is less sensitive[2]. The USA CDC Guidelines include only the CSF fluorescent treponemal antibody (FTA) test and the CSF Treponema pallidum particle agglutination (TPPA) assay as approved CSF treponemal tests. However, the sensitivity of treponemal tests in cerebrospinal fluid (CSF) is elevated owing to increased intrathecal production. However, the specificity is compromised due to potential spillover from systemic circulation[3,4]. In our patient, the high titers in both CSF RPR and VDRL tests were pivotal in confirming neurosyphilis as the underlying cause of LETM.

The first-line treatment for neurosyphilis is intravenous aqueous crystalline penicillin G, administered at 18–24 million units per day for 10-14 days. Alternative options include intramuscular procaine penicillin G at 2.4 million units once daily plus probenecid, or ceftriaxone at 1–2 g intravenously or intramuscularly daily for 10–14 days. Given that penicillin G was not available at our hospital, ceftriaxone emerged as the best alternative, ultimately resulting in a favorable prognosis.

Conclusion

This case sheds light on the rare occurrence of longitudinally extensive transverse myelitis (LETM) secondary to neurosyphilis. While LETM is often associated with autoimmune conditions, the case emphasizes the importance of considering less common infectious etiologies like syphilis. The patient's initial presentation was complicated by a prior diagnosis of L5-S1 spondylolisthesis and cauda equina syndrome, which could have masked the true cause. Elevated CSF RPR and VDRL titers confirmed neurosyphilis as the underlying issue. Due to the absence of first-line penicillin G, intravenous ceftriaxone emerged as an alternative option, resulting in a favorable prognosis for our patient. This case serves as a vital reminder for clinicians to include neurosyphilis in the differential diagnosis of LETM and highlights the value of a multidisciplinary approach for effective management.

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病例報告　112_C 33

瀰漫性膿瘍分枝桿菌乳突炎併中樞神經感染案例

Disseminated *Mycobacterium abscessus* Infection in A Woman

林敬堯[1] 湯其暾[2] 陳信傑[3] 趙載光[4] 陳燕麟[4] 王永志[5]
[1]三軍總醫院內科部 [2]三軍總醫院神經外科部 [3]三軍總醫院耳鼻喉頭頸外科部 [4]三軍總醫院病理部，
[5]三軍總醫院內科部感染及熱帶醫學科

Introduction

Nontuberculous mycobacteria (NTM) are microorganisms that can be found in both natural and man-made environments, such as soil, dust, lake water, tap water, food, and animals. Besides, NTM can endure exposure to a wide range of deleterious substances, such as antibiotics, antiseptics, biocides, sterilizing agents, and disinfectants, even resistance to chlorine. NTM infections, though uncommon, present diagnostic and therapeutic challenges. NTM-related otomastoiditis, particularly progressing to brain abscess, remains a rare but increasingly recognized entity. Current diagnostic criteria for NTM pulmonary infections do not readily apply to such cases, and the diagnostic process is often hindered by the slow growth of mycobacteria and potential contamination.

Case Presentation

The 66-year-old Taiwanese woman who denied any history began with a seemingly benign ear condition characterized by persistent ear discharge, a consequence of swimming pool exposure three months earlier. However, as time progressed, she experienced a decline in her left-sided hearing capacity and intermittent headaches. Physical examination raised concerns of left-sided hearing impairment, prompting further evaluation. Neuroimaging, specifically a computed tomography scan, unveiled a substantial soft tissue lesion (4.3 x 2.5 cm) with heterogeneous enhancement, accompanied by soft tissue thickening in the left external auditory canal. Most alarmingly, there were erosive changes and destruction of the left mastoid, occipital bone, and left mandibular fossa of the temporal bone. Additional diagnostic clues emerged from a computed tomography scan of the chest, revealing diffuse nodular opacities across all lung lobes. The patient underwent left modified radical mastoidectomy, tympanoplasty, and brain mass biopsy, ultimately confirming the presence of *Mycobacterium abscessus*. Treatment commenced with a multidrug regimen comprising clarithromycin, tigecycline, and imipenem-cilastatin, tailored to address the *Mycobacterium abscessus* brain abscess, otomastoiditis, and concurrent pulmonary disease. Challenges arose as the patient experienced adverse drug reactions, including acute pancreatitis, lactic acidosis, and infection lesion related hearing loss, prompting surgical intervention to remove the brain abscess. Microscopic examination revealed chronic granulomatous inflammation and multinucleate giant cells. Remarkably, the patient responded well to clarithromycin, low-dose linezolid, and amikacin therapy. Subsequently, treatment transitioned to azithromycin, rifabutin, and bedaquiline due to adverse event by previous multidrug therapy. Currently, follow-up MRI showed no disease progression and mild regression.

Discussion

This case underscores the intricate challenges posed by NTM-related otological infections,

particularly when complicated by intracranial involvement. NTM, ubiquitous microorganisms found in natural and man-made environments, are increasingly recognized for their capacity to cause illness, often affecting the lungs and other body regions. NTM-related otomastoiditis, though rare, has witnessed an uptick in prevalence, with *Mycobacterium abscessus* emerging as a prominent causative agent. Chronic otitis media or recurrent otitis can create an environment conducive to the growth of highly drug-resistant *Mycobacterium abscessus*, capable of forming biofilms and leading to longstanding otomastoiditis that may extend to the meninges and brain. Additionally, routes of infection can include tympanostomy tubes and tympanic membrane perforations. The diagnostic criteria for nontuberculous mycobacterial pulmonary disease primarily rely on radiological findings, microbiological results, and histopathological features. However, these criteria may not always be well-verified, leading to challenges in diagnosing NTM-related otomastoiditis and central nervous system infections. Slow mycobacterial growth and the possibility of contamination further complicate diagnoses. This case, with its atypical presentation featuring chronic granulomatous inflammation and soft tissue fibrosis, exemplifies these diagnostic challenges. In this unique case, guideline-based therapies for NTM infections were initially employed, but the patient experienced several adverse events, including acute pancreatitis and lactic acidosis. As a result, salvage therapy was considered, which involved a combination of bedaquiline, rifabutin, and azithromycin. Previous studies have highlighted the potential benefits of rifabutin and bedaquiline in the treatment of NTM infections. Rifabutin has shown promise in inhibiting the development of inducible macrolide resistance, demonstrating efficacy comparable to the first-line drug clarithromycin. Additionally, when co-administered with clarithromycin, rifabutin has been observed to have a synergistic effect. Furthermore, bedaquiline has proven its effectiveness in reducing the time required for sputum culture conversion and improving treatment outcomes, particularly in cases involving multidrug-resistant M. tuberculosis. These findings underscore the potential utility of these medications in the management of complex NTM infections, where conventional therapies may present challenges.

Conclusions

Managing NTM otological infections, especially when complicated by intracranial extension, remains a formidable clinical task. This case offers essential insights into the evolving landscape of NTM infections, emphasizing the crucial role of heightened clinical awareness, comprehensive diagnostics, and personalized treatment regimens. The multidrug-resistant nature of *Mycobacterium abscessus* necessitates a delicate balance between aggressive pharmacotherapy and the judicious management of adverse drug reactions. Success in this case was achieved through a combination of medical and surgical interventions, showcasing the significance of an interdisciplinary approach for optimizing patient outcomes. As challenges persist in diagnosing and managing NTM otomastoiditis, this unique and illustrative case contributes to our understanding of these complex infections, highlighting the need for ongoing research and clinical exploration in this domain.

病例報告　112_C 34

黏膜許旺氏細胞過誤瘤 – 非常罕見的腸胃道良性病兆

Mucosal Schwann Cell Harmartoma – A very rare benign lesion in the gastrointestinal tract

陳建安[1] 李怡瑩[2]
[1]大安婦幼醫院胃腸肝膽內科 [2]郭綜合醫院病理科

Introduction

Mucosal Schwann cell hamartomas (MSCH) are rare and are considered benign colon polyps. They were first described in 2009 to distinguish them as a distinct group of neuronal polyps primarily composed of S-100–positive Schwann cells. To the best of our knowledge, only 40 cases of MSCH have been reported to date. Herein, we describe a case an asymptomatic female with no prior history of inherited disorders, who was discovered to have a colonic polyp displaying pathological evidence of MSCH.

Case presentation

A 50-year-old woman with no personal or family history of colon cancer, and no known history of familiar adenomatous polyposis, multiple endocrine neoplasia type IIb (MEN IIb), neurofibromatosis type I (NF1), or Cowden syndrome, underwent a colonoscopy as part of the investigation into occult blood in the stool.

A 5 mm sessile polyp without ulceration was identified and removed from the descending colon using cold snare polypectomy method (Fig.1). The microscopic sections showed that the lesion with foci of nodular spindle cell proliferation within the lamina propria (Fig.2a, 2b). Immunostaining results showed strong diffuse staining of spindle cells with S-100 while negative for EMA and CD34 (Fig.3a, 3b, 3c). The polyp was diagnosed as MSCH.

Fig.1 sessile polyp under blue light image (BLI)

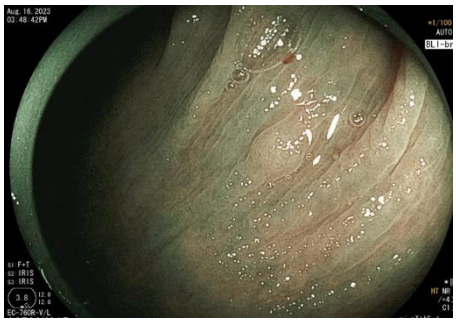


Fig.2a H&E 40x

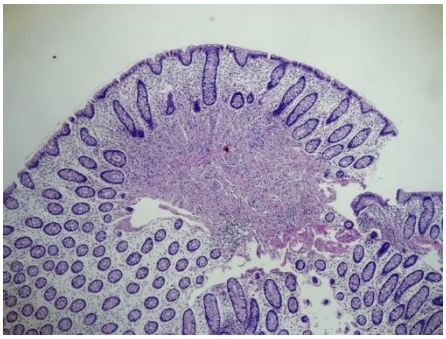


Fig.2b H&E (200x)

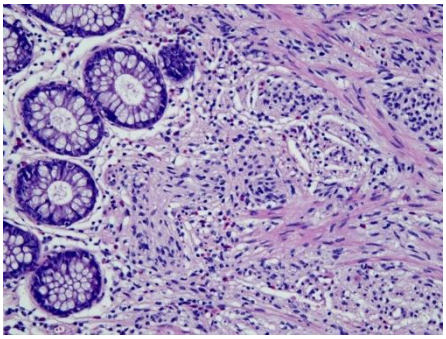


Fig.3a positive for S100 (100x)

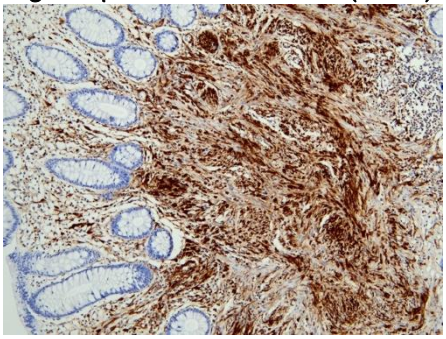


Fig.3b negative for CD34 (100x)

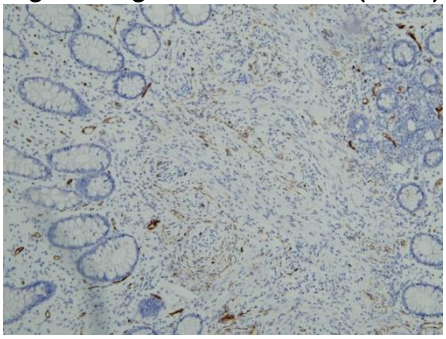
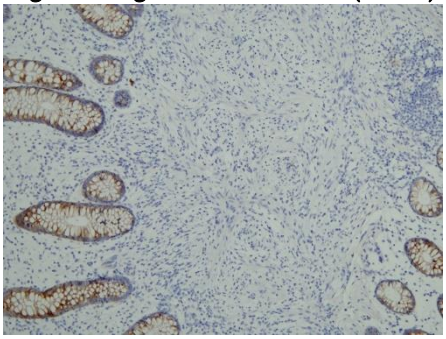


Fig.3c negative for EMA (100x)



Discussion

Benign neurogenic tumors are relatively common in the skin and somatic soft tissues, but they are exceptionally rare within the gastrointestinal tract. MSCHs, first characterized by Gibson and Hornick in 2009, were identified to establish them as a unique category of neuronal polyps primarily consisting of S-100–positive Schwann cells.
Typically, MSCH presents asymptomatically and is often discovered incidentally during routine colonoscopies. MSCH is not currently associated with any inherited disorders. These polyps originate from mesenchymal cells and are most commonly found in the left colon, with the sigmoid colon being the most frequent location in the GI tract. However, they can develop anywhere in the colon, and there has even been a rare case report of an MSCH identified in the stomach. Typically, the mucosa covering MSCHs remains intact, without erosions or ulcerations, and their size ranges from 1 to 8 mm. On average, patients diagnosed with MSCH are typically in their sixth decade of life, with a higher prevalence in females.
Diagnosis relies on histological features and immunohistochemical (IHC) patterns, which reveal spindle cell proliferation without ganglion cells in the lamina propria, with positive staining for S100 and negative staining for EMA.

Conclusion

Given the rarity of this lesion, there is a need for increased awareness and further studies to develop guidelines for its diagnosis, long-term screening, and follow-up.

病例報告　112_C 35

老年人 Henoch-Schönlein 紫斑病之複雜案例

A complex case of Henoch-Schönlein Purpura in an older adult

劉子瑜　羅陽
國泰綜合醫院皮膚科

Introduction

Henoch-Schönlein purpura (HSP) is a rare immunological disorder that primarily affects children but can occasionally manifest in adults, presenting a diagnostic challenge. This systemic vasculitis is characterized by a tetrad of symptoms: palpable purpura, abdominal pain, joint pain, and renal involvement. While often following an upper respiratory infection, its sudden onset in some cases can complicate diagnosis. We present a perplexing case of an 84-year-old woman, whose symptoms initially suggested a urinary tract infection. However, further investigations revealed a more complex and rare underlying condition.

Case Presentation

The 84-year-old woman, previously diagnosed with paroxysmal atrial fibrillation, coronary artery disease, and peripheral arterial occlusive disease, was admitted with a two-day history of intermittent fever and oliguria. Lab data showed leukocytosis (white blood cell count of 12.3 K/μL), a notable decline in renal function (creatinine: 0.7 mg/dL to 2.3 mg/dL), elevated C-reactive protein levels (8.0 mg/dL), and pyuria on urinalysis. Empirical treatment with cefuroxime was initiated, suspecting a urinary tract infection. Despite treatment, the fever persisted, pyuria subsided, and abnormal renal function persisted. Furthermore, purpuric rashes appeared on both legs and buttocks, leading to a dermatology consult. Skin biopsy results revealed vasculitis. Elevated serum immunoglobulin A levels (620 mg/dL) and immunoglobulin A deposition at vessel walls in renal biopsy confirmed the diagnosis of HSP.

Discussion

In this case, several differential diagnoses were considered, including other vasculitides, septicemia, and secondary causes of elevated immunoglobulin A such as liver disease. Thorough evaluation, including skin and renal biopsies, was essential to rule out these possibilities. HSP, although rare in adults, is characterized by immune-mediated vasculitis involving small vessels. Its etiology, often triggered by infections, leads to the deposition of immunoglobulin A immune complexes. Skin involvement, as evident in this case, ranges from purpura to necrotic lesions. Renal manifestations, common in HSP, underline the systemic nature of the disease, emphasizing the need for a comprehensive diagnostic approach.

Conclusion

In summary, HSP, though uncommon in older adults, should be considered in patients with unexplained fever, purpuric rashes, and renal involvement, even in the presence of underlying cardiac and peripheral vascular conditions. Timely and meticulous evaluation, including skin and renal biopsies, is crucial for accurate diagnosis and management. This case emphasizes the significance of a multidisciplinary approach in unraveling complex medical presentations, leading to improved patient outcomes and a deeper understanding of this enigmatic condition.

病例報告　112_C 36

無急性胰臟炎患者表現胰腺性脂膜炎之案例報告

A case of pancreatic panniculitis without acute pancreatitis

劉子瑜　林鳳玲
國泰綜合醫院皮膚科

Introduction

Pancreatic panniculitis often develops on the patient with pancreatitis, who present inflammation of adipose tissue. This article delves into a perplexing case involving a 40-year-old man who presented with multiple purpuric dermal plaques and papules on his lower legs. Despite lacking classic pancreatic symptoms, his condition led to a fascinating discovery of pancreatic panniculitis, a rare cutaneous manifestation without acute pancreatitis.

Case Presentation

This is a 40-year-old man, who is an alcoholism, with a history of Child C alcoholic liver cirrhosis and Hepatitis B carrier. He presented with multiple purpuric papules and plaques on his lower legs, accompanied by tenderness for several days. Notably, there was no fever, but his medical history, particularly his liver-related issues, raised concerns about underlying complications. Laboratory investigations revealed impaired renal function and abnormal liver enzymes. A skin biopsy to lower leg purpura was conducted. The pathology report revealed subcutaneous deposition of basophilia, calcification, necrotic fat, and epithelioid histiocytes, which were consistent with pancreatic panniculitis. It is a rare cutaneous manifestation of pancreatic disorders. Intriguingly, the diagnosis was complicated by the presence of "nonpancreatic pancreatic panniculitis," where pancreatic enzymes were released without evident pancreatic pathology.

Discussion

The differential diagnosis in this case included vasculitis, vasculopathy, pancreatic panniculitis, and invasive fungal infection. Vasculitis, characterized by blood vessel inflammation, usually presents with elevated inflammatory markers and specific autoantibodies. Vasculopathy, on the other hand, denotes vessel diseases without inflammation, requiring thorough clinical evaluation and imaging studies for differentiation. Invasive fungal infections demand special stains on skin biopsies and other relevant investigations. We could exclude these diagnoses by pathology review.

Pancreatic panniculitis, linked to pancreatic disorders, occurs when enzymes escape the inflamed pancreas, leading to subcutaneous fat necrosis. Clinically, it presents as tender nodules, primarily on the lower limbs. Remarkably, it can occur without acute pancreatic inflammation, posing diagnostic challenges. Histopathological analysis reveals unique features such as basophilic calcification and inflammatory infiltrates. Treatment targets the underlying pancreatic condition, emphasizing the need for systemic consideration in dermatology.

While typically associated with pancreatic diseases, it can occur in the absence of apparent pancreatic symptoms, as demonstrated in this case. The complexity deepened with the concept of "nonpancreatic pancreatic panniculitis," a phenomenon where pancreatic enzymes

are released into the bloodstream without evident pancreatic pathology. This intricate interplay of factors necessitates a holistic understanding of the patient's medical history and symptoms for accurate diagnosis and tailored management.

Conclusion

In conclusion, this intricate case illuminates the diagnostic complexities often encountered in clinical practice. The unexpected discovery of pancreatic panniculitis without active pancreatitis challenges conventional diagnostic norms, emphasizing the need for astute observation and thorough investigation. On patient with severe liver disease even with chronic pancreatitis, pancreatic panniculitis should take into consideration if the patient develops tender purpura at lower extremities.

病例報告　112_C 37

褥瘡病患合併疑似破傷風感染的病例個案

Suspected Tetanus with Subtle Symptoms in an Aged Patient with Pressure Sores

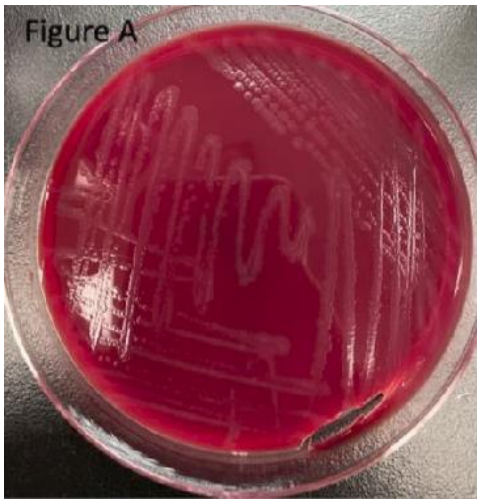
劉彥宏 [1,2] 盧雪珍 [3] 林芳媛 [3] 韋佳齡 [1]
[1] 新店耕莘醫院內科部 [2] 輔仁大學醫學院醫學系 [3] 新店耕莘醫院檢驗醫學科

Introduction

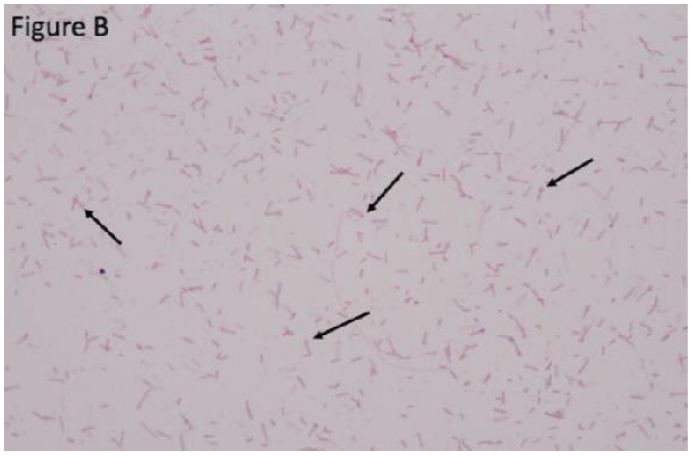
Tetanus is a toxemic illness caused by a neurotoxin produced by *Clostridium tetani* infection through skin injuries. It mainly manifests with neuromuscular dysfunction. The typical features include trismus, risus sardonicus, opisthotonus and autonomic overactivity. However, tetanus can begin with subtle symptoms, especially in aged people. Herein, we presented a elderly patient with suspected *Clostridium tetani* infection.

Case presentation

This 73 years old man with history of type 2 diabetes mellitus and hypertension presented with acute conscious disturbance for at least one hour prior to arrival to our emergency department (ED). According to patient's son, the patient had decreased oral and fluid intake in the past one month. Rapid cognitive function decline and bedridden status were also noted. Patient's son denied the patient had recent head trauma, cough, nausea or vomiting. Due to above mentioned complaints, the patient was brought to our ED by EMT. Laboratory studies reported leukocytosis 22700/uL, BUN 198 mg/dL, Cr 3.71 mg/dL, glucose 980 mg/dL, CRP 40 mg/dL and lactate 9.82 mmol/L. Under unstable condition, the patient was admitted to intensive care unit for further management.



After admission, multiple pressure ulcers over the lumbo-sacral area, hips and heels were found, about 10-30 x 10-30 cm in size, with foul smell and much yellow discharge. Piperacillin/tazobactam and Norepinephrine were prescribed for infection control and shock status. Insulin pump and IV hydration were used for hyperosmolar hyperglycemic syndrome (HHS) management as well. Plastic surgery team was consulted for debridement of multiple pressure ulcers. Sacral wound culture reported *Acinetobacter baumannii*, *Enterococcus faecium* and *Clostridium tetani*. (Figure A) Gram stain of *Clostridium tetani* revealed gram-positive bacillus with spore-forming.(Figure B, arrow). Based on the clinical presentation, tetani neurotoxin related cognition decline was suspected so that we consulted Neurology team for further evaluation. Brain MRA demonstrated recent lacunar infarctions in bilateral hemispheres with Watershed pattern. In addition, episodic of atrial fibrillation with rate 190-210 bpm was recorded on



ECG monitor and amiodarone for rhythm control was prescribed. Due to above findings, intravenous metronidazole was administrated for suspected tetanus for 10 days. Wound care and hyperbaric oxygen therapy were prescribed for multiple pressure sores as well. After above management, the patient's was GCS E4V1-2M4, oriented to person with smooth breathing pattern on room air. Then this patient was discharged with OPD follow-up.

Discussion

The incidence of tetanus varies throughout the world. Although tetanus vaccination does not generate long-term immunity, it dose reduce the incidence of tetanus in the USA, around 0.03 cases/100,000 persons[1]. Tetanus is a nervous system disorder caused by the toxin produced by *Clostridium tetani* (*C. tetani*). *C. tetani* is a gram- positive, anaerobic, rod-shaped bacterium, with a terminal spore, resembling a drumstick. The portal of entry of *C. tetani* is deep penetrating wounds, gunshot injuries, gangrene, and surgical intervention. But the organism entering through superficial skin injuries has been reported[2]. Although trismus is tetanus's most frequent presenting symptom, bulbar paralysis manifestations were more common than spasms in elderly patients[3]. Symptoms of autonomic overactivity, such as irritability, restlessness, sweating, tachycardia and arrhythmia, were also noted[4]. Laboratory culture cannot confirm or exclude the diagnosis while *C. tetani* was isolated in only 11.54% of cases[2]. Management of tetanus includes wound management, neutralizing the unbound toxin, antimicrobial therapy(metronidazole), controlling muscle spasms, managing dysautonomia, and supportive care.

An immunization program (diphtheria, tetanus, and pertussis vaccine) was launched in 1954 in Taiwan so that it is likely that our patient who was born in 1950 has never been vaccinated for tetanus, making him more eligible to tetanus. We did not observe the typical neurologic presentation of tetanus so that the diagnosis of tetanus cannot be made with confidence. However, there are still some clues suggestive of tetanus, including the pressure of deep pressure sore (portal of entry of *C. tetani*), poor oral intake (caused by dysphagia), arrhythmia (autonomic overactivity).

Conclusion

Although the presence of *C. tetani* in a wound does not indicate the diagnosis of tetanus, we should keep tetanus in the lists of differential diagnoses because clinical suspicion is the key to diagnosis and tetanus can mimic other medical conditions which are common in aged patients.

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病例報告　112_C 38

疑似巨大細胞病毒活化在一位接受類固醇治療的愛滋病合併肺囊蟲肺炎患者

Suspected CMV reactivation in an AIDS patient under steroid treatment for PJP

劉彥宏 [1,2,3]　姜之翎 [1]

[1]新店耕莘醫院感染管制中心 [2]新店耕莘醫院內科部 [3]輔仁大學醫學院醫學系

Introduction

Although the risk factors of cytomegalovirus (CMV) reactivation is not fully understood, severe dysfunction of the immune response is the key mechanism leading to CMV reactivation. HIV infection, sepsis and steroid administration all play important roles in dysregulation of the immune response. Here, we presented a patient with acquired immunodeficiency syndrome (AIDS) and *Pneumocystis jirovecii* pneumonia (PJP) treated by steroid, causing suspected CMV reactivation.

Case presentation

A 29-year-old male without medical history presented to our hospital with symptoms of fever, dry cough, and progressive dyspnea for two weeks. Upon admission, the physical examination revealed mild respiratory distress and tachycardia. Oxygen saturation level was 90% on room air. A CXR indicated reticular infiltration over bilateral basal lungs with subpleural sparing, leading to high suspicion of PJP. An HIV test was performed, confirming a positive result, with HIV viral load of 975,000 copies/mL and CD4 cell count of 28/mL. (Figure 1) Laboratory values showed plasma CMV viral load of 410 IU/mL, without evidence of co-infection with EBV or cryptococcosis. *PJP* was revealed by sputum through PCR examination. Treatment with Bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) was initiated for HIV infection, while Trimethoprim/Sulfamethoxazole was prescribed for PJP. Additionally, adjunctive dexamethasone was given for high A-a gradient. Empirical levofloxacin was used to cover suspected community-acquired pneumonia. Despite the treatment, the patient's dyspnea persisted. Furthermore, sputum culture yielded Mycobacterium avium complex infection, for which klarithromycin and ethambutol were administered. After four weeks of BIC/FTC/TAF treatment, HIV viral load decreased to 492 copies/mL, and CD4 cell count increased to 292/mL. However, no significant clinical improvement and persistent infiltration shown by CXR were noted. (Figure 2)

As evidenced by the increasing plasma CMV viral load, from 410 to 116,073 IU/mL, CMV reactivation was suspected. Consequently, the patient's dexamethasone was tapered to oral prednisolone. Eventually, the plasma CMV viral load dropped to 4,870 IU/mL without the use

Figure 1 Laboratory values and prescribed medications during the hospital stay

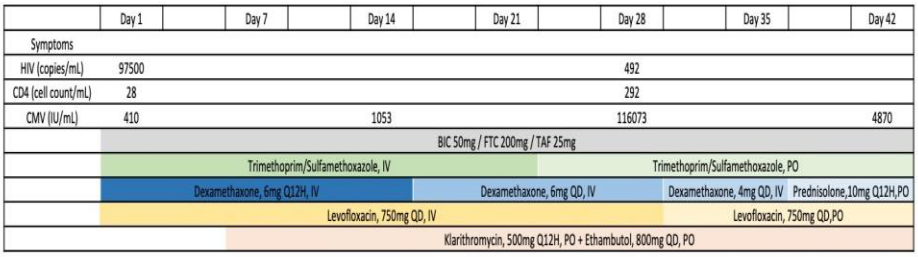
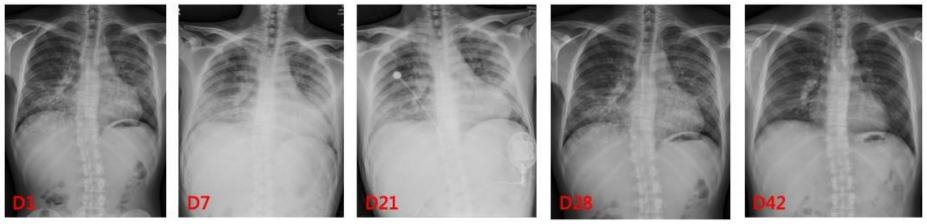


Figure 2 A series of chest X-rays during the hospital stay



of specific anti-CMV agents. The patient no longer experienced dyspnea and did not require oxygen supplementation. He was discharged in a stable condition, and follow-up tests at the outpatient department showed undetectable plasma CMV viral load.

Discussion

CMV, a double-stranded DNA virus and belonging to the fifth member of the human herpesvirus family, is one of the largest viruses and is the common viral pathogen in people living with HIV. In general, CMV is acquired during childhood to early adulthood and primary CMV infection is usually asymptomatic, although nonspecific illness or an infectious mononucleosis-like syndrome may be presented. After primary infection, CMV establishes latency in wide range of cells, including epithelial cells, endothelial cells, fibroblasts, and smooth-muscle cells. In individuals with functionally normal immune system, CMV reactivation occurs sporadically throughout life and it can be controlled via immunologic control. On the contrary, uncontrolled viral replication happens under immunocompromised status, such as impairment or loss function of CMV-specific CD4+ and CD8+ T-cells[1]. The risk factors for CMV reactivation include CD4 cell count < 50 cells/mL in AIDS patients, lack of pre-existing CMV-specific immunity in transplant patients, immunosuppressive drugs use, immature immune system in newborns and so on.[1,2] The most common presentation of CMV disease in AIDS patients is retinitis, possibly resulting in irreversible blindness. It can also cause pneumonitis, often with coinfections with *Pneumocystis jirovecii* and *Aspergillus fumigatus*.[1] Evidence of disseminated CMV infection was discovered in over 90% of AIDS patients during post-mortem examinations in the past[3].

In the presented case, steroid administration is based on international guidelines which suggest steroid prescription for PJP with hypoxemia or A-a gradient > 35~45 mmHg to down-regulate the hyper-inflammatory response. However, the increasing plasma CMV viral load with persistent dyspnea and infiltrations revealed by CXR were observed during the hospital stay. CMV reactivation was highly suspected despite it is not confirmed by solid evidence, such as detection of CMV DNA from BAL fluid or histopathologic exam of lung-tissue biopsy. The steroid dose was tapered off gradually without any change of medication therapy, and not only the clinical condition and the CXR improved but also the plasma CMV viral load declined, supporting our suspected CMV reactivation. Compared to other conditions associated with profound immunosuppression, the occurrence of CMV pneumonitis is infrequent in AIDS patients, but CMV reactivation should be taken into consideration when we prescribed steroid for PJP patient as steroids has been regarded as a possible risk for CMV reactivation[2].

Conclusion

This patient serves as a reminder of CMV reactivation when treating PJP with adjunctive dexamethasone. Proper monitoring is essential when managing such cases to ensure the best possible outcomes.

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病例報告　112_C 39

以突發性體重減輕為表現的腦下垂體中風: 病例報告及文獻回顧

pituitary apoplexy presenting as sudden weight loss : A case report and review of Literature

王寶妹 [1,2] 馬文雅 [1]
財團法人天主教新店耕莘醫院 [1] 內科及新陳代謝內分泌科 [2] 老年醫學科

Case presentation

A 74 years old post- menopausal woman came to our endocrinology out- patient department due to massive body weight loss 6-7 kg within six months. She had history of epilepsy with long term medication oral depakine 200mg 1# qd, 500 mg 1# hs at neurology department. She also had endometrial carcinoma and took abdominal total hysterectomy and bilateral salpingo-oophorectomy since 65 years of age. She also suffered from syncope once attempt at home on Mar 14, 2019 and was admitted to our hospital under impression of seizure. She had history of hyperlipidemia and took lipid lowering agents at our hospital.

At presentation, her consciousness was clear. Her arterial blood pressure revealed 114/68 mmHg and a heart rate of 94/min. She did not have fever nor sign of respiratory distress. Physical examination and comprehensive neurological examination were normal. Her eye movements were free and full. Eyebrows were slightly thinner. Her neck was supple. Hearts sounds were regular without murmurs.

The lungs were clear on both sides. The pigmentation of areola was diminished. The abdomen was soft and non-tender. There was sparse axillary and pubic hairs. The extremities showed mild edema but no clubbing. The peripheral pulsations were normal. Muscle powers and deep tendon reflexes of all four limbs were intact and symmetrical.

Complete blood count and serum chemistry tests were within normal limit. The data were summarized in table 1. Chest X ray flim showed no specific finding including tortuosity of thoracic aorta. Computerized tomography of brain revealed a 2.2cm mass in sellar turcica without obvious supra-sellar extension, presenting as T1 hyper-intensity and T2 hypo-intensity; pituitary apoplexy is more favored.

Figure 1

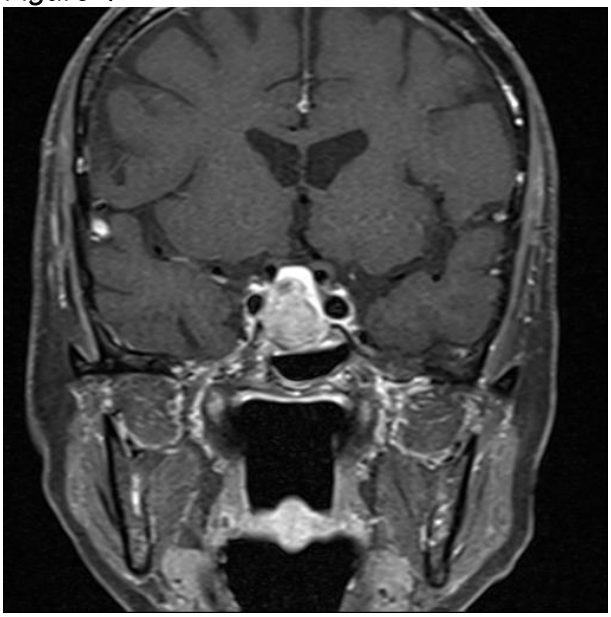
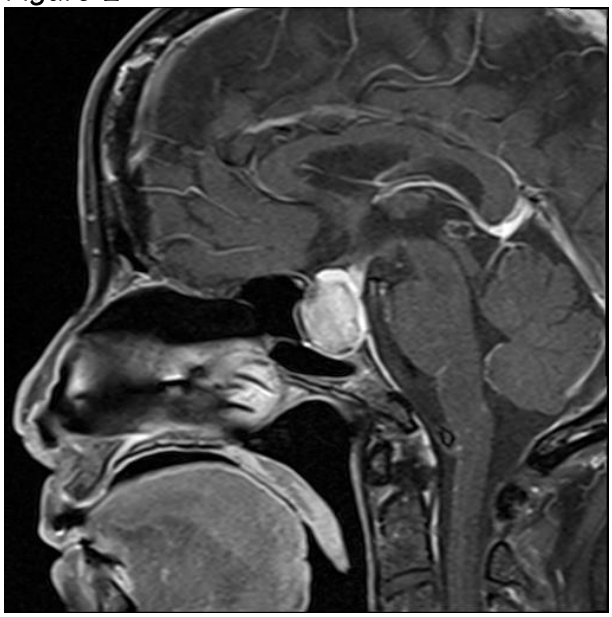


Figure 2



The hormonal profile was summarized in Table 2. The reduced morning cortisol, ACTH,

free thyroxine (free T4), thyroid stimulating hormone (TSH), reduced estradiol and follicular stimulating Hormone, luteinizing hormone were compactible with pan-hypopituitarism. The patient was given with thyroxine 100 mcg once daily for secondary hypothyroidism and oral glucocorticoid (prednisolone 10mg twice daily for secondary hypo-cortisolism. We add Dostinex (carbagoline) 1# weekly for high prolactin levels. Her general malaise and appetite were improved.

Complete blood counts		Normal range
White blood cells ,x109/L	6220	4-10x10^9
Hemoglobin, g/L 10.1	12.2	13.5-17.5
Hematocrit, % 39.2	35.0	41-53
Platelet x10^9	209	150-450 10^9
Biochemistry		
BUN, mg/dL	22	7-18
Creatinine, mg/dL	0.47	0.8-1.3
Sodium, mmol/L	139	136-145
Potassium, mmol/L	4.16	3.5-5.1

Table 1

Table 2

Hormone Profile	2021/10/19	2021/12/13	
Free T4 ng/dL	<0.25	1.22	0.89-1.76
TSH μIU/*mL*	-2.8		0.35-5.5
Cortisol (8:00) AM	1.87	3.68	5-23
ACTH (8:00) AM	10.2	11.5	0-46
Prolactin μg/L	28.43		2.1-17.7
FSH mIU/mL	-1.72		1-12
LH mul/mL	<0.2		1-12
E2 Pg/ml	<15.0		32.2
IGF1, ng/mL	114.0		35.1-216(70-79) years
HGH ng/mL	0.319		0.01-3.067
LDL mg/dL	161		<130
HDL mg/dL	107		>50

Discussion

Pituitary apoplexy, a rare clinical syndrome secondary to abrupt hemorrhage or infarction, complicates 2%–12% of pituitary adenomas, especially nonfunctioning tumors. Sudden headache and severe onset is the main symptom, sometimes associated with visual disturbances or ocular palsy. Precipitating factors (increase in intracranial pressure, arterial hypertension, major surgery, anticoagulant therapy or dynamic testing etcetera) may be identified[1].

Pituitary apoplexy is an endocrine emergency which requires immediate investigation and treatment. Despite its disastrous pathology, there have been cases where affected patients present with isolated visual disturbances or with no symptoms at all. It is therefore important to have early suspicion of pituitary apoplexy in stable patients with eye complaints as early detection and management are life-saving and significantly improve neuro-ophthalmic outcome[2].

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病例報告　112_C 40

後疫情時代的退伍軍人肺炎和新冠肺炎，是因果還是巧合

Post-COVID-19 Pandemic Legionella Disease and COVID-19 Pneumonia, Coincidence or Correlation

強舜慧[1] 周發揚[2] 張家豪[1,3]

[1]亞東紀念醫院內科部 [2]中國醫藥大學附設醫院醫學影像部 [3]亞東紀念醫院胸腔及重症醫學部

Introduction

As the increasing prevalence of COVID-19 with minor symptoms, flu-like transformation in the future would be expected, especially with the efficacy of vaccination. Emerging studies have shown that coinfection in COVID-19 patients was associated with poor outcomes and higher mortality rate[1]. Early detection of the dominant pathogen and timely effective treatment are crucial. Coinfection of COVID-19 and Legionella have been observed, especially during post-COVID-19 pandemic[2]. Stagnation of the water plumbing system during COVID-19 lockdown has been correlated to this phenomenon[3,4].

Case presentation

A 67-year-old male with diabetes mellitus, hypertension, and old ischemic stroke presented with intermittent fever, fatigue and dry cough for a week. He was tested positive for SARS-CoV-2. He took Chinese herbs and served home quarantine initially. Due to progressive dyspnea, he was sent to the emergency department. The chest radiograph showed consolidation at right lower lung (Figure 1). The chest computed tomography showed consolidation at right upper and lower lungs (Figure 2).

Figure 1 The supine chest radiograph displayed patchy consolidation at right lower lung field.

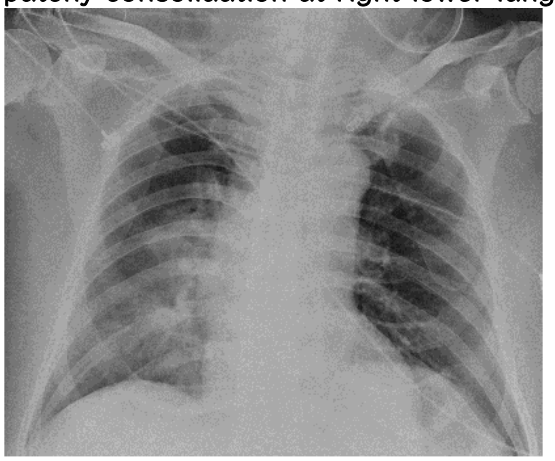
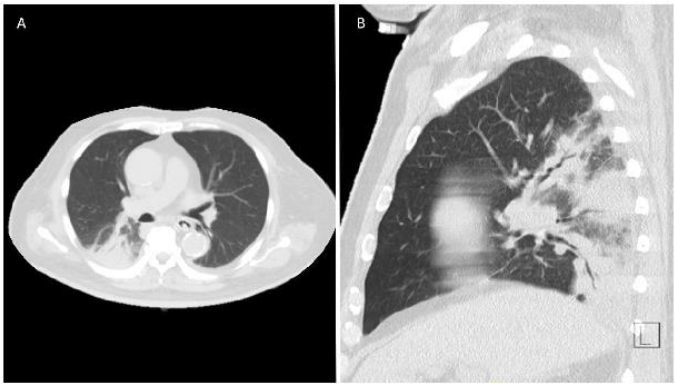


Figure 2 Chest computed tomography. Axial CT scan (A) and sagittal reconstruction (B) showed multifocal consolidation with air-bronchogram at posterior segment of right upper lobe and right lower lobe



Due to respiratory distress, intubation was performed. Subsequent examinations revealed negative for blood and sputum culture but a positive Legionella urinary antigen test. Moxifloxacin was prescribed. His oxygenation improved gradually, and was extubated successfully on day 9 of admission. He was discharged at room air condition after 14-days of Moxifloxacin treatment.

Discussion

The typical computed tomography findings of a COVID-19 patient were characterized by

bilateral, peripheral and basal ground-glass opacity. However, our case showed multi-lobar consolidative changes which are more compatible with Legionella pneumonia. This has raised the concern of the true pathogen leading to acute respiratory failure in the context of a COVID-19 patient. Where steroid has become the standard of care for critically ill COVID-19 patients, it might be controversial in the circumstance of bacterial and fungal co-infection. Especially when the evolving variants tend to become more akin to flu-like symptoms, it is crucial to acknowledge that the coinfection in COVID-19 patient might be the dominating pathogen instead.

Sporadic case reports regarding coinfection of COVID-19 and legionella pneumonia have been reported lately[2]. A meta-analysis reported a total 18/5035 coinfection cases of COVID-19 and Legionella pneumonia in Italy, of which, an increased risk ratio of 6.508 (95% CI 1.909–22.190) was observed as compared to the first semester of 2020[2]. A study comparing water samples during and after the COVID-19 lockdown has shown that water stagnation promotes the proliferation of Legionella, the relative abundance of Legionella in 2-months stagnation was 0.34% as compared with no stagnation[4]. Of note, a water sample taken from the household water system of a post-COVID-19 Legionella pneumonia patient was detected with Legionella pneumophila[5]. The timeline of which Legionella pneumonia infection 5 days after discharge further supported the hypothesis of water stagnation increased risk of Legionella infection.

We proposed that there is a correlation in the increased prevalence of Legionella pneumonia in post-COVID-19 pandemic. Stagnation of the water plumbing system, if not well-processed before reusing, might promote Legionella growth and subsequent infection. Poor maintenance of water resources during the lockdown period has contributed to increased waterborne pathogens contamination. This correlation that we proposed is applicable to all future infectious hazards involving extensive lockdown.

Conclusion

In COVID-19 patient, careful differential diagnosis to determine the true dominant pathogen is important to provide timely effective treatment. With previous lockdown and then reopening, increased risk of Legionella pneumonia infection in the near future needs to be considered. This concept of increased Legionella infection risk in post-lockdown timeline is an important public health issue to acknowledge. Adequate risk assessment and water sample testing may be helpful.

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病例報告　112_C 41

一位胸腺瘤合併重症肌無力危機的患者，以乾燥症症狀為起始臨床表現

A patient with diagnosis of thymoma and myasthenia gravis crisis present with initial symptoms of sicca complex

陳健良[1]　王旭輝[1,2]

[1]亞東紀念醫院內科部　[2]亞東紀念醫院胸腔內科

Introduction

In Taiwan, there are approximately 110 new diagnosed cases each year, with an estimated prevalence rate of about 0.5 per 100,000 population[1]. Half of the patients are asymptomatic, while the other half present with paraneoplastic syndrome (PNS). Among those with PNS, 25-40% exhibit symptoms of myasthenia gravis (MG)[2]. MG is a rare autoimmune condition that impacts the neuromuscular junction (NMJ), leading to the development of autoantibodies and damage to NMJ components[3]. An MG crisis is a severe condition in which MG progresses to affect the respiratory muscles, leading to respiratory failure, requiring intubation and mechanical ventilation[4]. Due to its antibody-mediated nature, treatment often involves the use of steroids and plasma exchange to achieve relief and bridges to thymectomy[5].

Due to the relationship between thymus and T-cell maturation, several articles in the past have suggested that the clinical manifestations of Thymoma-associated multiorgan autoimmunity (TAMA) are similar to those of Graft-versus-host disease (GVHD). When TAMA occurs in the eyes and mucous membranes, symptoms such as dry eyes and dry mouth like sicca complex can serve as initial symptoms of thymoma[6-8].

Case presentation

This 43-year-old female patient, with a previous medical history of gastroesophageal reflux disease, recently presented to outpatient clinics with progressive difficulty swallowing, dry mouth, dry eyes, blurred vision, ptosis, general weakness. The Schirmer test, which indicated 1/1 mm of wetting in 5 minutes, and keratitis were noted during ophthalmological examination. Nasopharyngoscopy and gastroscopy did not reveal any significant lesions. Hence, suspicion of Sjogren's syndrome led to outpatient follow-up. However, she experienced chocking while dinner, subsequently developing symptoms such as respiratory distress, chest pain, and cough. As a result, she was referred to the emergency department. Her blood oxygen level was found to be 87% upon arrival. A chest X-ray revealed increased infiltration in the lower right lung, and a CT scan identified a 3x2cm soft tissue mass in the anterior mediastinum. Blood tests indicated an elevated white blood cell count. She was admitted to the hospital for treatment of aspiration pneumonia. However, during her hospitalization, her excessive mucus production did not improve, and she experienced difficulty in clearing her throat. Neurologist suggested steroid therapy under the impression of MG. Due to worsening respiratory failure, the patient was intubated and transferred to the intensive care unit. The Neostigmine test yielded positive results, with improvements in eye blinking and swallowing, along with an increase in tidal volume. The repetitive nerve stimulation test showed a positive finding with a decremental response under 3-Hz test. Consequently, Pyridostigmine was administered. Plasma exchange was performed for four consecutive days, and thoracic surgeons were consulted to remove the 6.0 x 3.8 cm tumor. Anti-acetylcholine receptor (AChR) antibody

levels were elevated at 403.20 nmole/L, and auto-immune maker showed negative findings for Anti-Ro/La (6/9 AU/mL) but positive for ANA (Antinuclear Ab). Following surgery, the patient was successfully extubated and transferred back to the general ward. Pathological report showed thymoma, WHO type A, cT1bN0M0, pT1a, Modified Masaoka stage: stage IIa (Microscopic transcapsular invasion). She reported a significant improvement in overall weakness and a notable improvement in dry eyes and dry mouth symptoms. The patient was discharged smoothly and arranged radiotherapy for further treatment.

Discussion

Due to the close relationship between the thymus and the immune system, particularly in T-cell maturation, abnormalities in the thymus often manifest as autoimmune issues. Currently, the most extensively studied are those related to neurological diseases[9]. MG is a neuromuscular junction disease caused in 85% of the cases by AChR antibodies; in cases associated with thymoma, nearly all patients exhibit positive AChR antibodies. Furthermore, non-limb symptom such as bulbar, ocular, neck, and respiratory symptoms should raise the suspicion about the presence of thymoma in MG[10]. Other biomarkers in MG include lipoprotein-receptor related protein 4, ryanodine receptor, titin, and muscle-specific tyrosine kinase[3].

The proposed mechanism of TAMA is a breakdown in the immune regulatory function of the thymus and subsequent activation of T cells. These manifestations often focus on the skin (such as lichen planus) and blood (including pure red cell aplasia and Good syndrome). Connective tissue autoimmune diseases have also been mentioned. Sjögren's syndrome is an autoimmune disease primarily characterized by xerostomia and xerophthalmia, often resulting from lymphocytic infiltration in the glands and only few cases of Sjögren's syndrome and concurrent thymoma with MG have been reported[11]. Initially, the patient presented with xerostomia and xerophthalmia. This raised suspicion of Sjögren's syndrome although serological tests did not provide support for it. In sporadic case reports from the past, there have mentioned the presentation of keratoconjunctivitis sicca[12,13]. Currently, there isn't a specific antibody available to serve as a marker for these reasons[14]. However, considering the mechanisms of TAMA, sicca complex induced by T cells appears to be a more reasonable explanation. In our patient, these associated symptoms all improved following the removal of the thymoma. Therefore, we deduce that the mechanisms described above are likely involved.

Conclusion

We have described the typical treatment process for an MG crisis triggered by a thymoma. The diagnostic workup for MG includes serological tests, Neostigmine tests, repetitive nerve stimulation tests, and CT scan to ascertain the cause of MG. During an MG crisis, treatment involves the use of steroids, plasma exchange, and surgical removal of the thymoma. Subsequently, radiotherapy is scheduled, and the patient is followed up in outpatient care. Given the initial presentation of sicca complex, which improved after removal, there is reason to suspect that the symptoms were also part of PNS. We should remain vigilant regarding whether these presentations are caused by TAMA.

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病例報告　112_C 42

紅斑性狼瘡併發急性脊髓炎與急性肝炎-病例報告

SLE complicated with acute myelitis and acute hepatitis – A case report

崔東霖[1] 胡麗芳[2] 陳信榮[3] 呂敏升[4]

羅東聖母醫院[1]心臟內科 [2]風濕免疫科 [3]神經內科 [4]肝膽腸胃科

Introduction

The cause of SLE is not clear. It is thought to involve a combination of genetics and environmental factors. Female sex hormones, sunlight, smoking, vitamin D deficiency, and certain infections are also believed to increase a person's risk. Common initial and chronic complaints include fever, malaise, joint pains, muscle pains, and fatigue. Because these symptoms are so often seen in association with other diseases, these signs and symptoms are not part of the diagnostic criteria for SLE. When occurring in conjunction with other signs and symptoms, however, they are considered suggestive. We would like to present a case who had SLE complicated with acute myelitis and acute hepatitis.

Case report

This 32-year-old female patient denied other chronic illness. She suffered from intermittent fever for 2 weeks (since 2023/08/04), then oral ulcer (Ever visited infection specialist but no specific finding), Dry mouth, Muscle soreness, dyspnea, vaginal polyp. She came to AIR OPD for help, and autoimmune disease survey was done, on 8/29. She also complained of poor appetite, tea colored urine, body weight loss (7kg/recent month), malaise with weakness, and dyspnea. For the her symptoms progress, and lab found: E.S.R.:33, ANA:1:1280X(+), ANA: Homogeneous, Anti-dsDNA: Positive (>365.00), β2-GPI IgG:Positive. She came to our CV OPD for help due to palpitation sensation and angina, under the impression of palpitation and angina, suspected autoimmune disease such as SLE, and body weight loss (7kg/Month), oral ulcer suspected oral cancer, acute hpatitis, and leukopenia. She was admitted to our medical ward for further evaluation and management. Otherwise, she denied chills, conscious change, cough with sputum, nausea, vomiting, coffee ground vomitus, dysuria, tarry stool or bloody stool.

After admission, R/O SLE, oral medication included Imuran 1# qd, colchicine 1# qd, prednisolone 1# bid, Nincort ointment for disease control on the first day. We consulted ENT for oral ulcer with mass and do biopsy and pathology report revealed ulcer with chronic inflammation. Acute hepatitis was noted. Murphy sign positive test on 9/07. We arranged abdominal sonography which revealed negative test. Body weight loss with elevated tumor marker (CA-199:351.30 U/ml CA-153:20.87 U/ml CEA:5.70 ng/ml AFP:110.70 ng/ml CA-125 :22.42 U/ml) was noted. We arranged chest to pelvis CT revealed multiple small axillary lymph nodes, and a 0.43cm RLL lung nodule and mild pelvis ascites and cystic lesions in borderline sized ovaries. Lab data with Mycoplasma Pneumoniae IgM: Positive. We added Zithromax 1# po BID * 3days (9/11.12.13). However, the lab data showed elevated Amylase/Lipase (112/152->145/354->115/190); elevated bilirubin level (Bil D/T 3.9/3.8->3.5/3.5->4.3/4.2); elevated liver enzymes (GOT/GPT 594/182->415/141->473/131; Alk-P 255->269->360; r-GT 798->704->663). Silymarin was given and. Increased the Imuran dose to 1# bid and keep steroid. The symptoms of generalized weakness was still told and

we consulted neurologist. We arranged NCV and whole spine MRI which revealed Abnormal signal enhancement around T12 spinal cord. Inflammatory change is considered on 9/15. We discussed with neurologist and do lumbar puncture on 9/16 for CSF study, which revealed no protein or WBC. Consulted neurologist that Please check brain MRI, VEP for r/o MS or Devic's. The VEP and brain MRI were normal. So methylprednisolone 500mg iv BID x 5 days for acute myelitis. In a relatively stable condition, arrange discharge on 9/25 and OPD follow up.

Discussion

About SLE, the common initial and chronic complaints include fever, malaise, joint pains, muscle pains, and fatigue. Because these symptoms are so often seen in association with other diseases, these signs and symptoms are not part of the diagnostic criteria for SLE. When occurring in conjunction with other signs and symptoms, however, they are considered suggestive. Females tend to have a greater number of relapses, a low white blood cell count, more arthritis. A lot of organ involvement was reported; however, concurrent acute myelitis and acute hepatitis were found in our case.

Conclusion

SLE is one of several diseases known as "the great imitator" because it often mimics or is mistaken for other illnesses. SLE is a classical item in differential diagnosis, because SLE symptoms vary widely and come and go unpredictably. Diagnosis can thus be elusive, with some people having unexplained symptoms of SLE for years. We need to pay more attention to patient with fever of unknown origin, especially in young female.

病例報告　112_C 43

嚴重冠心症出現在患有源自肺動脈之右冠狀動脈的病患 – 罕見先天性心臟病的不尋常表現

Severe CAD in ARCAPA - Unusual presentations in a rarely congenital heart disease

崔東霖[1] 陳明聰[2] 林明賢[3]

羅東聖母醫院[1]心臟內科 [2]醫學影像科 [3]核醫科

Introduction

Anomalous origin of coronary arteries are rare which are found in approximately 1–2% of the general population. Anomalous origin of the right coronary artery from the pulmonary artery (ARCAPA) was first described by the Irish anatomist John Brooks in 1885. The embryological basis of ARCAPA remains unclear while it is generally thought with malformation of coronary artery development during the fourth to sixth week of gestation. The incidence of ARCAPA in patients undergoing coronary angiography was found to be 0.002%. Now it is considered as the second most common type in the coronary anomalies of pulmonary artery origination, second to the ALCAPA. In contrast to ALCAPA with high mortality rate early in childhood, the clinical manifestations in patients with ARCAPA are variable. Surgical intervention is recommended even in asymptomatic patients. Only about 200 cases about ARCAPA have been reported.

Case report

The 89-years-old male suffered from chest pain and tightness, cold sweating and hypertension(180/79) on 6/07 after dinner, thus he visited ER at the same day, after treatment he felt improved, thus discharged from ER, but he still felt chest tightness off and on, thus visited to CV OPD for help on 6/08, impression of angina pectoris suspect CAD, he was admission for CAG on 20230609. After admission to CV ward, for angina pectoris under DAPT with Aspirin + clopidogrel treatment, the heart echo showed preserved LV systolic function 63.9%, and thallium scan showed moderate to severe IHD & myocardial ischemia in diffuse septal, apical & diffuse inferior walls (severe reduction of uptake) of LV was demonstrated and large areas of reversible perfusion defect in diffuse septal, apical & diffuse inferior walls. The coronary CTA revealed right coronary artery derived from pulmonary artery and significant calcifications along LM and left anterior descending coronary artery. We arrange percutaneous coronary intervention and balloon dilatation with stenting was done for ostium to proximal LAD with drug-eluting stent successfully. Due to his clinically condition stable, then discharge and OPD follow up. Conservative treatment for the ARCAPA because of extremely old age which was suggested by cardiovascular surgeon.

Discussion

The patients with ARCAPA present variable clinical manifestations. According to previous review, about 38% of patients with ARCAPA were asymptomatic at the time of diagnosis. There is a bimodal distribution of the age at presentation as one peak centered near after birth and another peak centered around 40 to 60 years of age. Soon after birth in patients with ARCAPA, the high pulmonary pressure keeps antegrade perfusion with deoxygenated blood. Myocardial anoxia of RCA territory causes collateralization development between the left and right coronary systems As pulmonary pressure decreases and collateralization

develops, blood from left coronary system flows retrogradely into the pulmonary artery and results in "coronary steal" phenomenon. If collateralization has not sufficiently developed, the patients may present with myocardial ischemia. Left coronary system supplies adequate oxygenated blood to the entire heart and the patients survive and may grow up asymptomatically. Single coronary system is more prone to atherosclerosis and left to right shunt is more prone to cardiac dysfunction.

Angiography is considered as the golden standard for the diagnosis of ARCAPA. Typical features of ARCAPA observed by angiography include retrograde flow though the RCA, extensive collateralization, dilated coronary system with increased flow as well as flow from RCA into pulmonary artery. Echocardiography and coronary CT angiography are of important diagnostic value. There is consensus about early intervention in patients with ARCAPA to prevent later complications such as cardiac dysfunction and myocardial ischemia. The aims of treatment are to eliminate the "coronary steal" and establish dual coronary system originating from aorta.

Three surgical strategies are commonly applied, included of simple RCA ligation, RCA ligation with CABG, and RCA reimplantation onto aorta. Simple RCA ligation usually took place in patients who were not deemed good candidates for CABG. RCA reimplantation is thought to provide higher patency rate compared with RCA ligation with CABG. Because of the complete cardiac arrest and sufficient collateralization, simple RCA ligation was thought acceptable without compromised myocardial perfusion. After eliminating the "coronary steal" phenomenon, the patient received good results as 5-year postoperative coronary CT angiography showed both left ventricle and coronary system decreased in size without evidence of myocardial ischemia.

Conclusion

As patients with ARCAPA could be asymptomatic, we emphasize the suspicion in patients with dilated coronary arteries and retrograde flow in RCA when detected by echocardiography. Early intervention is necessary even in asymptomatic patients and RCA ligation with CABG or RCA reimplantation are preferred in such patients as they provide favorable long-term outcome. Anomalous origin of the right coronary artery originating from the pulmonary trunk (ARCAPA) is a rare congenital coronary anomaly with an estimated prevalence of 0.002% ARCAPA may lead to myocardial ischemia and/or sudden cardiac arrest. Origin of the RCA from the pulmonary artery (ARCAPA) is a rare congenital malformation with a potentially malignant outcome for the patient. In our case, the chest discomfort was due to occlusion of the LAD and was probably unrelated to the coronary malformation.

病例報告　112_C 44

半相合造血幹細胞移植術後併發罕見非感染性猛爆性器質化肺炎

A rare non-infectious pulmonary complication of organizing pneumonia with fulminant presentation after haploidentical stem cell transplantation

葉士源[1]　黃聖娟[2,3]

佛教慈濟醫療財團法人花蓮慈濟醫院[1]內科部　[2]血液腫瘤科　[3]臨床病理部

Introduction

Pulmonary complications are common among patients after allogeneic transplantation due to the use of immunosuppressant therapy (IST) and dysregulated immunity. While infection is the primary etiology of pulmonary complications, late-onset non-infectious pulmonary complications (LONIPCs) pose a significant threat due to the challenges associated with timely diagnosis and treatment. Organizing pneumonia (OP), previously known as bronchiolitis obliterans organizing pneumonia (BOOP), can occur in patients after transplantation with a delayed onset, typically around 148 days after transplantation.

In this case, we present a patient who developed a fulminant course of OP approximately 5 months after transplantation. His condition rapidly deteriorated, necessitating extracorporeal membrane oxygenation (ECMO) support. Timely diagnosis and appropriate treatment are crucial factors contributing to a successful outcome in this patient.

Case presentation

A 26-year-old male with Philadelphia-positive acute lymphoblastic leukemia (Ph+ ALL) underwent haploidentical transplantation on 2 December 2022 (day 0). Following the transplantation, only mild and transient acute graft-versus-host disease (GVHD) developed, and thus, IST was rapidly tapered off since day 82. CMV viremia was detected but did not progress to CMV disease. He maintained complete molecular remission (CMR) with imatinib as maintenance therapy, alongside prophylactic drugs including sulfamethoxazole/trimethoprim and valacyclovir. There was no evidence of chronic GVHD and he successfully returned to work five months after transplantation.

On May 9, 2023 (day 158), he underwent a follow-up bone marrow (BM) examination and reported no discomfort. However, the following day, he began experiencing shortness of breath while climbing stairs, along with non-productive cough and low-grade fever. He denied any other associated symptoms, but he did recall experiencing a prolonged upper respiratory tract infection lasting approximately one month the previous month.

On 11 May 2023, he went to the emergency department, presenting with fever (38°C), tachycardia (102 beats per minute), dyspnea (20 breaths per minute), and desaturation (94% under ambient air). Pneumonia was impressed based on the presence of bilateral patchy consolidations observed on a chest X-ray. Rapid tests for influenza and COVID-19 both yielded negative results. Consequently, he was empirically treated with piperacillin/tazobactam and admitted to the hematology ward on the same day. He had no history of smoking, alcohol consumption, betel nut use, herbal use, or known drug allergies. His body weight was 73 kg, and his height was 169 cm, with a normal BMI of 25.6. The only notable physical findings were bilateral crackles upon examination. Laboratory results indicated Hb 12.3 g/dL, MCV 88.5 fL, PLT 63K/uL, AST 21 U/L, ALT 23 U/L, ALP 127 IU/L, GGT 187 U/L,

TBI 1.7 mg/dL, DBI 0.4 mg/dL, lactate 0.7 mmol/L, CRP 17.68 mg/dL, PCT 0.22 ng/mL, WBC 8.55K/uL (with a normal differential count). A recent BM examination revealed CMR in ALL. Chest CT was performed, revealing bilateral peripheral consolidations, air bronchograms, and a suspected reverse-halo sign. In the suspicion of pulmonary aspergillosis and atypical infection, voriconazole and azithromycin were added.
On 14 May 2023, he had persistent fever accompanied by progressive desaturation with SpO2 92% under venturi mask 10L/80%. The chest X-ray revealed denser and larger consolidations over bilateral lung fields. By May 15, 2023, his hypoxemia worsened even under high-flow nasal cannula support. Consequently, he was transferred to the MICU, where endotracheal intubation was performed on the same day. The PaO2/FiO2 Ratio was only 73 under FiO2 of 100%. The ARDS protocol was initiated. However, profound shock accompanied by tachycardia was observed during prone position. Therefore, the prone position was discontinued, and venous-venous ECMO was applied.
The cardiac echo revealed a left ventricular ejection fraction (LVEF) of 62% without obvious wall motion abnormalities, which ruled out congestive heart failure and cardiogenic shock. To provide a broader spectrum of coverage, meropenem and teicoplanin were added, voriconazole was switched to isavuconazole for mold infection, and levofloxacin and amikacin were introduced for potential tuberculosis.
Given the lack of identified pathogens in previous sputum samples, bronchoalveolar lavage (BAL) was performed. The aspirated sputum was light orange with WBC ranging from 5 to 10 per high-power field (HPF), RBC exceeding 100 per HPF, lymphocytes accounting for 51%, neutrophil segments at 37%, monocytes at 9.5%, and eosinophils at 0.5%. Biopsy was not conducted due to the anticoagulant use during ECMO. All previous expectorated sputum and BAL sample yielded negative results, which suggested that the etiology of fulminant ARDS might not be infectious in nature. Given the clinical impression of OP, oral prednisolone was initiated at a dosage of 40mg/day(approximately 0.5mg/kg/day), starting on May 17, 2023.
The patient's ventilator settings were successfully reduced from FiO2 70% to 40% on the following day, and follow-up chest X-rays displayed remarkable improvement. The ECMO was removed after 7 days and he was also successfully extubated after 14 days. Follow-up chest X-ray showed resolution of consolidations. He could walk and even climb stairs after transferred back to ward.

Discussion

OP is one of the LONIPCs that can develop without concurrent GVHD. Similar to cryptogenic organizing pneumonia (COP) in patients without known underlying diseases, the onset is usually insidious or subacute, with typical symptoms including fever, non-productive cough, and dyspnea. These clinical manifestations closely resemble those of infections, which can make timely diagnosis challenging. Once the OP being correctly diagnosed, most patients respond well to systemic steroid, at a dosage of 0.5-1mg/kg/day of prednisolone.
Biopsy is considered the gold standard for diagnosis of OP but is usually reserved for situations where the clinical course does not align with the diagnosis due to its potential complications. In our case, the patient's disease progression was rapid, requiring mechanical ventilation along with VV ECMO within just 4 days. This situation is relatively uncommon. However, with the addition of immediate broad-spectrum antibiotic treatment and guided by the patient's clinical course and the patterns observed on chest CT, we made the confident decision to initiate steroid therapy. This ultimately led to a favorable recovery.

Conclusion

OP is an uncommon non-infectious pulmonary complication that can occur at a later stage following stem cell transplantation. When promptly recognized and treated with steroids, a favorable outcome is anticipated, even in patients necessitating ECMO support.

病例報告　112_C 45

個案報告-葛瑞夫氏症導致肺動脈高壓造成頑固型肋膜積水-病例報告

Refractory Pleural Effusion Secondary to Pulmonary Hypertension Caused by Graves' Disease - A Case Report

賴致和[1] 李晏榮[2] 周威宇[2] 楊政達[3]

[1]林口長庚紀念醫院內科部 [2]林口長庚紀念醫院內科部新陳代謝暨內分泌科 [3]桃園長庚紀念醫院胸腔內科

Introduction

Hyperthyroidism related pulmonary hypertension (PHTN) could be due to hyperdynamic heart failure (group 2), pulmonary artery hypertension (PAH) (group 5), or both by 2018 World Health Organization classification. Solely symptomatic PAH due to Graves' disease is rarely reported.

Case presentation

A 58-year-old hypertensive woman presented with progressive palpitation and exertional dyspnea for 2 weeks. Accompanied symptoms include orthopnea, insomnia, diarrhea, abdominal bloating, lower limbs edema and body weight gain (42 kg to 52 kg in 1 month). Initial blood pressure140/80 mmHg; HR 145/min with atrial fibrillation (AF) on ECG. SpO2 92% in ambient air. Neither enlarged thyroid gland nor exophthalmos were noticed. Liver and kidney function were adequate but borderline BNP (543 pg/mL); low TSH (<0.008 uIU/mL) and high free-T4 (1.83 ng/dL). Graves' disease was confirmed by positive anti-TPO antibody (Ab), anti-TSHR Ab, and anti-thyroglobulin Ab. A chest radiograph (CXR) showed moderate right pleural effusion with cardiomegaly (Figure 1). Echocardiography revealed normal left ventricular wall motion, LVEF 70%; PHTN with severe TR (systolic PAP 53 mmHg). Abdominal echo showed massive ascites without portal hypertension. The thyroid appeared hypoechoic Swiss-cheese like features, favoring autoimmune thyroiditis.

Figure 1. Persistent moderate amount of right-sided pleural effusion and cardiomegaly after 2 weeks of diuretics and thoracentesis for 1000 ml of transudative effusion.

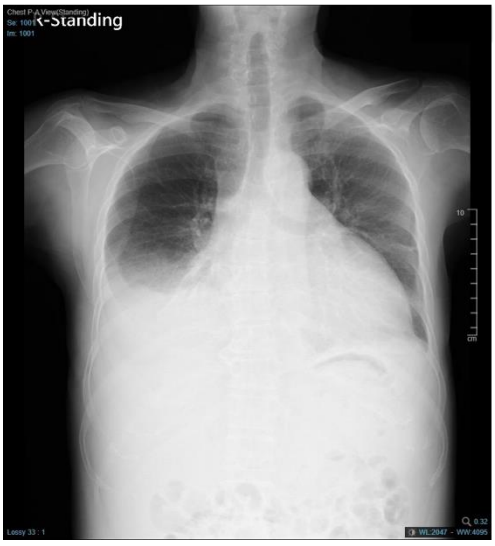
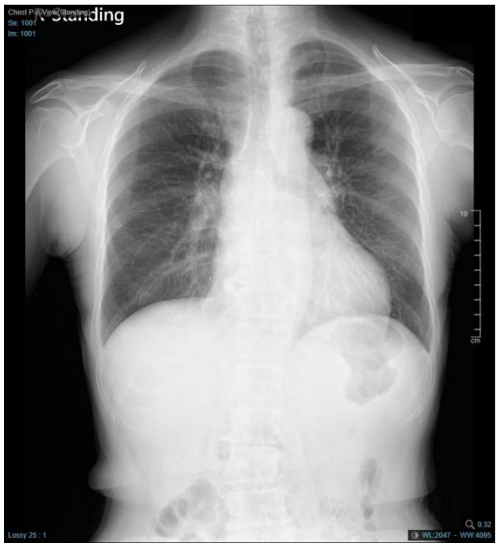


Figure 2. Complete remission of pleural effusion and normalized heart size after 3 weeks of Methimazole.



After 2 weeks of diuretics, her edema improved but with refractory pleural effusion. Methimazole and atenolol were initiated for hyperthyroidism, ECG soon returned to sinus rhythm. The CXR on the 3rd week of anti-thyroid showed complete remission of effusion with normal heart size (Figure 2). No recurrence of pleural effusion on 3rd and 6th week follow-up.

Discussion

Our report highlights a unique case of Graves' disease presented with refractory pleural effusion and ascites for 2 weeks but dramatically improved only since the 3rd week of treatment, the clinical course is less likely to be the effect of diuretics. We are interested whether her refractory pleural effusion comes from left heart failure or right heart failure secondary to pulmonary hypertension. Although AF was noticed at the beginning, the heart rhythm soon returned to sinus and cardiac echo exhibited normal LV contractility; on the contrary, severe PAH was found, which can explain her refractory effusion and was most likely secondary to her hyperthyroidism.

PAH is rarely reported as a first manifestation of hyperthyroidism, while most cases are asymptomatic. Early thionamides reverse hyperthyroidism related PAH with fair outcome, as in our case. Several theories have been proposed for the pathophysiology, including endothelial dysfunction with remodeling, increased cytokines release, immune dysfunction, or enhanced catecholamine sensitivity. In our case, rapid and complete regression of PAH favors a reversible etiology, such as catecholamine effect. To our knowledge, this is the first case reported in Asia having symptomatic PAH secondary to Graves' disease.

Conclusion

Hyperthyroidism related PAH should be considered in patients with refractory pleural effusion. It is usually reversible with good prognosis after early control of thyroid dysfunction.

病例報告　112_C 46

嗜麥芽窄食單胞菌：院內性蜂窩性組織感染於免疫不全患者

Stenotrophomonas maltophila: nosocomial soft-tissue infection in an immunocompromised patient

戴睿暉[1]　陳智皓[1,2]

[1]中國醫藥大學附設醫院內科部　[2]中國醫藥大學附設醫院內科部感染科

Introduction

Stenotrophomonas maltophilia (S.maltophilia) is an opportunistic Gram-negative bacillus, which is also well-known as a multidrug-resistant nosocomial infection pathogen, especially in immunocompromised patients[1]. Over the last few years, the prevalence of S.maltophilia has increased, potentially due to the improvement of cancer treatment, high frequency of antibiotic use and the increase amount of catheter and device placement. While most of the S.maltophilia cases were reported with ventilator-associated pneumonia, it could also cause bacteremia, urinary tract infections(UTIs) and skin and soft tissue infections (SSTIs)[2]. We presented a 63-year-old female with S.maltophilia SSTI in order to call for the importance of early differential diagnosis and treatment for those at-risk hosts with cutaneous infections.

Case presentation

A 62-year-old female with underlying history of diabetes mellitus, hypertension, arrhythmia, atopic dermatitis under topical steroid use, and end stage renal disease under regular hemodialysis, came to Infectious out-patient department(OPD) due to bilateral lower limbs multiple ulcerative wound with pus formation, accompanied with right ankle erythematous change and tenderness. At first, she got treatment as non-complicated SSTI at OPD for half a month, with empirical antibiotic as clindamycin capsules. However, after 2 weeks of OPD following, the wound condition progressed. Thus, pus culture or bacterial, and fungus, and Gram stain were arranged for further diagnosis. The result turned out to be Cutaneous fusariosis. Because of the patient underlying QT prolong (QTc > 500ms) finding via electrocardiography, oral voriconazole or posaconazole was not suitable for her. Admission was then suggested for intravenous antibiotic therapy.

Fig 1. The right heel ulcerative wounds with surrounding erythematous change and pus formation

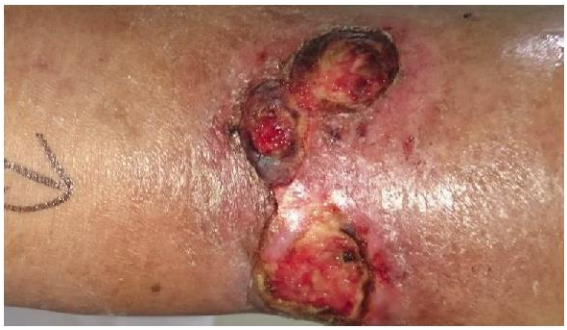
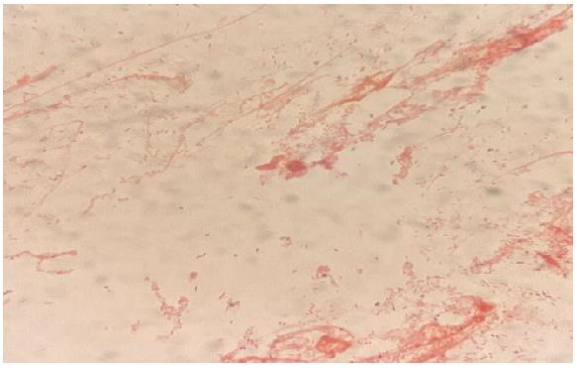


Fig 2. Superficial wound pus Gram stains showed GNB 4+ with phagocytosis (100x)



Amphotericin B was used for Cutaneous fusariosis. Local debridement was done and we de-escalated antibiotic to oral form isavuconazole after 10 days of liposomal Amphotericin B treatment course. However, newly developed wound with pus formation was observed on right heel(Figure 1). Empirical antibiotic as ceftazidime was given at first, which was based on the Gram stain result—Gram-negative bacillus 4+ with phagocytosis(Figure 2). At last, the superficial pus culture turned out to be S. maltophilia.

Under the impression of secondary bacterial infection, we switched antibiotic to trimethoprim/ Sulfamethoxazole (*Sevatrim*) according to the susceptibility results. Second time of surgical debridement was done smoothly for better wound infection control. After 10 days of antibiotic treatment, the bilateral lower limbs ulcerative wounds were healing well. No more discharge was noted from the wounds and the local signs of inflammation was improving. After total 24 days of admission, the patient discharged and kept follow-up on our infectious OPD, without evidence of recurrence.

Discussion

S.maltophilia is an ubiquitous bacterium which could be isolated from water, soil, plants and medical devices. It is an opportunistic nosocomial pathogen, and thus, the most important risk factors for developing S.maltophilia infection are associated with immunocompromised status and various medical treatments, including intravascular catheter positioning, mechanical ventilation, and exposure to broad-spectrum anti-microbials[3]. Therefore, high morbidity and mortality could be observed in these patients.

While the pneumonia and bacteremia are the most common manifestations of infection, the SSTI took the third most common cause, accounting for up to 10% of the cases, particularly in patients with severe neutropenia[4,5]. Our patient neither neutropenic or having hematological malignancy disease, but was immunocompromised due to end stage renal disease and diabetes mellitus, s, and the impairment of cutaneous immunity due to long-term topical steroid use. Despite S.maltophilia was considered to be a nosocomial pathogen, our patient was not admitted due to the S.maltophilia cutaneous infection initially, but fusariosis. She was later diagnosed as secondary S.maltophilia SSTI during second part of the admission course. The patient might be infected during the iatrogenic procedure, such as operation or wound dressing.

Treatment of S.maltophilia is a big challenge. With a high rate of mutation, this bacterium is well-known for its intrinsically resistant to most antibiotics. In our case, the S.maltophilia was cephalosporin or β-lactams resistant, according to the susceptibility testing, which is compatible to the reported data[6].

Conclusion

Since S.maltophilia was a rare and opportunistic infection pathogen, it could be difficult to be taken into consideration and diagnosed by the clinicians, consequently. As a result, Thus, timely and precise identification of the bacteria(i.e. culture, Gran stains) is important to make early diagnosis and targeted therapy.

For the increasing amounts of nosocomial SSTIs, clinicians should be more awareness to the pathogens less commonly encountered, such as S.maltophilia.

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病例報告　112_C 47

第一位以腦膿瘍為表現的 *Streptococcus cristatus* 心內膜炎案例

The first case of *Streptococcus cristatus* endocarditis presenting with brain abscess

張舒評[1] 周家卉[2] 許怡婷[3] 何茂旺[2] 薛博仁[2,4]
中國醫藥大學附設醫院[1]內科部 [2]感染科 [3]神經醫學中心 [4]檢驗醫學部

Introduction

Viridans group *Streptococci* are the predominant organisms of infective endocarditis, but *Streptococcus cristatus* is an infrequent cause of infective endocarditis in that group. In this case report, we aimed to introduce the first case of *S.cristatus* endocarditis presenting with brain abscess.

Case presentation

A 34-year-old man with a history of mitral valve prolapse (MVP) and mitral regurgitation presented to our emergency department with intermittent fever, chills and headache for one month. He had no nausea, vomiting, stiff neck or recent head trauma. He had received local steroid injections for pain control of his herniated disc in the past few years.

On examination, he had clear consciousness without focal neurological deficits. Cerebrospinal fluid (CSF) analysis revealed: 20 white blood cell/μL (3% neutrophils, 71% lymphocytes, 25% monocytes, and 1% eosinophils), glucose 38 mg/dL, total protein 66 mg/dL, and no pathogen was identified from Gram's stain, acid-fast stain, India ink stain or culture. The CSF multiplex polymerase chain reaction panel for meningitis, including herpes simplex virus (HSV) and varicella-zoster virus (VZV), detected no pathogens. Combo test for human immunodeficiency virus (HIV) screening was also negative. A focal hypodensity in the left parietal lobe was found from non-contrast-enhanced computed tomography (CT) of brain. Contrast-enhanced magnetic resonance image (MRI) reported a 2.5 cm lesion with peripheral enhancement and surrounding edema, which was compatible with brain abscess. Therefore, two sets of peripheral blood culture were sampled and empirical antibiotic with ceftriaxone was administered.

However, both sets of blood culture later yielded *S. cristatus* identified by matrix-assisted laser desorption and ionization-time of flight (MALDI-TOF). Echocardiogram demonstrated mitral valve prolapse with severe mitral regurgitation, which was similar to ten years before. No vegetations were noted. With the clinical presentations mentioned above meeting the modified Duke criteria, the patient was diagnosed with infective endocarditis complicated with brain abscess.

As the fever subsided under four week ceftriaxone treatment, the patient was discharged with oral linezolid for continuing treatment of brain abscess. Linezolid was continued two weeks later. The MRI of brain examination three months later showed reduced in size of the abscess and the peripheral enhancement had disappeared.

Discussion

In this case, mitral regurgitation associated with mitral valve prolapse was a predisposing condition for infective endocarditis. As a community-acquired endocarditis, viridans group *Streptococci* stand for the most common pathogen. Some species of the group have a

proclivity to produce abscess formation and metastatic infection foci, both within the heart and in extracardiac locations. In comparison to other pathogens, extracardiac manifestations may be the only presentation without significant valvular destruction.
The extracardiac complications with central nervous system involvements carries a higher morbidity and mortality. They are classified into the following: meningitis/encephalopathy, ischemic events, cerebral hemorrhage, and brain abscess. Among neurological complications, brain abscess was rare and no previous cases of endocarditis associated brain abscess had been reported with *S. cristatus*. Therefore, we shared the first case of *S. cristatus* endocarditis induced brain abscess.

Conclusion

Among patients with viridans group *Streptococci* bacteremia and brain abscess, careful history taking and physical examination are essential to determine if endocarditis is present. Once diagnosed, treatment should be carried out promptly and adequate follow-up strategies be proposed.

病例報告　112_C 48

腹膜透析癌症患者接受 Cabozantinib 併發罕見 Hungatella Hathewayi 腹膜炎成功保留腹膜透析之個案報告

Unveiling Rare Hungatella Hathewayi Peritonitis and Successful Preservation of Peritoneal Dialysis Following Cabozantinib Treatment: A Case Report

李思霈 [1] 林詩怡 [2]
中國醫藥大學附設醫院 [1] 內科部 [2] 內科部腎臟系

Introduction

In recent years, the landscape of cancer therapy has undergone a revolutionary transformation, offering newfound hope to patients grappling with various malignancies. Traditional treatments, such as chemotherapy and radiation therapy, have been integral in cancer management; however, they often come with a plethora of side effects and limited specificity. The advent of targeted therapies, dendritic cell therapies, immunotherapy, and radiopharmaceuticals, et al, which exploit molecular markers or immune cells to selectively inhibit cancer cell proliferation, has marked a significant leap in improving patient outcomes with fewer claimed off-target effects. Patients undergoing dialysis are at an elevated risk of developing cancer, and furthermore, they exhibit a higher likelihood of presenting with advanced-stage malignancies. Consequently, patients on dialysis have increased accessibility to these advanced treatment regimens than ever before. However, it is worth noting that the complications of these cancer treatments as well as how to manage the complications in the context of dialysis are infrequently reported in the scientific literature, especially those receiving peritoneal dialysis. It should be emphasized that the management of treatment-related complications in cancer patients undergoing dialysis, particularly those on peritoneal dialysis, is less frequently addressed in scientific literature compared to non-dialysis populations.

In this report, we present a patient undergoing peritoneal dialysis for renal cell carcinoma (RCC) metastasis, who developed an uncommon instance of Hungatella hathewayi peritonitis after receiving treatment with Cabozantinib, and successfully cured with preserving peritoneal dialysis.

Case presentation

A 76-year-old male with a history of ESRD on peritoneal dialysis, metastatic clear cell renal cell carcinoma with lung and T6 metastasis receiving oral Cabozantinib, hypertension, and type 2 diabetes, presented to the emergency department with diffuse abdominal pain, fever, chills, nausea, and vomiting. Peritoneal effluent was turbid. Laboratory investigations showed pancytopenia and elevated hsCRP levels. Ascites analysis revealed leukocytosis with a predominance of neutrophils. The patient was admitted to the nephrology ward under the diagnosis of CAPD peritonitis.

Upon admission, empirical antibiotics were initiated, comprising intraperitoneal Cefepime (1000 mg QD) and Vancomycin (1500 mg Q5D). Ascites culture subsequently isolated Hungatella hathewayi, necessitating the addition of intravenous Metronidazole (500 mg Q12H) to the treatment regimen. Despite this antimicrobial therapy and termination of Cabozantinib, persistent leukopenia and hypotension indicated that severe sepsis was unlikely the singular

etiological factor. Granulocyte Colony-Stimulating Factor (G-CSF) was administered on the fifth day post-admission, and colloid fluid resuscitation with albumin was employed for a four-day duration.

Hemodynamic status improved without the necessity for additional vasopressor support and the decline in ascites white blood cell (WBC) count to less than 100 cells/mm³ was also noted. (Table 1)

The patient remained on a tailored antibiotic regimen under stringent monitoring. Over a three-week interval, consistent clinical and laboratory improvements were observed, including the resolution of pancytopenia and stabilization of vital signs. The patient was discharged upon the successful completion of the antibiotic course. The patient continued to undergo peritoneal dialysis smoothly, without any observed impairment to the peritoneal membrane's permeability function.

Table 1. Serial Changes in Ascites Routine Parameters in the Patient During the Treatment Period with Hungatella Hathewayi Peritonitis

	Day 2	Day 5	Day 9	Day 13
G-CSF administration		Start	End	
Ascites routine				
Appearance	Cloudy	cloudy	clear	clear
Color	yellow	Light-yellow	Light-yellow	Light-yellow
RBC count	1242	91	83	7
WBC count	2419	1374	150	46
Differential count (%)				
Neutrophil	92	88	58	34
Lymphocyt	1	5	23	47
Monocyte	6	6	15	17
Eosinophil	1	1	3	2
Basophil	0	0	1	0

Discussion

In the context of the presented case, Hungatella hathewayi emerges as a seldom-observed pathogen in peritonitis episodes. Our observations suggest that the patient's oral regimen of Cabozantinib, a tyrosine kinase inhibitor typically prescribed for metastatic clear cell renal cell carcinoma, may have played a pivotal role in the onset of pancytopenia, subsequently heightening the patient's susceptibility to peritonitis.

Given that Hungatella hathewayi, this Gram-positive, endospore-forming, rod-shaped bacterium, is also as an glycosaminoglycan-degrading firmicutes in the human gut, it is reasonably postulated that the route of peritonitis infection in this patient stemmed from gastrointestinal tract translocation of Hungatella hatheway.

In this case, several mechanisms facilitate the translocation of bacteria from the gastrointestinal tract, including but not limited to intestinal bacterial overgrowth, deficiencies in host immune defenses, and impairment of the intestinal barrier integrity. Diarrhea is a prevalent adverse effect associated with Cabozantinib treatment, manifesting in approximately 72–75% of patients. This occurrence is potentially attributable to the high expression levels of Vascular Endothelial Growth Factor (VEGF) and Vascular Endothelial Growth Factor Receptors (VEGFR) in the intestinal tissue, which may result in mucosal disruption. Additionally, although less common, myelotoxicity represents another clinically significant adverse event linked to Cabozantinib use, elevating the risk for infection and possible sepsis.

In the present study, we observed a marked improvement in patient hemodynamics following the administration of granulocyte colony-stimulating factor (G-CSF). Specifically, a gradual stabilization of hemodynamic parameters was noted, corroborated by the decline in ascites white blood cell (WBC) count to less than 100 cells/mm³. These findings not only substantiate the efficacy of G-CSF in modulating the host immune response but also lend credence to our hypothesis regarding the septic condition observed in this case. We suspect that the sepsis

is linked to the myelotoxic effects of Cabozantinib. Termination of Cabozantinib administration, coupled with targeted antibiotic intervention and G-CSF use, has been shown to effectively resolve the infection in our patient.

Conclusion

We report a unique case of Hungatella hathewayi peritonitis in a patient with ESRD on peritoneal dialysis following the administration of Cabozantinib for metastatic clear cell renal cell carcinoma. Prompt recognition, discontinuation of the offending medication, and appropriate antibiotic therapy were crucial in achieving a favorable outcome. This case highlights the importance of vigilant monitoring and consideration of medication-related complications in patients with complex medical histories. The safety implications of these advanced cancer therapies in the dialysis population extend beyond merely assessing their therapeutic efficacy and call for more comprehensive awareness of related complications.

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病例報告　112_C 49

一位嚴重類鼻疽感染導致之敗血性休克及使用葉克膜輔助救治之個案

A case of fulminating melioidosis resuscitated by the assistance of venoarterial extracorporeal membrane oxygenation

姚京含[1] 陳智皓[2] 吳秉儒[3]
中國醫藥大學附設醫院[1]內科部 [2]內科部感染科 [3]內科部胸腔暨重症系

Introduction

Melioidosis, caused by intracellular Gram-negative pathogen *Burkholderia pseudomallei*, is endemic in Southeast Asia and Northern Australia. This organism is widely distributed in soil or surface water in endemic regions. However, the true worldwide incidence is unknown because a large proportion of infection is likely to be underdiagnosed in resource-limited area[1]. The main routes of transmission include direct skin inoculation, inhalation and ingestion. Melioidosis is known as " the great mimicker " because of its manifestations, ranging from localized skin lesions, pneumonia and organ abscess to fulminant septic shock[2]. In Taiwan, the endemic regions are southern and central suburban and rural areas. The peak incidence in 5 years happened in 2019 after typhoon strike with cluster of cases[3]. We reported a case of melioidosis complicated with septic shock and cardiac arrest. Extracorporeal cardiopulmonary resuscitation (ECPR) was applied for sepsis-induced cardiogenic shock and helped the patient survive this catastrophic event.

Case presentation

The patient is a 66-year-old male construction worker with past history of primary hypertension and gouty arthritis. He presented to our emergency department (ED) with intermittent fever for 7 days and intolerable dyspnea for 1 day. He complained muscular soreness, rhinorrhea and cough with purulent, sticky yellow sputum in recent days. On arrival at ED, the temperature was 37.3°C, the pulse 134 beats per minute, the blood pressure 148/72mmHg, the respiratory rate 22 breaths per minute, and oxygen saturation 78% while he was breathing ambient air. On examination, crackles were heard over bilateral lung without heart murmur. No skin rashes or wound were disclosed. He did not contact ill people or traveled to rural area nor contact soil directly with skin but he was breeding pigeons at home. Chest radiograph revealed that there were diffuse nodular lesions over bilateral lung fields and the density increased in the lower area (Figure 1-A). Complete blood count showed leukocytes: 17700/L, neutrophils: 95.4%, red blood cells (RBCs): 2860000/L, hemoglobin (Hb): 7.9g/dL. Biochemical tests revealed high sensitivity C-reactive protein (hsCRP): >40mg/dL, alanine transaminase (ALT): 45U/L, creatinine (Cr): 9.05mg/dL, sodium (Na): 134mmol/L, potassium (K): 5.3mmol/L, lactate: 26.0mg/dL. Venous blood gas showed pH: 7.26, pCO2: 22mmHg, pO2:109mmHg under FiO2:100%, bicarbonate: 9.9mmol/L, BEvt: -15.6mmol/L. However, the patient was found to be unresponsive and pulseless during the computed tomography (CT) scan (Figure 2). Cardiopulmonary resuscitation was activated and he gained return of spontaneous circulation (ROSC) 43 minutes later. Profound shock after using vasopressor and low cardiac output were found thus venoarterial extracorporeal membrane oxygenation (ECMO) was placed. He was transferred to intensive care unit and high dose norepinephrine was used. We chose initial antibiotics regimen with ceftriaxone plus

levofloxacin for septic shock caused by community-acquired pneumonia with septic emboli. Continuous renal replacement therapy was started for his acute kidney injury and severe metabolic acidosis. 4 days later, the blood culture showed the growth of *Burkholderia pseudomallei* and we changed the antibiotics to ceftazidime plus levofloxacin for more than 8 weeks. Oral trimethoprim-sulfamethoxazole (TMP-SMX) plus levofloxacin was used for eradication. Echocardiography showed left ventricular ejection fraction (LVEF) around 18.7% on day 3 and severely reduced biventricular systolic function. Transesophageal echocardiography (TEE) performed 2 days later revealed no vegetation on valves and LVEF already improved to around 30%. We let the patient weaned from ECMO with improved LVEF >40% on hospitalization day 10. His consciousness recovered without impairment was transferred to ordinary ward for future eradication therapy. Positron emission tomography/computed tomography (PET/CT) scan showed no evident metastatic infection sites. He was finally discharged after hospitalization for 3 months and chest X-ray showed resolution of pulmonary lesions (Figure 1-B).

Figure 1. (A) Chest x-ray on admission day with diffusely distributed nodular lesion over bilateral lung fields (B) Chest x-ray 2 months later after treatment showed resolved septic emboli.

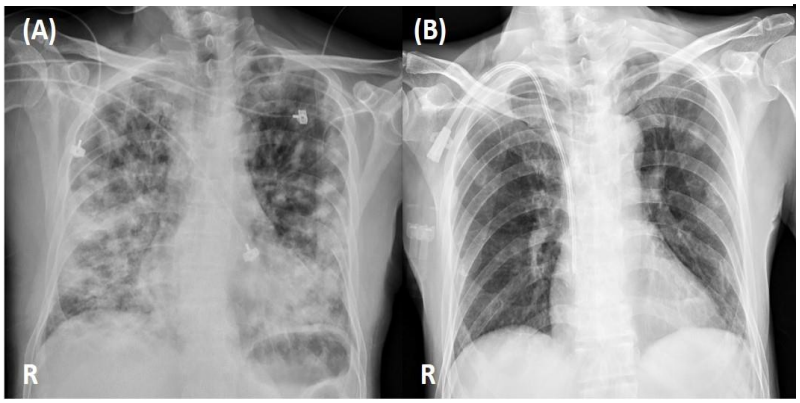
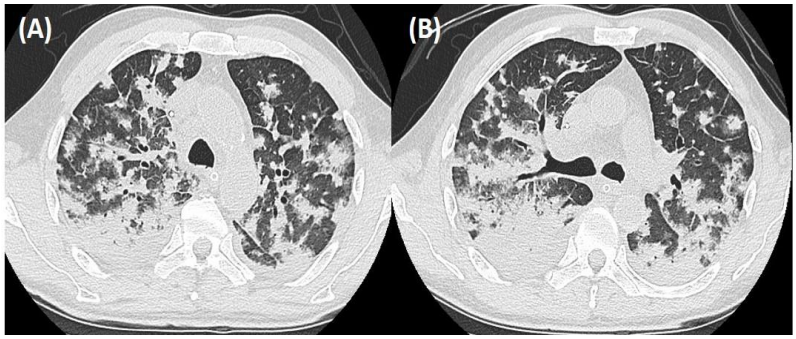


Figure 2. (A)(B) Different cross-section views of chest computed tomography on admission day with diffuse septic emboli and bilateral consolidations.



Discussion

Melioidosis is a possible cause which should not be forgotten of severe community-acquired pneumonia in Taiwan. It confers high mortality ranging 10-50%[4] and was usually unidentified initially or kept in the physician's mind, which may lead to inadequate treatment. In this case, we kept the empirical antibiotics until positive report of *Burkholderia pseudomallei*. If not with levofloxacin, this patient would probably miss the chance to survive. There was identical pathogen isolated from the sputum. Occupational exposure with inhalation of pathogen was highly suspected. Comorbidities, in one aspect, determine the severity and fatality of melioidosis[4-6]. This patient's glycated hemoglobin A1c (HbA1c) level is 5.7% and may have chronic kidney disease based on his bilateral small kidney sizes (around 7cm in the longest axis). In the Darwin prospective study, 27% of melioidosis patients have different extent chronic kidney diseases[4].

Pneumonia is the most common form of melioidosis and accompanied with the 63% of concurrent bacteremia[7]. Besides, multilobar presentation is associated with poor prognosis[8]. Our case presenting diffuse discrete lesions was a rather fulminant form. This pathogen was reported to hide inside human body for a long period and cause relapse of the disease. In

Australia, the recurrence rate is reported at 5.7% with a median time to relapse of 9.4 months (range, 3.6 to 28.0)[9]. Recurrent *Burkholderia pseudomallei* bacteremia was recorded 2 months later. There was no presence of resistance and his clinical condition was stable except recurrent fever. Emergence of resistance during therapy has been documented with all the therapeutic options[12-18] and practitioner should be alert to the signs of infection relapse. In 2023, Wu et al reported a case of melioidosis with emergence of resistance to levofloxacin and meropenem during treatment period. Amino acid substitution in GyrA and deletion in AmrR responsible for quinolone and carbapenem resistance respectively were identified[19]. This case highlights the importance of adequate empirical treatment for a severe community-acquired pneumonia (CAP) patient with unusual pattern and the clinician's alertness to endemic diseases.

Conclusion

Melioidosis should be considered for severe CAP in endemic regions. Though resistant strains were reported occasionally in Taiwan, *Burkholderia pseudomallei* were largely susceptible to carbapenems, ceftazidime but fluoroquinolones were unknown. Venoarterial ECMO could be life-saving in strictly selected patients with severe septic shock combining cardiac dysfunction after infection. More meticulous studies are urgently needed to define exact hemodynamic parameters which could recognize the potential sepsis patients requiring VA-ECMO support.

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病例報告　112_C 50

個案報告: 在一位七十歲女性以血便為臨床表現的十二指腸鉤蟲感染

Case report: Ancylostoma duodenale infection with presentation of bloody diarrhea in a 67-year-old female

姚京含[1]　江承源[2]

[1] 中國醫藥大學附設醫院-內科部　[2] 亞洲大學附設醫院-內科部消化系

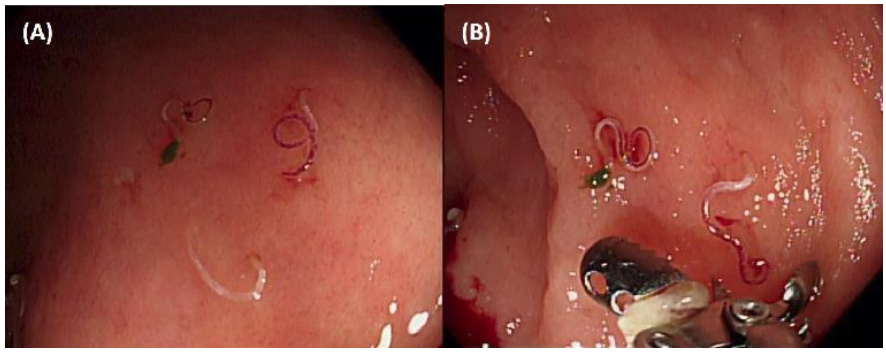
Introduction

Hookworm infection is prevalent in tropical and subtropical areas such as the Middle East, Southeast Asia and tropical Africa. However, owing to the improvement of environment, sanitation and hygiene after the advent of the 21st century, parasitic infections are disappearing in developed countries. Intestinal hookworm disease in humans is caused by *Necator americanus, Ancylostoma duodenale,* and *A. ceylanicum*. *A. duodenale* and *N. americanus* were considered the two primary intestinal hookworm species worldwide, but *A. ceylanicum*, is also emerging parasite infecting humans in some regions according to newer studies[1]. It is recognized as the only zoonotic hookworm that can mature into adult stage[2] in human. Other zoonotic species infections, *Ancylostoma caninum*, *A. braziliense,* and *Uncinaria stenocephala* manifest as extraintestinal symptoms like cutaneous larva migrans (CLM). In Taiwan, there are still occasional reports of protozoan and helminthic infections but without comprehensive and detailed statistics in recent years. We report a case of *Ancylostoma duodenale* infection with the presentation of bloody diarrhea and abdominal cramping pain in a 60s woman.

Case presentation

The patient is a 67-year-old housewife and she presented to our emergency department (ED) with intermittent abdominal and diarrhea several times for 3 days. She described the pain as colicky and not related to food intake and persisted even after fasting. She mentioned that her stool appeared watery with mucus and dark red blood. She also complained pruritis and had skin rashes. She denied recent traveling to rural areas, cluster history and walking barefoot in the field but confessed that she had eaten salad containing uncooked vegetables. She visited out patient department at first and oral ciprofloxacin was prescribed under the tentative diagnosis of infectious colitis. Due to persistent symptoms and decreased appetite, she went to our ED for further evaluation.

Figure 1. (A)(B) Hookworm found in the cecum with blood discharged from the mucosa breaks caused by the parasites.



Her initial vital signs were temperature 36.3 Celsius degree, pulse rate 83 beats per minute, blood pressure 126/63 mmHg, respiratory rate 14 breaths per minute, oxygen saturation 98%. Physical examination revealed epigastric mild tenderness, negative rebound pain,

hyperactive bowel sound and no pale conjunctiva. Some rashes were found on her legs and abdomen with scratching scars and scabs formation its nature could not be determined. The hemogram showed mild leukocytosis, microcytic red blood cells (RBCs) and the eosinophilic percentage was significantly elevated (Leukocytes: 12500/ L, neutrophils: 68.9%, eosinophils: 12.9%, hemoglobin: 12.2 g/dL, mean corpuscular volume of RBCs: 64.4 fL). Biochemical tests showed mild hypokalemia (Potassium: 3.4 mmol/L) without other significant abnormalities including normal liver enzymes, high sensitivity C-reactive protein, blood urea nitrogen, and creatinine level. She was admitted under the impression of infectious colitis and intravenous (IV) antibiotics ciprofloxacin was given. Her epigastric pain improved after symptomatic treatment but she still presented intermittent red and loose stool with much fluid discharge.

We arranged esophagogastroduodenoscopy (EGD) for her but it only showed mild superficial gastritis without active bleeding lesions. Therefore, a colonoscopy was conducted and an unexpected diagnosis was made. At the site 80cm distal from the anal verge, there were multiple white, linear and crawling creatures (Figure 1 (A)(B)). Hookworm infection of the cecum was suspected and biopsy of the tissue confirmed the ancylostomiasis. Microscopic examination disclosed parasites eggs and larvae in the stool specimen. Mebendazole 100mg, BID was prescribed for 3 days and the patient's diarrhea improved without recurrence. 2 weeks later, hookworm eggs were eliminated from her stool.

Discussion

Soil-transmitted helminths (STH) diseases are more prevalent in the tropics and subtropics. It is estimated that approximately 500 million people are infected with hookworms worldwide[3]. Globally, hookworm infections exert a major impact on morbidities rather than mortality[4,5]. However, the exact annual incidence and prevalence of local populations are unknown due to lack of formal statistics. Most epidemiological studies are conducted in low-income countries. There was one nationwide survey of China in 2014 to 2015 and reported weighted prevalence of STH was 4.49% (95% confidential interval (CI): 2.45%-6.53%), including 2.62% (95% CI: 0.86%-4.38%) hookworm infections. Out of 3,579 hookworm cases with species differentiation, 479 cases (13.38%) were infected with only *Ancylostoma spp.*, 2,808 cases (78.46%) with only *Necator americanus*, and another 292 cases (8.16%) with both species[6]. Probably due to rare incidence, there was no similar studies or related fromal statistics in Taiwan after 2000.

Humans acquire ancylostoma infection mainly from cutaneous penetration of larvae when contacting contaminated soil barefoot. Notably, *A. duodenale* could infect the human host by oral ingestion[7] and directly mature inside the small intestine. After breaking the integument, the larva migrated into the blood vessels, carried to the heart and then the lungs. They exit the circulation of the lungs, coughed out and then swallowed into the digestive tract[1]. They developed into adult worms that feed and breed in intestines. Clinical manifestations range from cutaneous pruritic maculopapular eruption, migration tracks, cough to unspecific gastrointestinal symptoms. Some articles described *A. duodenale* as "wasteful feeder" that differs it from *N. americanus* with heavier blood loss in clinical manifestation[8,9]. The gastrointestinal symptoms usually develop 5-9 weeks after the initial infection. Finally, chronic and high-burden hookworm infection leads to iron deficiency, protein loss, and malnutrition.

Diagnosis mainly relies on stool examination which eggs are detected and unexplained

eosinophilia may be a clue. Polymerase chain reaction (PCR) assays were also invented commercially with superior sensitivity[10-12]. In our case, colonic infestation of *A. duodenale* is a rather atypical presentation of the hookworm infection though there were already cases reported[13-15]. The first-line treatment is benzimidazoles and albendazole is preferred. Comparative studies and Meta-analysis[16] showed a higher cure rate of up to 80% when using albendazole. The mebendazole cure rate decreased to only 15% in a WHO report[17]. Our patient received the treatment and eggs were not detectable 2 weeks later.

Conclusion

Hookworm infection is also a possible diagnosis of diarrhea in rural and endemic regions in Taiwan. *Ancylostoma duodenale* could reside in the cecum and colon, though the upper GI tract predominates. Benzimidazoles is the mainstay of anthelmintics but healthcare practitioners should beware of its variable efficacy and risks of treatment failure. Albendazole 400mg daily is the recommended choice.

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病例報告　112_C 51

新冠病毒感染及使用瑞德西韋後相關之急性胰臟炎

Acute pancreatitis following SARS-CoV-2 infection and the use of Remdesivir

姚京含[1] 陳永芳[2] 楊凱介[3]
中國醫藥大學附設醫院 [1]內科部 [2]醫學影像部 [3]內科部風濕免疫科

Introduction

In the era of the COVID-19 pandemic, respiratory tract infections have emerged as the primary clinical manifestation of this rapidly spreading disease. The SARS-CoV-2 virus binds to the ACE2 receptor on cell surfaces and enters epithelial cells after priming the spike protein with TMPRSS2[1]. Notably, ACE2 receptors are expressed in various organs, including the kidneys, gastrointestinal tract epithelial cells, and pancreatic acinar cells[2]. While there have been case reports documenting the incidence of pancreatitis following SARS-CoV-2 infection[3-6], there is still a lack of well-designed, large-scale epidemiological studies on this matter[7-8]. The issues of prevalence, the precise mechanism, and risk factors for COVID-19-related acute pancreatitis remain unresolved to date. Some case reports have also suggested that pancreatitis could be triggered by the use of antiviral medications, such as Remdesivir[9-12]. In this context, we present a case of acute pancreatitis that occurred after SAR-CoV-2 infection. The patient received Remdesivir during hospitalization and subsequently developed acute pancreatitis.

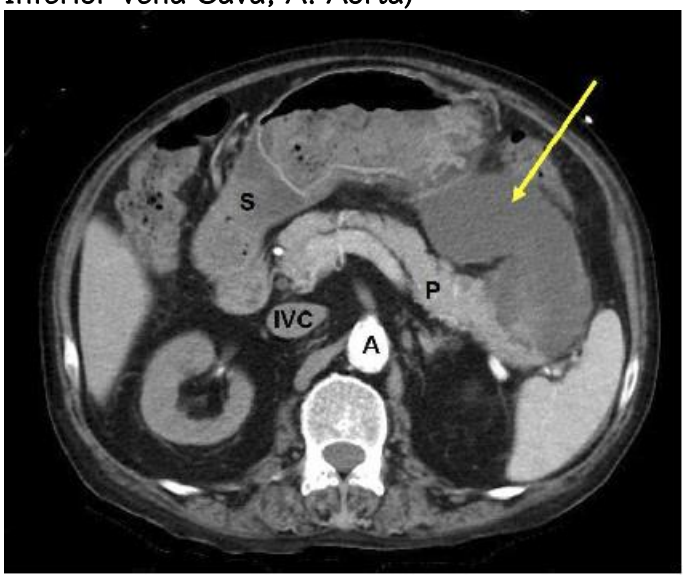
Case presentation

A 61-year-old married man with medical history of systemic lupus erythematosus (SLE) diagnosed for 6 years, with presentation of nephritis (patient refused renal biopsy), positive of anti-nuclear antibodies positive (ANA+: 1:160x speckled pattern), anti-Smith (anti-SM) antibodies, and exhibited low complement level (C3 and C4), along with thrombocytopenia at other hospital. He had been receiving regular outpatient treatment consisting of methylprednisolone (6mg daily) and mycophenolic acid (360mg twice daily). On April 22, 2023, he was admitted through the emergency department for community- acquired pneumonia (CAP). Yet, his condition worsened and he was intubated for respiratory failure due to *Pneumocystitis jiroveci* pneumonia and decompensating congestive heart failure. Since then, he received regular hemodialysis. Pneumonia improved after prescription of piperacillin-tazobactam and trimethoprim-sulfamethoxazole. His SLE remained relative stable, with negative ANA, anti-DS-DNA, and normal complement level during admission. He was extubated and transferred to regular ward on 17 May, 2023.

On May 23, 2023, the patient experienced intermittent fever spikes, sore throat, and myalgia. A diagnosis of COVID-19 was confirmed through a positive nasopharyngeal swab SARS-CoV-2 antigen test. In response, Remdesivir was administered for a 4-day course to manage moderate COVID-19 symptoms. Remarkably, the patient's fever and discomfort significantly improved by the second day of treatment. However, four days after completing the Remdesivir therapy, the patient suddenly developed acute epigastric pain and tenderness in the left upper quadrant, accompanied by rebounding pain. Laboratory tests indicated elevated levels of amylase (429 U/L; normal range: 29-103 U/L), lipase (416 U/L; normal range: 8-58 U/L), AST (60 U/L; normal range: 50-40 U/L), ALT (51 U/L; normal range: 50-40 U/L), Alk- P (151 IU/L;

normal range: 38-126 U/L), r-GT (245 U/L; normal range: 8-50 U/L), hsCRP (5.65 mg/dL; normal: <1.0 mg/dL), triglycerides (222 mg/dL; normal: <150 mg/dL), and total bilirubin (0.48 mg/dL; normal range: 0.2-1.3 mg/dL). The platelet count was reduced (124 x 10^3 /μL; normal range: 130-400 x 10^3/μL), but prothrombin and activated partial prothrombin times remained within normal limits. Further investigation via contrast-enhanced abdominal computed tomography (CT) revealed pancreatic swelling with adjacent fat stranding and a heterogeneous density mass lesion at the pancreatic tail, suggesting the presence of a hematoma (see Figure 1). Notably, there were no gallstones or common bile duct dilatation. In response, percutaneous drainage was performed, yielding dark-red effusion. A drainage tube was inserted to facilitate continuous drainage.

Figure 1. Contrast-enhanced abdominal computed tomography (CT): Hematoma formation (indicated by an arrow) around the pancreas tail with hypodense content and partial contrast enhancement, consistent with acute necrotic fluid accumulation (S: Stomach, P: Pancreas, IVC: Inferior Vena Cava, A: Aorta)



However, no microorganisms were cultured from the effusion. The patient was ultimately diagnosed with acute pancreatitis complicated by necrosis and a hematoma located at the pancreatic tail. Conservative therapy was administered, and the hematoma gradually resolved before the patient's discharge. Given the patient's history, imaging, and lab results, this acute pancreatitis episode could be associated with either COVID-19 or Remdesivir treatment.

Discussion

In this case, the intra-abdominal event was unexpected and complicated the care of this patient, who has multiple underlying diseases. The etiology of acute pancreatitis was typically confirmed by exclusion. Abdomen CT showed neither gallstones nor bile duct/pancreatic duct dilatation. Although no further examinations, such as endoscopic ultrasonography (EUS) or magnetic resonance cholangiopancreatography (MRCP), were conducted to rule out possible microlithiasis or bile tract abnormalities, there was no history or clinical symptoms/signs of biliary tract lithiasis or obstruction. Furthermore, he experienced acute onset of abdominal pain just four days after receiving Remdesivir and with a recent COVID-19 infection; thus, his pancreatitis was highly related to COVID-19 infection or drug-induced. We checked the SARS-CoV-2 PCR of the drained fluid, but it was negative, even though there was a record of a positive result before[13]. A possible explanation for pancreatitis associated with COVID-19 is that the SARS-CoV-2 virus enters pancreas acinar cells, causing inflammation and swelling of pancreas tissue. The release of digestive enzymes destructed the cells and led to the development of pancreatitis. The question of whether the incidence of pancreatitis is higher in COVID-19 patients is still debated[7,14]. The incidence rate of pancreatitis in COVID-19 patients is 0.27%, as reported in the retrospective cohort study published by S. Inamdar in 2020[7]. Among the patients with pancreatitis, 69% were idiopathic. A meta-analysis reported that the prevalence of post-COVID-19 acute pancreatitis is around 6.7%, with idiopathic

pancreatitis comprising a larger proportion than in the group without COVID-19. The mortality rate and disease severity were also increased in the COVID-19 group[15]. Regarding Remdesivir-induced pancreatitis, however, there were scanty case reports, and establishing a causality link between the drug and pancreas destruction, let alone the mechanism, is challenging. Remdesivir was the only suspected drug in nine cases, and the time to onset of pancreatitis ranged from one to nine days, with a median of four days[16]. This study highlights the possibility of acute pancreatitis occurring four to five days after the administration of Remdesivir, even in patients without underlying diseases[17]. Therefore, further research is needed to fully understand the relationship between Remdesivir and acute pancreatitis during therapy for COVID-19 infection.

Conclusion

Extrapulmonary manifestations and gastrointestinal (GI) symptoms are frequent among COVID-19 patients. SARS-CoV-2 and Remdesivir should be considered as possible causes of acute pancreatitis if other common etiologies have been ruled out, such as gallstones, alcohol, hyperlipidemia, or autoimmune diseases. Well-conducted studies on the relationship and precise molecular mechanisms of pancreatitis with COVID-19 or Remdesivir are still needed.

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病例報告　112_C 52

麩質敏感性腸病與類肉瘤症並存: 一個罕見的案例報告

Celiac disease concomitant with sarcoidosis: Report of a rare case

朱襄[1] 周仁偉[1,2] 洪偉哲[1,3] 陳旆聿[4]
中國醫藥大學附設醫院 [1]內科部 [2]消化醫學中心胃腸科 [3]風濕免疫科 [4]病理部

Introduction

Celiac disease is mainly prevalent in Western countries due to the consumption of wheat-based diets, whereas in Asia, it is relatively rare due to the rice-based diet culture. However, the popularity of wheat-based diets in Asia, due to the introduction of Western dietary habits, has led to an increase in the prevalence of abdominal diseases. Moreover, sarcoidosis is a systemic inflammatory disease that can affect any organ in our body. In this present report, we introduce a rare case of refractory celiac disease, despite maintaining a gluten-free diet. This case subsequently developed sarcoidosis and treatment-related small bowel perforation.

Case Presentation

A 56-year-old male with a history of beta-thalassemia presented to our hospital because of several months' history of watery diarrhea. Moreover, he also had a weight loss of 20 kilograms and poor appetite. Esophagogastroduodenoscopy and colonoscopy performed and showed no definite diagnosis. After hospitalization, laboratory tests showed positivity of neutral fat in his stool, anemia (hemoglobin 9.2 g/dL), hypoalbuminemia (albumin: 3.1 g/dL), and elevated ESR (118 mm/hour), indicating steatorrhea with a hidden chronic inflammatory bowel disease. We performed double-balloon enteroscopy and found diffuse edematous and erythematous mucosa with short villi in the jejunum and ileum (Figure 1). Multiple biopsy specimen from the small intestine were taken for pathology. Histopathology of biopsy specimens revealed diffuse and marked villus blunting, increased lymphoplasma cells in the lamina propria, and scattered intraepithelial lymphocytes, supporting the diagnosis of celiac disease (Figure 2). In addition, we checked the serum profiles of celiac disease and found a 15-fold increase of the upper normal limit of anti-tissue transglutaminase IgA.

Figure 1 Double-balloon enteroscopy demonstrated diffuse edematous and erythematous mucosa with short villi in the jejunum (left) and ileum (right).

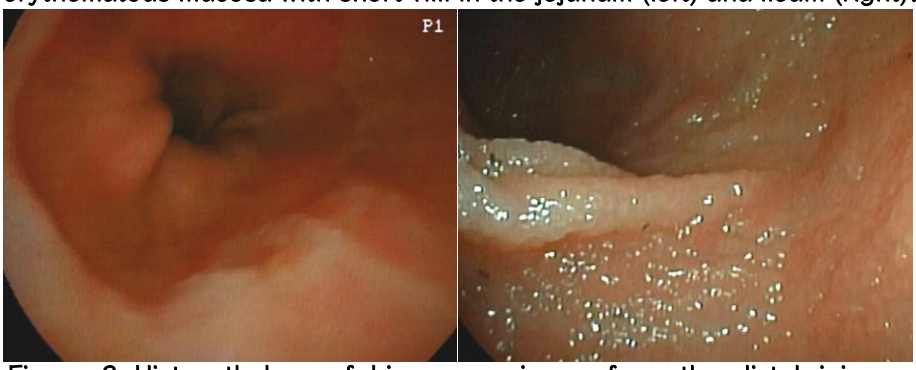
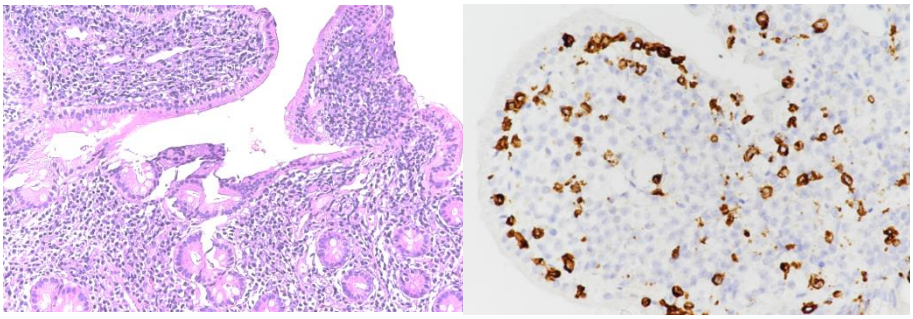


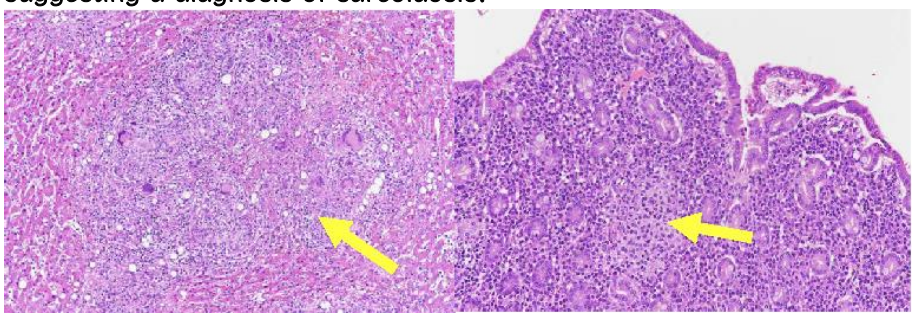
Figure 2 Histopathology of biopsy specimens from the distal jejunum showed marked villus blunting, increased lymphoplasma cells in the lamina propria (left) and scattered intraepithelial lymphocytes (right). Intraepithelial lymphocytes (IEL): 23/per 100 enterocytes.



The patient was kept on a gluten-free diet in the subsequent year, and his diarrhea improved. However, the diarrhea relapsed and became refractory despite the gluten-free diet in the next year. Abdominal computed tomography scan showed several hypervascular nodules in the right lobe of the liver. Moreover, wall thickening of the small bowel and lymphadenopathy adjacent to the mesenteric artery were also identified. Histopathology of a biopsy specimen from the liver nodule showed non-caseating granulomatous inflammation, consistent with sarcoidosis (Figure 3). We started steroid therapy for his sarcoidosis. However, the patient suffered from small bowel perforation two weeks later and underwent emergency laparotomy. Histopathology of specimens from the resected small intestine also showed sarcoidosis with focal involvement (Figure 3). We attributed this to the significant response of intestinal sarcoidosis to steroid therapy. Despite the nutrient support and a gluten-free diet, the patient died of malnutrition several months later.

Discussion

Figure 3 Histopathology showed non-caseating granulomas (yellow arrows) in the liver (left) and the resected small intestine (right), suggesting a diagnosis of sarcoidosis.



Celiac disease is once considered a disease that only affects people in Western countries due to their dietary habits. However, as Western diets have become more popular in Asia, celiac disease is no longer rare in this region. A meta-analysis conducted by Singh P et al found that the seroprevalence and the prevalence of celiac disease in Asia are 1.6% and 0.5%, respectively[1]. The diagnosis of celiac disease is mainly based on small bowel biopsy and serum tests[2]. Clinical symptoms of celiac disease include chronic diarrhea, steatorrhea, bloating, indigestion, constipation, and weight loss[3]. When a patient presents with symptoms similar to celiac disease, clinicians should start by checking the serum anti-tissue transglutaminase IgA level[2]. Tissue transglutaminase repairs intestinal mucosal breaks and prevents gluten from penetrating into the body. Once gluten enters the human body, it is transformed into deamidated gliadin. A 10-fold increase in the upper normal limit of anti-tissue transglutaminase IgA is considered significant[4].

The presence of DQ2 and DQ8 haplotypes enables the presentation of gluten antigens by antigen-presenting cells[2]. This can trigger an immune response and lead to the onset of celiac disease. The combination of serum anti-tissue transglutaminase IgA level, HLA typing, and response to a gluten-free diet is helpful for making the diagnosis[4]. However, IgA deficiency often presents in patients with celiac disease and makes serologic testing unreliable[5]. Enteroscopic biopsy should be performed if clinically and serologically inconclusive. Typical pathological features include intraepithelial lymphocytosis, villus atrophy, and crypt hyperplasia[6].

Sarcoidosis is a multisystem granulomatous disorder that often involves both lung parenchyma and adjacent lymph nodes. Gene-environment interaction plays a major role in the development of sarcoidosis. Once genetically predisposed individuals are exposed to specific antigens, antigen-presenting cells activate downstream T cells and cause the release of several cytokines and chemokines[7]. Finally, a granuloma consisting of a core of multinucleated giant cells surrounded by CD4+ T cells and some CD8+ T cells is formed[7]. The

class II haplotype HLA-DR3/DQ2 has been proven to be related to both sarcoidosis and celiac disease[8]. Therefore, a patient with celiac disease carries a higher risk of sarcoidosis. Likewise, patients with a prior history of sarcoidosis should be screened for celiac disease if they present with typical symptoms. Although the coexistence of celiac disease and sarcoidosis is uncommon, our case supports this hypothesis. The question of whether to screen for celiac disease as a routine in patients with sarcoidosis is currently under discussion[9].

Conclusion

The prevalence of celiac disease has grown in recent years due to the popularity of Western dietary habits. The concomitant expression of celiac disease and sarcoidosis might influence the treatment protocol. Regardless of whether it is celiac disease or sarcoidosis, once a patient is diagnosed with one of them, we should be alert to the other one.

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病例報告　112_C 53

心臟射頻消融術後之食道心包膜簍管，一個少見但致命的併發症

Post radiofrequency catheter ablation esophageal-pericardium fistula, a rare and fatal complication

朱襄[1]　吳宏彬[1,2]

[1]中國醫藥大學附設醫院內科部 [2]中國醫藥大學附設醫院心血管系

Introduction

Atrial fibrillation (AF) is a common tachyarrhythmia in elderly patients. Radiofrequency catheter ablation (RFCA) is considered the preferred treatment for patients with both atrial fibrillation and heart failure with reduced ejection fraction[1]. However, RFCA itself carries the risk of causing thermal injury to the atrium and esophagus. Atrio-esophageal fistula (AEF) or pericardial-esophageal fistula (PEF) is a rare complication of RFCA, and its mortality rate is extremely high[2]. In this report, we present a case of pericardial-esophageal fistula following RFCA. This case highlights the importance of early surgical debridement in such cases and underscores the need for vigilant thermal monitoring during RFCA.

Case Presentation

A 66-year-old male presented to our hospital with progressive exertional dyspnea. Holter's EKG showed paroxysmal atrial fibrillation and atrial flutter. Echocardiography revealed heart failure with reduced ejection fraction (HFrEF) and bilateral atrial enlargement. Left ventricular ejection fraction was measured at 31.1%, with a wall motion severity index of 2 and a left atrial volume index of 51.75 cm^3/m^2. Functional mitral regurgitation and tricuspid regurgitation were also observed. We performed ablation of the cavotricuspid isthmus and bilateral pulmonary vein isolation (Figure 1), which resulted in successful ablation and exclusive one-way conduction from the atrial septum to the right low atrium during left atrium pacing. However, 19 days after RFCA, the patient complained of acute onset chest pain. Physical examination revealed hypotension, bradycardia, distal heart sounds, and pericardial friction rubs. Emergent CT scan revealed pneumopericardium. Purulent pericardial effusion with food content was drained from the pericardium (Figure 2), and culture of the pericardial effusion soon revealed the growth of Enterococcus faecalis.

We performed sternotomy and irrigated the pericardial space with warm saline, keeping the sternal wound open with passive drainage (Figure 3). During the operation, we used an endoscope to inspect the mucosa but found no remarkable findings. No water leakage was observed in the

Figure 1 Aortic CT revealed pneumopericardium with pericardial effusion(Average Hounsfield units 40.6).

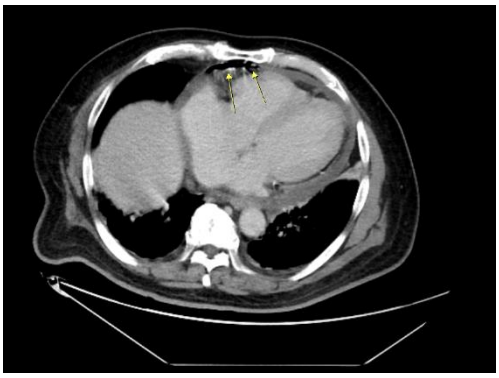
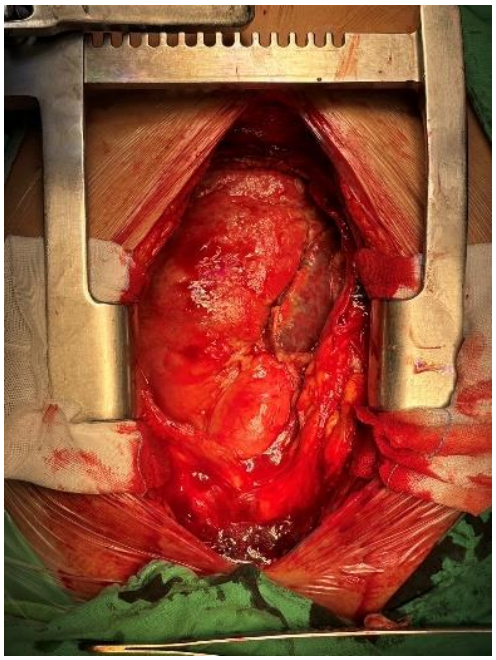


Figure 2 Purulent pericardial effusion.

esophagus when warm saline flowed through the pericardial space. We suspected that the previous catheter ablation had caused delayed thermal injury, resulting in the formation of a transient pericardial-esophageal fistula. The patient developed refractory ventricular tachycardia with cardiogenic shock during treatment and underwent a twelve-day course of V-A ECMO support and a seventeen-day course of mechanical ventilation. Parenteral nutrient support was maintained for twenty days, and a subsequent esophagram revealed no contrast leakage, indicating complete healing of the esophagus. The patient was discharged thirty-two days after the onset of chest pain without any complications. We followed up with this case for three months, during which no recurrent pericarditis, atrial fibrillation or flutter was observed.

Figure 3 After sternotomy, a turbid red pericardial effusion with a significant amount of fibrin coating emerged.



Discussion

AEF and PEF are rare but potentially fatal complications of catheter ablation. The estimated risk of AEF is between 0.03% and 0.08%[3,4]. AEF can occur within a range of 0 to 60 days after the procedure, with a median onset time of 21 days[2]. It can result in active hemorrhage if there is a communicating fistula. Negative pressure during inspiration can also lead to the suction of air or food into the pericardial space, causing air embolization or pericarditis. Clinical symptoms may include fever, neurological symptoms, gastrointestinal bleeding, and chest pain. CT scan is an effective diagnostic tool, with abnormalities detected in around 98% of cases[2]. Although enteroscopy could be a useful method for directly assessing mucosal breaks, it is contraindicated due to the risk of introducing air into the communication, leading to pneumopericardium or air embolization. Approximately 28% of patients experience clinical deterioration either during or shortly after the procedure[2]. In our case, we performed enteroscopy only after opening the pericardium.

Surgical debridement is considered the gold standard treatment and has been shown to decrease mortality to 33% compared to no intervention (97%) or endoscopic stenting (65%)[2]. In cases where surgical sternotomy is contraindicated, esophageal stenting with pericardial drainage may be an alternative option. It is recommended to place a pericardial drainage before performing endoscopy to prevent further hemodynamic instability[5]. Additionally, migration of the esophageal stent remains a concern. To address this, Eitel C. et al suggest using clips to secure the proximal end of the stent tulip and prevent stent displacement.[5] The treatment approach consisted of systemic antibiotics, closure of the communication, and adequate drainage, forming the complete therapeutic paradigm.

Conclusion

AEF and PEF are rare but fatal complications of RFCA (Radiofrequency catheter ablation). Early and adequate surgical drainage should always be considered as the primary treatment option. If a patient is not suitable for surgical intervention, endoscopic stenting with pericardial drainage could be an effective salvage therapy.

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病例報告　112_C 54

第三期肺腺癌接受同步放射化學治療後引起之乳糜胸

Chylothorax after concurrent chemoradiotherapy in lung adenocarcinoma carcinoma

賴致源　鄭文建
中國醫藥大學附設醫院

Case Report

A 62-year-old housewife developed a palpable nodule in right lower neck. Chest radiograph and chest computed tomographic (CT) reveal a mass in RUL up to 8.6 centimeters in diameter. Bronchoscopic biopsy pathology examination showed evidence of adenocarcinoma, T4N3M0, stage IIIc. She was treated with concurrent radiotherapy and systemic chemotherapy consisting of cisplatin, pemetrexed and bevacizumab. Then she received consolidation therapy with durvalumab and pemetrexed.

Fourteen months later, the patient developed chest discomfort and dyspnea. A chest radiograph showed a new right pleural effusion. Durvalumab and pemetrexed was shifted to doxetacel plus ramulizumab due to suspection of progression of disease. Computed tomography (CT) scan of the chest showed an increase in the size of the right pleural effusion and thoracentesis was performed. Pleural fluid analysis showed triglyceride 111 mg/dL consistent with chylothorax. However, no malignant cells were identified on cytology. Positron emission tomography (PET) scan showed no FDG-avid locoregional recurrence nor distant metastasis.

In these two years, she was clinically stable. There was no apparent disease relapse. We believe the chylothorax was caused by concurrent radiotherapy.

Discussion

Chylothorax is usually attributed to congenital abnormalities, trauma, surgery, and neoplastic processes. Radiotherapy is rarely described as a cause of chylothorax[1]. Radiotherapy can lead to narrowing of lymph vessels and impairment of lymph flow. Fibrosis following irradiation is therefore a potential cause of chylothorax. The incidence of chylothorax as a side-effect of other oncological management approaches may rise as use of neoadjuvant or concomitant chemotherapy with radiotherapy increases[2]. This may be due to radiosensitisation by chemotherapeutic agents such as epirubicin, cisplatin, and fluorouracil[1]. Our patient received cisplatin. Treatment options for chylothorax include dietary modification, pleurodesis, retrograde lymphatic embolization and thoracic duct dilation[3].

Post-radiotherapy chylothorax has been described infrequently in the medical literature. A previous study [4] published in 2021 described a case of an 81-year-old man with locally advanced esophageal carcinoma treated with concurrent radiation therapy. After two months. He developed large bilateral chylothorax with severe atelectasis without evidence of recurrence of his malignancy.

A more recent case report [5] published in 2023 reported a case of a 73-year-old male with stage IIIb (T4N3M0) non-small cell lung cancer-adenocarcinoma of the right upper lobe. He developed chylothorax five years after he was treated with concurrent radiation therapy.

There was no malignancy detected in the pleural effusion. This is similar to our case. However, our patient developed chylothorax 14 month after concurrent radiation therapy.
These reports and our case imply that chylothorax in people with mediastinal irradiation is not necessarily a manifestation of disease progression; however, an attempt should be made to exclude a herald of relapse.

Conclusion

Chylothorax is a rare complication that can result from radiotherapy. This diagnosis should be considered in the differential diagnosis in patients present with recurrent pleural effusion after radiotherapy to the mediastinum. Disease progression should be excluded, but chylothorax is not necessarily a manifestation of recurrence.

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病例報告　112_C 55

新冠肺炎後急性腎衰竭為表現的 IgA 腎病變患者

Acute kidney injury in IgA nephropathy who suffered for SARS-CoV-2 infection

黃兆逢[1] 張菀容[1] 張育瑞[2]
[1]中國醫藥大學附設醫院教學部 [2]中國醫藥大學附設醫院腎臟內科

Introduction

SARS-CoV-2 infection has been an important public health issue with a prevalence of 33.7-47.9% globally and high morbidity after the infection. SARS-CoV-2 can cause multiple organ damage including lung, heart (10-20%), kidney (0.5%-29%) and even gastrointestinal tract (12%-61%) via inflammatory pathways, such as angiotensin-converting enzyme 2 (ACE-2) receptors. Within the renal manifestations, glomerulonephritis causes burden with 19.5 -72.9% increased risk of progression to ESRD. IgA nephropathy is one of the most common primary glomerular diseases, with up to 50% in Asian countries. IgA nephropathy, typically characterized by slow progression, can worsen as acute kidney injury (AKI) due to viral upper respiratory tract infections (URI).

So far, there have been some reports, with a total of 6 patients, describing the correlation between IgA nephropathy and SARS-CoV-2. But there has been still no report about AKI event of IgA nephropathy patient after the infection of SARS-CoV-2. Here, we will discuss a case about a patient with IgA nephropathy and SARS-CoV-2 infection complicated with AKI during the infection event.

Case presentation

This is a 25-year-old male with past history of IgA nephropathy and thalassemia came to our hospital due to gross hematuria, left flank pain and mild URI symptoms. Lab data, performed at emergency department showed hematuria (>1000 /uL), pyuria (49 /uL), and mild elevation of hsCRP (1.97 mg/dL). Furthermore, AKI was noted according to the baseline creatinine (0.93mg/dL) and new creatinine (1.48mg/dL). Last but not least, SARS-CoV-2 rapid test showed positive and the PCR result is Liat Ct:13.4. With impression of SARS-CoV-2 infection complicated with AKI, he was admitted for the treatment and quarantine.

After admission, we treated the patient with Molnupiravir and flumarin. After follow-up two days later, the pyuria has improved (11 /uL), as well as the hematuria (127 /uL). Fever also subsided on the third day. Under relative stable status, the patient was discharged and arranged to follow up at the outpatient department. One week later, the follow-up data at outpatient department showed improvement in urine analysis (RBC: 15 /uL; WBC: 4 /uL), ACR (719.55 ug/mg Creatinine), micro albumin (25.4 mg/dL), urine protein (1116.15 mg/g). (Figure 1 and figure 2)

Figure 1

	Creatinine (mg/dL)	GFR (mL/min/1.73㎡)
111/09/02	0.961.48*	95
111/11/19	1.48*	57*
111/11/21	0.90	102
112/01/07	0.92	99

Figure 2

	Creatinine (mg/dL)	Microalbumin (mg/dL)	Protein (mg/dL)	ACR (ug/mg Creatinine)	Urine protein / (creatinine/ 1000) (mg/g)
2022/08/06	41.6	18.7*	29.8*	449.52*	716.35*
2022/11/21	103.3	74.4*	137.8*	720.23*	1333.98
2022/11/30	35.3	25.4*	39.4*	719.55*	1116.15
2022/01/07	39.9	8.8*	15.6*	220.55*	390.98

Discussion

Renal involvement which is related to COVID-19, including increased serum creatinine (SCr), variable degrees of proteinuria and hematuria, or even renal fibrosis. These renal complications have a prevalence from 0.5% in China by Guan et al. to 80% in critically ill COVID-19 patients in France by Rubin et al, which mostly associated with age, sex, or other underlying diseases. Furthermore, when the renal damage progressed to acute kidney injury (AKI), it can contribute to worse outcome at about 5.3-fold higher mortality risk than those without AKI. Moreover, severe renal impairment is more common among patients with chronic comorbid conditions, especially patients with chronic kidney disease, like in our case.

IgA nephropathy (IgAN) is a common primary glomerular disease in Asia area. It can be exacerbated by lots of factors, such as infection episodes, especially upper respiratory and gastrointestinal mucosal infections. Although several kinds of pathogen in respiratory tract infection were noted to be related to the exacerbated IgA nephropathy, and past research reveals the role of APOL-1 gene between SARS-CoV-2 infection and exacerbation of glomerular disease, there has been one report so far about the exacerbation of IgA nephropathy after the SARS-CoV-2 infection.

There is a case series of 5 IgA nephropathy patients in Japan presented with either gross hematuria, proteinuria, or AKI after the infection of SARS-CoV- 2. We presented a young male with the past history of IgA nephropathy, and had received three dosages of vaccine. However, this case presented with all three symptoms of IgA nephropathy exacerbation, gross hematuria, proteinuria and AKI. Although our patient recovered after a series of treatment, we should beware of glomerulonephritis flare up in SARS-CoV- 2.

This study has a few limitations. First, this patient's acute kidney injury was confirmed by the lab data, but we did not get the value of the serum IgA. Second, we did not perform kidney re-biopsy to confirm the mesangial change degree as other experts' advice: If a patient with IgA nephropathy suffered from exacerbation of the renal function damage with the presence of gross hematuria, oliguria, or even anuria, flare up of the underlying should be alarmed and the re-biopsy of the kidney should also be arranged to include or exclude the rapid progression of IgA nephropathy. In the future, more studies should be needed for further understanding the mechanism of SARS-CoV-2 affecting the glomerular mesangium.

Conclusion

IgA nephropathy can be exacerbated after the infection of SARS-CoV-2. It is important to detect the AKI event of these patients, which implicits a worse outcome.

病例報告　112_C 56

魔鬼藏在細節裡！以糖尿病為初始表現的庫欣氏病患者

The devil is in the details! A patient with Cushing's disease presenting initially with diabetes

黃兆逢[1] 謝富淇[1] 曾睿玉[2]
[1]中國醫藥大學附設醫院教學部 [2]中國醫藥大學附設醫院新陳代謝科

Introduction

Hyperglycemia is a prevalent clinical issue, with our primary focus being the regulation of blood glucose levels. Nonetheless, the equilibrium of insulin and blood glucose is not the sole factor, as numerous medical conditions can contribute to the disruption of glucose regulation. In this context, we will discuss a case that initially presented with a hyperglycemic state, but further investigation during the clinical course revealed additional endocrine disorders.

Case presentation

This is a 43-year-old female nutritionist with past history of hypertension under regular medical control was presented to the emergency department with fever and generalized weakness for approximately one day. About the accompanying symptoms, she also reported shortness of breath, diarrhea, dysuria, nausea, vomiting, and lower back pain. Upon examination in the emergency department, her vital signs showed sinus tachycardia and tachypnea, with a fever of 39.1 degrees Celsius. Laboratory data revealed leukocytosis with neutrophil predominant and acute kidney injury. Her hsCRP and procalcitonin levels were also significantly high, suggesting a severe infection. Venous blood gas analysis showed metabolic acidosis and the other laboratory data confirmed high lactate levels and elevated ketone bodies. Based on these findings, we suspected the patient was in septic shock and diabetic ketoacidosis(DKA) due to an infection. Subsequent bacterial cultures revealed a urinary tract infection with a unique strain of E.coli, present in both the urinary tract and blood. A computed tomography(CT) scan showed feeling defect in the left kidney, consistent with emphysematous pyelonephritis, which likely led to the patient's septic shock and the DKA. Due to the severity of her condition and the need for the closely monitor, she was admitted to the intensive care unit for further observation and treatment.

After admission, the patient's blood sugar level gradually stabilized with the use of insulin pump. Consequently, the insulin pump was removed. Furthermore, the patient was treated for an infection with cefoperazone sodium and sulbactam sodium. However, due to the development of cholestasis, the treatment was switched to ciprofloxacin, which is sensitive to E.coli we cultured. The infection was gradually brought under control. During the hospital stay, the patient exhibited signs of Cushing's syndrome, such as moon face and buffalo hump. The patient also had generalized edema, leading us to suspect Cushing's syndrome. A myriad of tests were arranged, revealing dexamethasone suppressed test results, elevated 24-hour urine and free cortisol levels, and a loss of diurnal variation in AM and PM cortisol levels. (figure.1)

Considering these findings and the results of a high-dose dexamethasone test, along with high ACTH levels, we concluded that the patient had ACTH-dependent Cushing's syndrome. (figure.2) According to a review in the New England Journal of Medicine, the patient's situation

is more correspond to the corticotrophin dependent Cushing's syndrome. However, the patient was not suitable for Inferior Petrosal Sinus Sampling(IPSS) due to her severe infection event. Therefore, we used other diagnostic methods, including a high-dose dexamethasone test and MRI (Image1). An adenoma was found in the patient's pituitary gland. After discussing with the patient, she received transsphenoidal removal of pituitary tumor under navigator. The final pathology of the pituitary tumor revealed a Rathke's cleft cyst.

Post-surgery, the patient's symptoms significantly improved, including the moon face and buffalo hump. Currently, the patient continues to receive treatment and is being monitored at our outpatient clinic.

Figure 1

- ✓ Cortisol PM (07/29): 16.43 * ug/dL (<10)
- ✓ Cortisol AM (07/30): 22.53 ug/dL (6.7-22.6)
- ✓ ACTH(AM) : 18.1 pg/mL (<46)
- ✓ Urine 24 hrs total volume: 2700 mL
- ✓ Urine Free Cortisol: 27.20 ug/dL
- ✓ Urine 24Hrs Free Cortisol: 734.40* ug/24Hrs (58~403 ug/24Hrs)

Figure 2

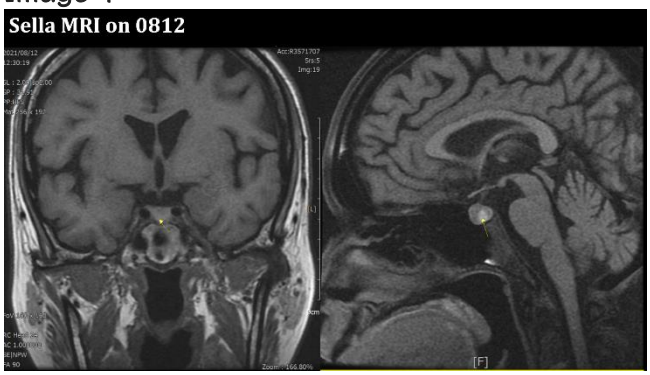
1mg dexamethasone suppression test

- ✓ Cortisol AM (07/31): 9.86 ug/dL

Figure 3

- ✓ Cortisol AM (after 1 mg dexamethasone suppression test): 9.86 ug/dL (6.7-22.6)
- ✓ Cortisol AM (after high dose dexamethasone suppression test) : 1.87 * ug/dL (6.7-22.6)

Image 1



Discussion

Endogenous Cushing's syndrome(CS) is a rare but life-threatening endocrine disorder characterized by excessive cortisol secretion. The annual incidence of CS remains low, ranging between 1.8 and 3.2 cases per million in the population. Among the various subtypes, Cushing's disease(CD) is the most common and exhibits a notable female predominance. In a study conducted in China, the overall female-to-male ratio for CS patients was 3.6 : 1.

Interestingly, male CD patients tended to be younger than their female counterparts at the time of their initial admission (33.1±14.0vs.36.9±12.5, P<0.01), which is consistent with findings reported in previous studies in Europe. Despite its significance, the hyperglycemic status, with a prevalence of up to 50%, is often overlooked in all presentations of CD.

In the present case, the patient had not been diagnosed with diabetes mellitus over the past four decades, with the initial manifestation of the underlying Cushing's disease presenting as a hyperglycemic crisis. Our initial approach involved treating the patient for diabetic ketoacidosis, which we presumed was induced by urosepsis. It was only upon observing her central obesity that we initiated surveillance for Cushing's syndrome. Following the guidance of senior clinicians, we conducted further investigations, which revealed ACTH-dependent Cushing's syndrome, leading to a final diagnosis of Cushing's disease.

However, there were certain limitations to this case. Firstly, the patient's frail condition precluded the use of Inferior Petrosal Sinus Sampling(IPSS). Consequently, we relied on the high-dose dexamethasone suppression test(HDDST) and MRI imaging for confirmation. Secondly, the final pathology of the pituitary tumor revealed a Rathke's cleft cyst, which was

challenging to reconcile with the clinical presentation.
This case underscores the importance of considering potential underlying conditions or events that may be masked by a hyperglycemic event, beyond the obvious infectious etiology.

Conclusion

A hyperglycemic episode is a significant clinical occurrence within our healthcare setting. Nevertheless, it is crucial to delve deeper into the underlying factors contributing to elevated blood glucose levels through comprehensive past history acquisition, meticulous physical examination, and detailed laboratory data analysis. This approach is essential to minimize the risk of diagnostic oversights.

病例報告　112_C 57

社區性肺炎裡潛藏感染性心內膜炎的個案呈現

A case of concealed infective endocarditis in the community acquired pneumonia

黃兆逢[1] 黃禹馨[1] 施文心[2]
[1]中國醫藥大學附設醫院教學部 [2]中國醫藥大學附設醫院感染科

Introduction

Mycoplasma pneumonia stands as a prevalent etiological agent contributing to community-acquired pneumonia. In accordance with the IDSA, the primary course of action involves the judicious administration of suitable antimicrobial agents to effectively combat pneumonia. In cases where clinical improvement is not observed, a prudent approach entails reevaluating the ongoing antibiotic therapy and contemplating the presence of alternative infectious etiologies, notably infective endocarditis.

It is imperative to recognize that infective endocarditis has emerged as a formidable global public health concern. This condition poses a significant threat to afflicted individuals, often resulting in severe clinical complications and, in some instances, catastrophic outcomes.

In this context, we present a compelling clinical case that exemplifies the diagnostic challenges posed by the coexistence of infective endocarditis and pneumonia. The intricate interplay between these two distinct pathologies underscores the importance of heightened clinical vigilance in identifying obscured infectious conditions, particularly when managing cases of pneumonia.

Case presentation

This is a 38-year-old female patient with a medical history of Sicca syndrome managed with hydroxychloroquine at other hospital for approximately 5 years presented to our emergency department(ED) with a two-week history of persistent fever accompanied by headaches, chillness, and shortness of breath. Initial laboratory assessment in the ED revealed normal white blood cell count(7800/uL) but an elevated high-sensitivity C-reactive protein(hsCRP) level. Additionally, the patient tested positive for Mycoplasma IgM antibodies. A chest X-ray(CXR) demonstrated increased opacities, infiltrations, and pleural effusions in the bilateral lower lung fields. With these clues, a diagnosis of community-acquired pneumonia was established, prompting the patient's transfer to our inpatient ward for pneumonia management.

Upon admission, the patient received ceftriaxone in combination with azithromycin, later transitioning to ceftriaxone alongside levofloxacin for pneumonia treatment. Ine week later, the patient's symptoms improved, as evidenced by clinical improvement and resolution of CXR abnormalities. However, while at home, the patient experienced palpitations, shortness of breath, and chest tightness during sleep. Subsequently, she attended a cardiology outpatient clinic as scheduled, where a new-onset heart murmur was detected. Further evaluation with transthoracic echocardiography revealed vegetations on the anterior mitral leaflet with perforation. Blood culture results from the previous admission identified Streptococcus mitis bacteremia. A diagnosis of infective endocarditis was established, leading to the patient's readmission for both medical and surgical management.

During the second hospitalization, ceftriaxone therapy was tailored according to drug

sensitivity testing. Additional diagnostic assessments, including transesophageal echocardiography(TEE), carotid sonography, ankle-brachial index measurement, peripheral vascular sonography, and coronary angiography, were performed. TEE confirmed the presence of vegetations on A3 associated with severe mitral regurgitation, with vegetation dimensions measuring 18.9x3.2mm. Considering the presence of mitral valve rupture, severe mitral regurgitation, and the patient's relatively stable hemodynamic status, surgical intervention was recommended. The patient selected transcatheter aortic valve replacement(TAVR). Subsequent to the procedure, her symptoms, including shortness of breath, chest tightness, and palpitations, gradually ameliorated.

Discussion

Infective endocarditis(IE) is a rare but is associated with high morbidity and mortality disease if late recognition and improper treatment. From an epidemiological perspective, it prevails more in elder people with age above 60 years and more in men than women. The characteristics of IE patients are older age, with prosthetic valves or other cardiac devices. There are several risk factors for IE, including people with congenital heart disease, diabetes mellitus, or human immunodeficiency virus, an intravenous drug abuser, undergo hemodialysis and so on. For the identified pathogen, Streptococci still seems to be the predominant pathogen. Numerous research studies have brought attention that autoimmune disease such as systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) may contribute to the occurrence of IE and that is because the antibodies could have the potential to modify the surface of cardiac valves and make it easier for pathogens to attach tightly to the valve. In a case report, they hypothesize poor oral hygiene in a patient with Sicca syndrome in which saliva production is relatively insufficient. In diagnosis, IE can present with unspecific signs such as fever, dyspnea, fatigue, palpitation, or chest pain, which sometimes can be mistakenly treated as pneumonia or complicated with pneumonia since community-acquired pneumonia prevails more often.

Mycoplasma pneumonia presents radiographic characteristics on CXR imaging, including bilateral lung involvement with peribronchial and perivascular interstitial infiltration. Alveolar consolidation may also occur, frequently accompanied by pleural effusions, indicative of greater severity. However, image can also be seen in patients with IE. On the other hand, identification of any bacterial strain in blood cultures, especially endocarditis-associated species, physician should be aware of diagnosis of IE and initiates IE survey. According to the 2023 ESC guideline, pharmacological regimens should be lasting 6-8 weeks; however, some patients require surgical intervention due to symptomatic heart failure, medication failure, or highly pathogenic microorganisms. Besides, left-sided vegetations exceeding 10mm in length may warrant surgical indication.

In our patient, initial admission for suspected mycoplasma pneumonia resulted in improvement of the right lower lobe patch with antibiotic treatment. However, retrospective examination of her medical records revealed subtle and unusual clues in the form of unresolved bilateral pleural effusions. While severe pneumonia induced by Streptococcus mitis has been reported, it is more common in immunocompromised patients. Given our patient's non-immunocompromised status, the persistence of pneumonia or pleural effusion should have alerted us to the possibility of an underlying condition beyond pneumonia.

Conclusion

When we deal with pneumonia, once the pneumonia improved slowly or not as scheduled, we should reevaluate whether we judiciously choose antibiotics or there are other episodes conceal within the shadow such as infective endocarditis.

病例報告　112_C 58

罕見的大細胞性神經內分泌瘤，對吉舒達反應顯著的個案呈現

A rare large cell-type neuroendocrine carcinoma case with remarkable response to pembrolizumab

黃兆逢[1]　連銘渝[2]
[1]中國醫藥大學附設醫院教學部　[2]中國醫藥大學附設醫院血液腫瘤科

Introduction

The incidence of neuroendocrine tumors (NETs) has exhibited a substantial six-fold increase over time, notably marked by a predominance of localized tumors as opposed to metastatic cases. Primary tumor sites predominantly involve the gastrointestinal tract, no matter in the world or in Taiwan, and the prevailing histological subtype is small cell-type neuroendocrine carcinoma (SCNEC). The conventional therapeutic approach entails a regimen incorporating etoposide and platinum-based therapy. In this context, we shall present a case of large cell-type neuroendocrine carcinoma (LCNEC) in the endometrium characterized by an exceptional response to the conventional treatment regimen augmented with immunotherapeutic intervention, specifically pembrolizumab.

Case presentation

This is a 39-year-old nulliparity female with a past history of uterine myoma complicated with abnormal bleeding under treatment who came to our outpatient department with chief complaints of epigastralgia, hiccups and postprandial nausea for 2 weeks. During the physical examination, a palpable mass over upper abdomen was found. History of family was her mom's colon rectal cancer and hepatocellular carcinoma. Abnormal value was found in the tumor marker, CA-125 (110.5 U/ mL) and PIVKA-II (107.86 mAU/mL); but no abnormality was noted in other blood chemistry data (liver function, bilirubin, or renal function). The abdominal CT scan reveals a 13.6cm*9.4cm heterogeneous density in uterus, accompanying mass in the liver (12.7 *13.3), intra-abdominal lymph nodes and peritoneum. The patient then received operation of transcervical resection on 10th Dec,2021, and the pathology sample showed positive IHC of CK, SYN, chromogranin A, CD56, and negative IHC of LCA, vimentin, TTF-1, GFAP, S100, which is matched to the neuroendocrine tumor. Finally, the NGS (Next-Generation Sequencing) data showed TMB-H, MSI-H and MMR biallelic inactivation. Furthermore, the ascites sample also confirmed the metastasis of the primary tumor. After the operation, the patient suffered from post renal AKI and the reevaluation of the abdominal and pelvis computed tomography revealed the invasion of upper third ureter. The situation improved after the arrangement of the temporary percutaneous nephrostomy.

After diagnosis of NET, and the confirmation of NGS, the patient received three times of etoposide and carboplatin during December 17th, 2021, to December 24th, 2021. And then immunotherapy of pembrolizumab has been added since January 9th, 2022 and then chemotherapy and immunotherapy was given every three weeks since January 9th, 2022. After the forth use of pembrolizumab, the following up pelvic CT showed shrinkage of the tumor size at liver and pelvis and evaluated as partial response. Furthermore, laparoscopic partial hepatectomy and uterine resection were both arranged and the pathological report revealed the picture of neuroendocrine tumor. Then other cycles of pembrolizumab was given

every one month, and the latest CT scan done on August 9th, 2022 showed complete response.

Discussion

Endometrial neuroendocrine tumors, also referred to as endometrial small cell carcinoma or endometrial neuroendocrine carcinoma, represent a rare form of uterine cancer originating in the endometrium. These tumors are relatively infrequent, constituting less than 2% of all endometrial cancers. Notably, they exhibit an aggressive and rapid growth pattern, primarily afflicting women over the age of 50 who possess a history of endometrial hyperplasia, mirroring the characteristics of the case at hand which presented with the tumor at the endometrium and metastasis of the liver.

Within this category, large-cell neuroendocrine tumors of the endometrium are exceptionally rare, with only a handful of documented cases in medical literature. Treatment strategies for this specific cancer subtype typically involve a regimen consisting of etoposide and platinum-based therapy. Alternatively, a regimen combining platinum-based drugs and gemcitabine is considered, with the former approach demonstrating a more favorable prognosis.

To enhance the therapeutic efficacy of LCNEC, the incorporation of immune checkpoint inhibitors merits consideration. Several trials have underscored the promising outcomes associated with the administration of Pembrolizumab in patients grappling with advanced endometrial cancer. However, to date, there have been no randomized controlled trials conducted to elucidate the impact of immune checkpoint inhibitor utilization in patients with LCNEC. Only a solitary case report has explored this treatment approach, demonstrating favorable outcomes. Consequently, we administered a regimen comprising etoposide, carboplatin, and pembrolizumab in our case, resulting in a noteworthy response with complete remission observed within one year.

In our case, the patient initially presented with LCNEC affecting both the endometrium, the liver, and the upper third ureter which led to post-renal acute kidney injury (AKI). The response to the combined chemotherapy and immunotherapy treatment was remarkable. However, several limitations persist within this case. Firstly, while the follow-up CT imaging displayed no evidence of tumor recurrence, the long-term prognosis of the patient remains uncertain due to the lack of sufficient data to substantiate this claim. Secondly, it is important to note that this report represents a singular case, rendering it impossible to definitively ascertain whether immune therapy-associated adverse events, such as Immune-Related Adverse Events, may manifest in other patients following the same treatment regimen.

Notwithstanding the numerous uncertainties surrounding the use of pembrolizumab in LCNEC, this case presentation has provided a novel opportunity to address this rare and malignant neuroendocrine tumor.

Conclusion

We reported a rare case of LCNEC with TMB-H mutation, MSI-H status, and biallelic MMR inactivation under chemotherapy and pembrolizumab. The patient exhibited a complete response lasting for 13 months. This notable outcome underscores the potential efficacy and safety of Pembrolizumab plus chemotherapy in LCNEC, particularly in cases featuring TMB-H or MSI-H. However, more research should be done to confirm the role of pembrolizumab in neuroendocrine tumor.

病例報告　112_C 59

固體器官移植受贈者因 Neoscytalidium dimidiatum 引起的侵襲性真菌感染：兩例個案報告與文獻回顧

Invasive Fungal Infection due to Neoscytalidium dimidiatum in Solid Organ Transplantation Recipients: Two Cases Report & Literature Review

李昆峰[1] 蘇浤傑[2] 陳怡臻[2] 周家卉[2] 張廖年峰[3] 李原地[4] 何茂旺[2] 曾坤浩[5] 林瑜姿[6] 薛博仁[2,5]
[1]中國醫藥大學附設醫院內科部 [2]中國醫藥大學附設醫院內科部感染科 [3]中國醫藥大學附設醫院皮膚科 [4]中山醫學大學附設醫院內科部感染科 [5]中國醫藥大學附設醫院檢驗醫學部 [6]中國醫藥大學醫學檢驗生物技術學系

Abstract

Solid organ transplantation is a way to solve the end organ diseases in modern medicine. To prevent or treat organ rejection after transplantation, the recipients need to take immunosuppressive agents for a long time. This may induce opportunistic infection (OI) in the transplant recipients even long time after transplantation. Invasive aspergillosis and candidiasis are two of the most common OIs after solid organ transplantation. Neoscytalidium species are demantiatious mold and rarely reported as invasive infection in recipients after solid organ transplantation. We report two cases of invasive subcutaneous infection of N. dimidiatum after solid organ transplantation and review the literatures.

Introduction

This study focuses on the impact of Mycoses, particularly Neoscytalidium dimidiatum, on immunosuppressed hosts such as transplant recipients. The study presents two cases of organ transplant recipients, one liver and one kidney, who developed invasive Neoscytalidium dimidiatum infection. The aim is to contribute to the limited literature on this topic and highlight the need for increased awareness of this potential infectious complication in liver transplant recipients.

Case Presentation

The first case involves a 53-year-old man with a history of alcoholic liver cirrhosis who underwent a liver transplant. He presented with progressive swelling of his right lower limb, nodules, and pustules. The second case involves a 75-year-old male farmer who underwent a kidney transplant and presented with persistent skin lesions on his forearms. Both patients were diagnosed with Neoscytalidium dimidiatum infection.

Discussion

The study discusses the classification of Neoscytalidium infections and highlights the importance of considering invasive Neoscytalidium infection in liver transplant recipients. The study also compares the two cases, noting that the liver transplant recipient experienced a more rapid onset of symptoms and was taking more immunosuppressive agents. The study concludes by suggesting that the management of Neoscytalidium infection in liver transplant recipients may be more challenging than in other immunosuppressed hosts, such as renal transplant recipients.

病例報告　112_C 60

一個免疫健全感染新冠肺炎重症併發巨細胞病毒結腸炎之個案

Cytomegalovirus colitis followed by COVID-19 critical illness in an immunocompetent patient

陳聖富[1] 鄧紀綱[2] 鄭孟瑜[3] 何茂旺[3] 廖偉志[2]

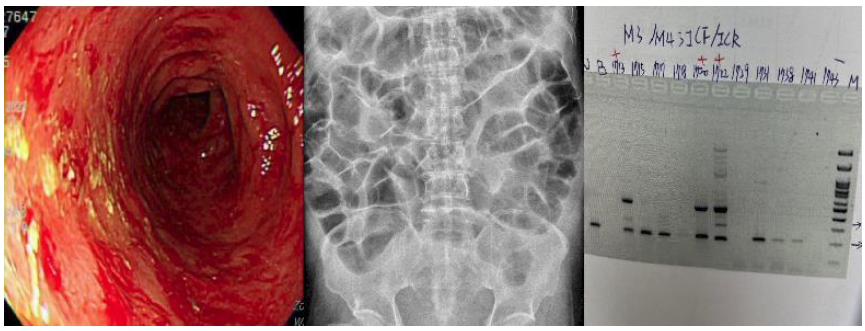
[1]中國醫藥大學附設醫院內科部 [2]中國醫藥大學附設醫院胸腔科 [3]中國醫藥大學附設醫院感染科

Introduction

Cytomegalovirus (CMV) infection is common in immunocompetent hosts, with seroprevalence rates ranging between 40 and 100 percent of the adult population. Although high serology prevalence of CMV, most CMV primary infection is generally asymptomatic or may present as a mononucleosis syndrome. Most cases of CMV disease occur in the setting of advanced immunosuppression. CMV disease localized to a single organ has been described in immunocompetent hosts. These cases are rare and limited to small series and case reports. In immunocompetent adults, CMV infection usually appears due to reactivation of latent infection rather than primary infection. In this case, we present a case of CMV colitis in a COVID-19 patient who is regarded as an immunocompetent patient.

Case presentation

Fig1 Fig2 Fig3



The patient is a 65-year-old male retired worker without any COVID-19 vaccine history, presented with sore throat, cough, sputum, and rhinorrhea for 2 weeks. The patient had progressing dyspnea and visited to emergency room. Under the tentative diagnosis of COVID-19, critical illness, initial PCR Ct level 17.6, complicated with acute respiratory failure and ARDS, the patient was intubated with mechanical ventilator support and admitted to the intensive care unit. He received Remdesivir and Tocilizumab for COVID-19 treatment, along with intravenous Dexamethasone 6mg for a week. Meanwhile, the patient was being treated as moderate ARDS under protective lung strategy. For moderate ARDS, an equivalent glucocorticoid above 30mg of prednisolone per day was kept for around a month.

After 20 days of admission to the ICU, watery stool for days with blood-tinged stool was noted, without peritoneal signs. We arranged abdominal CT and it revealed diffuse swelling of the colonic wall. Subsequently, colonoscopy was performed and found multiple tiny ulcers and mucosa hyperemia(Fig.1). Though persistent water diarrhea, the patient complained of progressing abdomen flatus and then developed to constipation after few days, KUB(Fig. 2) compatible with ileus. The previous biopsy showed non-specific ulcer of cecum, and the immunohistochemical stain for CMV was negative. However, the stool CMV PCR(Fig. 3) showed positive findings. Serum CMV viral load elevated to 2.6*10^4 IU/ml, compared with negative findings one month ago. Therefore, the patient was started on Ganciclovir 5mg/kg Q12H intravenously for 14 days; Erythromycin and Metoclopramide were also prescribed as prokinetic agents. Clinical symptoms of ileus and serum CMV viral load indeed improved

under the above treatment. In the meantime, the patient received tracheostomy for chronic respiratory failure and was gradually stepped down to home care in 71-day hospital course.

Discussion

CMV infection is defined as virus isolation or detection of viral antigens or nucleic acid in any body fluid or tissue specimen. CMV disease refers to evidence of CMV infection with attributable symptoms or signs, including viral syndrome and end-organ disease. Due to the lack of studies, viral load cut-off levels have not yet been defined, while some of the studies regarded that viral load greater than 1000 copies/mL as cutoff value. Proven CMV gastrointestinal disease requires gastrointestinal symptoms plus macroscopic mucosal lesions plus CMV documented in tissue. CMV documented in blood by NAT or antigenemia or CMV documented by PCR from tissue biopsies is not sufficient for the diagnosis of CMV GI disease, and could be defined as possible GI disease.

In this case, the patient is considered as an immunocompetent host, with serum Anti-CMV IgG level 89.2 U/ml, negative CMV PCR, indicating latent CMV infection. Gastrointestinal involvement with CMV is uncommon in immunocompetent hosts. CMV colitis usually presents with hematochezia, abdominal pain, diarrhea, nausea, vomiting, melena, and fever. There was some case study that reported CMV colitis presented with ileus. According to the clinical course, high titer of CMV viral load, and good treatment response, the patient's GI symptoms meet the definition as possible CMV GI disease. The negative finding of cecum ulcer immunohistochemical stain may result from inappropriate biopsy site.

The patient may also had some relative immunocompromised etiology such as ICU-acquired immunosuppression and high-dose glucocorticoid used. Some studies pointed out CMV infection was five-fold higher in patients with sepsis. However, the risks of CMV infection and CMV end-organ disease are not generally applicable because of heterogeneity. None of the disease severity scores(e.g. APACHE II or SAPS II score) correlated with a risk of CMV infection. COVID-19, as a novel global pandemic of coronavirus disease, is rather heterogeneous, ranging from no symptoms to critical illness. Numerous studies have demonstrated that the severity and outcomes are closely related to hosts immune responses. Immune disorders are common in severe infections and sepsis and are characterized by developing a high inflammation state to immunosuppression. There are some case reports presented about CMV colitis followed by COVID-19 infection in immunocompetent patients, even in mild to moderate degrees of COVID-19 infection. So, COVID-19 infection may be considered as an independent risk factor to immunocompromised conditions.

Conclusion

CMV colitis is a rare event in immunocompetent hosts. In this case, COVID-19 infection may be regarded as a trigger or risk factor for relatively immunocompromised condition. A well-designed trial and hypothesis should be established for better understanding of immunity and its regulation in response to SARS-CoV-2 infection. Before that, we should consider CMV colitis in COVID-19 patients as a differential diagnosis of gastrointestinal symptoms in clinical practice.

病例報告　112_C 61

以胃麻痺為表現的免疫相關不良事件：一位 66 歲小細胞肺癌患者接受 Durvalumab 的治療案例

Gastroparesis as an Immune-Related Adverse Event in a 66-year-old Small Cell Lung Cancer Patient with Durvalumab Treatment

張庭毓[1]　鄭文建[1,2]
[1]中國醫藥大學附設醫院內科部　[2]中國醫藥大學附設醫院胸腔科

Introduction

Immunotherapy, a method that enhance a patient's immune system to fight disease, has recently been a source of promising new cancer treatments. Immune checkpoint inhibitors (ICIs) have remarkable benefits in treating a variety of cancer types. This method enhances anti-tumor immunity by inhibiting intrinsic down-regulators of immunity, such as cytotoxic T-lymphocyte antigen 4(CTLA-4) (ipilimumab) and programmed cell death 1(PD-1)(pembrolizumab, nivolumab) or its ligand, programmed cell death ligand 1(PD-L1)(avelumab, atezolizumab, durvalumab)[1,2]. The use of ICIs has significantly improved the outcomes for patients with various types of cancers. However, this treatment is also associated with unique immune-related adverse events. It has been observed that up to 65% of patients experience one or more of these adverse events, which affect various organs such as the skin, thyroid, liver, gastrointestinal tract, and lungs. Among these, dermatologic and gastrointestinal toxicities are reported with the highest incidence[3,4]. While luminal GI toxicities, particularly enterocolitis, have been well-documented, gastroparesis has been less frequently reported[3]. Thus, in this report, we will outline a case of a patient who developed gastroparesis following a 9-month course of durvalumab treatment.

Case Presentation

A 66-year-old Taiwanese heavy smoker(1PPD for 40 years) with Small cell lung cancer(SCLC) at an extensive stage with bone, adrenal gland, and brain metastasis receiving 6 cycles Durvalumab 360mg, Etoposide, Cisplatin, 4 cycles maintenance durvalumab 360mg, whole brain radiotherapy presented with poor intake, vomiting, especially 1-2 hours after meals.
The upper GI endoscopy report showed mild pylorus deformity and no significant change. The biopsy of the pylorus deformity also revealed neither malignancy nor glandular dysplasia. In addition, we also placed a nasogastric tube for the patient and found that almost all food was not emptied after being drained from the nasogastric tube three hours after feeding. Therefore, gastroparesis was suspected. The patient has no history of abdominal surgery, and none of the medications have side effects that could cause gastroparesis. Blood sugar is under well controlled. Laboratory data are as follows: TSH:0.448uIU/mL(0.34-5.60), Serum Free T4:1.18ng/dL(0.54-1.40), Serum Free T3:3.15pg/mL(2.0-4.0), ACTH(AM):5.13pg/mL(<46), Cortisol AM:1.14ug/dL(6.7-22.6), Sodium(Na):135mmol/L(135-147), Potassium(K):3.8mmol/L(3.5-4.9), Corrected calcium(Ca):9.2mmol/L.
Therefore, we initially increased the use of oral steroids (Cortisone acetate 75 mg/day), but there was no improvement after 7 days of initiation with systemic steroids. Hence, immune-related adverse events of gastroparesis were suspected. After the placement of the nasoduodenal tube, the patient's digestion improved significantly. No food drainage was observed from the nasoduodenal tube three hours post the last meal, and symptoms of

nausea and vomiting subsided.

Discussion

Immunotherapy with ICIs has improved cancer treatment by using the immune system to target cancer cells. However, it also cause side effects like skin problems, gastrointestinal events, liver inflammation, hormonal imbalances, and rare inflammatory events affecting different organs[5]. While luminal GI toxicities, particularly enterocolitis, have been well described, gastroparesis has not been previously reported[3,4].

Common causes of gastroparesis include drugs, abdominal surgery, endocrine disorders, and electrolyte imbalances. Other articles have mentioned that paraneoplastic syndrome can also manifest as gut motility disorders[7]. This is particularly prevalent in patients with SCLC and is associated with anti-Hu, also known as type 1 anti-neuronal nuclear antibodies(ANNA-1)[3,7].

In our case, the patient developed gastroparesis nine months after the initial use of durvalumab. A review of other related articles shows that gastroparesis caused by the use of ICIs occurs between 3-12 months, but the cases of ICIs in that article were ipilimumab(CTLA-4 inhibitors), pembrolizumab(PD-1 inhibitors), and nivolumab(PD-1 inhibitors)[3]. The ICI mentioned in our report is durvalumab(PD-L1 inhibitors), and there have been no previous articles mentioning gastroparesis caused by durvalumab. Even gastrointestinal-related adverse events are rarely reported and are mostly characterized by diarrhea[5,6]. Previous article used Scintigraphic Gastric Emptying Tests for diagnosing gastroparesis[3], but considering our patient's severe vomiting, we used nasogastric tube drainage amounts after meals and upper GI endoscopy images as the basis for judgment. The ANNA-1 data was not obtained from our patient due to the lack of the relevant antibody test in our hospital. Furthermore, the previous case series about gastroparesis caused by ICIs also did not conduct the antibody test either[3].

Although our patient cannot undergo gastric scintigraphy due to severe vomiting, it is still recommended for screening symptoms of gastroparesis if indicated. To confirm ICI-related gastroparesis, it is essential to rule out other common causes of gastroparesis. Additionally, an ANNA-1 test can be conducted to exclude the possibility of paraneoplastic syndrome. Deep gastric biopsies may be considered for patients with gastroparesis as an immune-related adverse event to enhance our understanding of the underlying pathophysiology, suggesting that gastroparesis may result from an immune-related adverse event.

Conclusion

Gastroparesis as an immune-related adverse event is rare. We present a case of small cell lung cancer that developed after the administration of durvalumab. This case can serve as a reference for differential diagnosis for physicians in the future.

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病例報告　112_C 62

成功以 Anti-PD-1 治療高微衛星不穩定性同步下咽和食道鱗狀細胞癌

Successful Anti-Programmed Cell Death-1 (anti-PD-1) treatment of microsatellite instability-high Synchronous Hypopharyngeal and Esophageal Squamous Cell Carcinoma: A case report

林芳妤[1]　連銘渝[1,2]
[1]中國醫藥大學附設醫院內科部　[2]中國醫藥大學附設醫院血液腫瘤科

Introduction

Synchronous multiple primary malignancies refer to the diagnosis of two or more primary malignancies within a six-month timeframe. Each of these cancers originates from a unique primary site and is not an extension, recurrence, or metastasis. The co-occurrence of synchronous esophageal squamous cell carcinoma (ESCC) and head and neck squamous cell carcinoma (HNSCC) is approximately 2.7% among HNSCC patients. Patients with supraglottic and pyriform sinus cancers, or with a history of moderate to heavy alcohol consumption, have a higher risk (15~23%) of developing synchronous ESCC. Synchronous cancer is generally associated with a poor prognosis. There is no universally effective treatment for this dual primary cancer, making the selection of effective treatment strategies crucial for these patients. (Szu-Ying Pan, Chi-Ping Huang, et al., 2020)

Case presentation:

A 66-year-old male patient presented with initial presentation of lump sensation in the throat and odynophagia for half a year. An esophagogastroduodenoscopy done at local medical doctor revealed an exophytic tumor over the bilateral supraglottic, right hypopharynx, and a tumor of the upper esophagus. Transoral laser microsurgery was performed on April 23, 2020. The pathological findings of hypopharynx, right supraglottic, and right pyriform sinus showed moderate to poorly differentiated squamous cell carcinoma (SCC). A computed tomography and upper Mini probe endoscopic ultrasonography on April, 2020 reported upper- to lower/3 esophagus cancer with mediastinum lymph node involvement. The esophageal biopsy showed SCC. A positron emission tomography scan (PET) confirmed no distant metastasis. However, he was diagnosed with synchronous hypopharynx cancer, SCC, cT2N0M0 and upper- to lower/3 esophagus cancer, SCC, cT3N2M0.

The patient was treated with neoadjuvant concurrent chemoradiotherapy with paclitaxel 50mg/m2 plus cisplatin 30mg/m2 weekly for four cycles, with curative radiotherapy to the esophageal tumor with margin and involved lymph nodes for 45 Gy/25Fr from May 13, 2020 to June 19, 2020. After one month, PET scan showed Right upper lobe, multiple lymph nodes, and left adrenal gland metastasis and spine metastasis. Thus, the patient received Nivolumab 2mg/kg body weight plus chemotherapy with PF regimen four times at 2-week interval since July 2020. Also, local radiotherapy to bone and abdominal metastatic lesion for 40 Gy/15Fx was done. A follow PET on Oct 2020 showed disease progression with new bone and brain metastasis. (Sacrum and left fronto-parietal region of cerebrum)

The result of comprehensive genomic profiling by next-generation sequencing revealed the expression of high tumor mutational burden (13 mutations) and ERBB2 amplification. Thus, we planned to treat the patient with pembrolizumab (100 mg on day 1 once every 3 weeks) plus afatinib 30mg daily due to high tumor mutational burden and ERBB expression since Oct

2020. After four cycles of pembrolizumab plus afatinib, an enhanced PET scan showed that the sacrum and left fronto-parietal of cerebrum metastasis were significantly reduced. The effectiveness of immunotherapy plus targe therapy led us to decide to maintain the treatment regimen. Owing to the severe side effect of skin, Afatinib was held on Dec 2020. He continues with pembrolizumab treatment at a dose of 100mg as maintenance therapy at 3-week intervals. Over his clinical course from 2020 to 2023, there was radiographic evidence of complete remission, and maintenance pembrolizumab therapy was continued for two years. The image and esophagogastroduodenoscopy consistently confirmed complete remission until July 03, 2023. Hypopharyngeal cancer was also followed up by laryngoscopy regularly and no recurrence was noted.

Discussion

Surgical resection is typically used to treat early-stage esophageal cancer. For more advanced stages or metastatic ESCC, the standard treatment has been neoadjuvant or definitive chemoradiotherapy with fluorouracil and platinum-based chemotherapy. However, this approach has a low overall efficiency and often leads to drug resistance after the first round of chemotherapy, resulting in disease progression. (Yi Yang, Xiangliang Liu, et al., 2022)

The KEYNOTE-181 study compared advanced/metastatic ESCC patients treated with chemotherapy (paclitaxel, docetaxel, or irinotecan) to those treated with pembrolizumab. The results indicated that patients treated with pembrolizumab had a median overall survival of 10.0 months, compared to 6.5 months for those treated with chemotherapy, and experienced fewer treatment-related adverse events. PD-L1 (Programmed Cell Death-Ligand 1) CPS (combined positive score) ≥1 was identified as a suitable cut-off and a predictive marker of pembrolizumab's effectiveness in Asian patients with ESCC. (Y Cao, S Qin, et al., 2021)

The KEYNOTE-048 study showed that first-line pembrolizumab and pembrolizumab-chemotherapy continued to offer survival benefits over cetuximab-chemotherapy in recurrent/metastatic head and neck squamous cell carcinoma, even after a 4-year follow-up. (Kevin J Harrington, Barbara Burtness, et al., 2022) The significant correlation between CD8+ TIL (tumor infiltrating lymphocyte) and PD-L1+ TPS (Tumor proportion score) in HNSCC and ESCC suggests that PD-L1/PD-1 (programmed death-1) associated immunotherapy could be a potential treatment option for synchronous esophageal squamous cell carcinoma and hypopharyngeal cancer. (Tseng-Cheng Chena, et al., 2020) The KEYNOTE-158 study also indicated that high tissue TMB could be a new and useful predictive biomarker for robust response to pembrolizumab monotherapy in patients with previously treated recurrent or metastatic advanced solid tumors (Aurélien Marabelle, Marwan Fakih, et al., 2020).

Conclusion:

We presented a case of microsatellite instability-high Synchronous Hypopharyngeal and Esophageal Squamous Cell Carcinoma treated with anti-PD-1 successfully. In conclusion, as the patient with high tissue tumor mutation burden, immunotherapy with Pembrolizumab may have a sustained survival benefit. But many actual clinical studies are still needed to explore and discover better treatment decisions for such patients.

病例報告　112_C 63

接受福斯利諾治療腹膜透析病患併發憩室破裂導致腹膜炎: 一個被忽略的腹膜炎感染原因

Diverticulum rupture related peritonitis in an elderly woman under the treatment of lanthanum carbonate: a neglected cause of peritonitis

林于智[1] 林信宏[2] 王怡寬[3]

[1]中國醫藥大學附設醫院-內科部 [2]中國醫藥大學附設醫院新竹分院-內科部腎臟科 [3]中國醫藥大學附設醫院-內科部腎臟科

Introduction

Peritonitis is a common complication of peritoneal dialysis, which is associated with significant morbidity, catheter loss, transfer to hemodialysis, transient loss of ultrafiltration, possible permanent membrane damage, and occasionally death. Patients with peritonitis may present with fever, abdomen pain, nausea/vomiting, cloudy effluent or even consciousness disturbance. Peritonitis may be directly related to peritoneal dialysis (most of the cases) or secondary to a nondialysis-related intra-abdominal or systemic process (less than 6 percent in peritoneal dialysis (PD) patients)[1]. Sporadic case of diverticulum rupture related may be neglected when presenting with common peritonitis presentation. We reported a colon diverticulum rupture related peritonitis case in a PD patient.

Case Description

A 59-year-old female with a history of 1. diabetes mellitus type 2, 2.end stage kidney disease under PD since 2014 due to diabetes nephropathy, 3. gastroesophageal reflux disease, 4. hypertension, 5. hyperlipidemia, 6. colon diverticulum, 7. hyperphosphatemia under lanthanum carbonate use came to emergency department due to progressive diffuse abdominal pain for 3 days. The patient initially presented with acute onset diffuse abdominal pain, chills, cloudy dialysate and decreased ultrafiltration. The origin physical examination showed diffuse abdominal tenderness, muscle guarding, rebounding pain, and lower limbs pitting edema 1+ and lab data revealed elevated hsCRP (16.08 mg/dL). Ascites routine showed cloudy appearance, and leukocytosis (WBC: 525/ul) with neutrophilia (89%) and ascites culture yielded E.coli later. The patient was treated as PD peritonitis with intraperitoneal cefazolin and gentamycin and soon shifted to cefepime according to ascites culture. However, cloudy ascites fluid and diffuse abdominal tenderness, peritoneal sign still persisted despite under antibiotics therapy for five days. Refractory peritonitis was suspected and we arranged abdomen computed tomographgy (CT) for further survey, which revealed 1. radiopaque agents over entire bowel and diverticulum in non-

Figure 1A

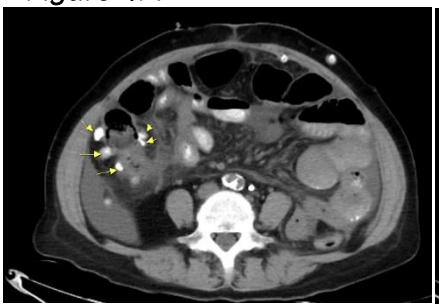


Figure 1B

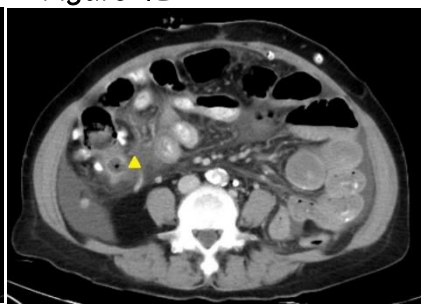
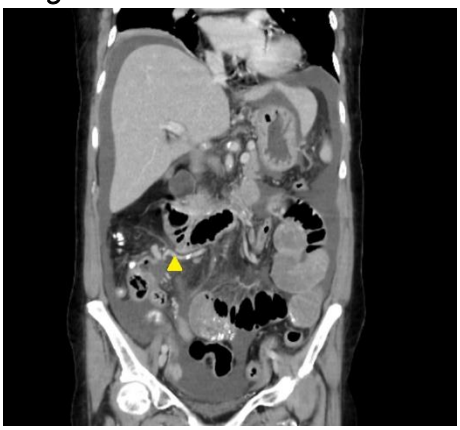


Figure 1C



contrast view, suspected lanthanum related (arrow) (Figure 1A) 2. a perforation hole, suspected from diverticulum of ascending colon (arrowhead) (Figure 1B and 1C) 3. several diverticula in the ascending colon, cecum, descending colon and sigmoid colon. We consulted colon and rectal surgeons and kept antibiotics treatment was suggested due to stable vital signs and improved abdominal pain. After two weeks antibiotics treatment, the patient was discharged due to improved abdominal pain without peritoneal sign and decrease in WBC counts (75/ul, neutrophil 44 %) in ascites routine.

Discussion

In Taiwan, *PD* starts since 1984 and accounted for 8.1 % of all dialysis patients according to Taiwan Renal Registry Data System in 2020. The great limiting factor to the use of CAPD is poor long-term effectiveness because of the development of complications such as peritonitis, catheter malposition, peritoneal herniation or leakage and so on. Of all complications, peritonitis is the most common one. Peritonitis may be directly related to peritoneal dialysis or secondary to a non-dialysis-related intra-abdominal pathology including ruptured diverticulum, appendicitis, bowel perforation and incarcerated hernia or systemic process[1,2]. The intra-abdominal pathology is responsible less than 6% of cases of peritonitis[1]. Diverticulum size more than 10 mm, location in the ascending, transverse or descending colon also significantly increases the risk of developing peritonitis of enteral origin[3]. A clinical report also found the association between lanthanum use and colonic diverticulosis[4]. Emergent surgical intervention, peritoneal lavage or antibiotics treatment would be considered if diverticulum related peritonitis was diagnosed[5]. Thus, early diagnosis was important. Peritonitis from enteric causes can lead to diagnostic challenge and delays in appropriate treatment, which may increase morbidity and mortality rate of approximately 50%[6]. The International Society for Peritoneal Dialysis (ISPD) guidelines in 2022 suggest that identification of multiple organisms is highly suggestive of an enteric cause for peritonitis and early surgical evaluation should be obtained. Besides, ISPD defined refractory peritonitis as failure of the PD effluent to clear after 5 days of appropriate antibiotics[6]. Based on the concept of ISPD recommendations, perforated peritonitis should be suspected in PD patient with refractory peritonitis and further survey should be done immediately[7]. A prospective study comments that Multi-detector computed tomography (MDCT) is relatively higher sensitivity and specificity for predicting the site of gastrointestinal tract perforations among diagnosis tools. Common image feature of perforation includes concentrated bubbles of extra-luminal air in close proximity to the bowel wall, a focal defect in the bowel wall and segmental bowel wall thickening[8].

Conclusion

A early image study is recommended in patients with refractory peritonitis to differentiate the causes and possibility of secondary peritonitis.

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病例報告　112_C 64

以 Abatacept 治療免疫檢查點抑制劑相關心肌炎
Abatacept Treatment of Immune Checkpoint Inhibitor–Related Myocarditis

蔡佳妤 [1]　連銘渝 [1,2]
[1] 中國醫藥大學附設醫院內科部　[2] 中國醫藥大學附設醫院血液腫瘤科

Introduction

Immune checkpoint inhibitor (ICI) is a promising form in cancer therapy by activating the immune system to target cancer cells. However, this immune activation can lead to rare but severe side effects, known as immune-related adverse events (IRAEs). We present a case of esophageal carcinoma recurrence treated with ociperlimab and tiselelizumab, resulting in ICI-related myocarditis. Diagnosis was confirmed through the patient's response to steroids and immunosuppressants.

Case

A 49-year-old housewife with history of alcohol drinking and heavy smoking was diagnosed of lower esophageal squamous-cell carcinoma(SqCC), cT3N0M0,stage 3 in January, 2022, with initial presentation of dysphagia and body weight loss in one month.

The patient received thoracic esophagectomy and gastric reconstruction on 22,Jan,2022. Several cycles of adjuvant concurrent chemoradiotherapy with cisplatin and 5-fluorouracil were administered. Radiotherapy was administered to the esophageal tumor bed and anastomosis with margin. However, PET scan reported relapse over the posterior mediastinal region seemingly along the route of native upper/middle thoracic esophagus. Due to progressing disease, the patient received nine times of ICI therapy with Ociperlimab 900 mg and Tislelizumab 200 mg during 18 July, 2022 to 3 Jan,2023.

The patient presented with chest tightness, shortness of breath and fever for one week. Electrocardiogram (ECG) revealed aVR, V1-2 ST elevation with diffuse T wave inversion (Fig. 1). The level of hs-troponin-I (25.1944 ng/mL) and NT-pro BNP(15492

Figure 1 Initial ECG
ST elevation over aVR, V1-2 with diffuse T wave inversion

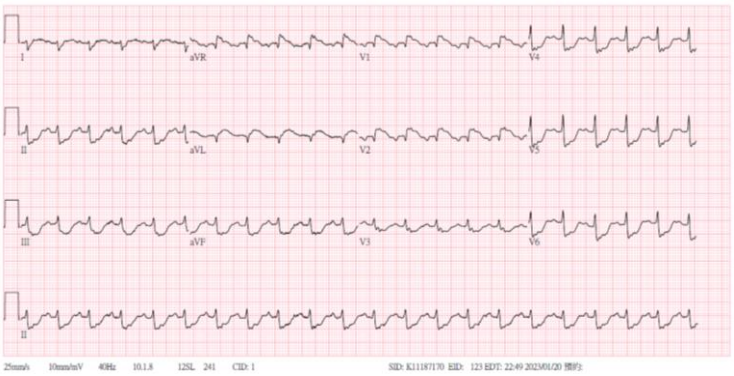
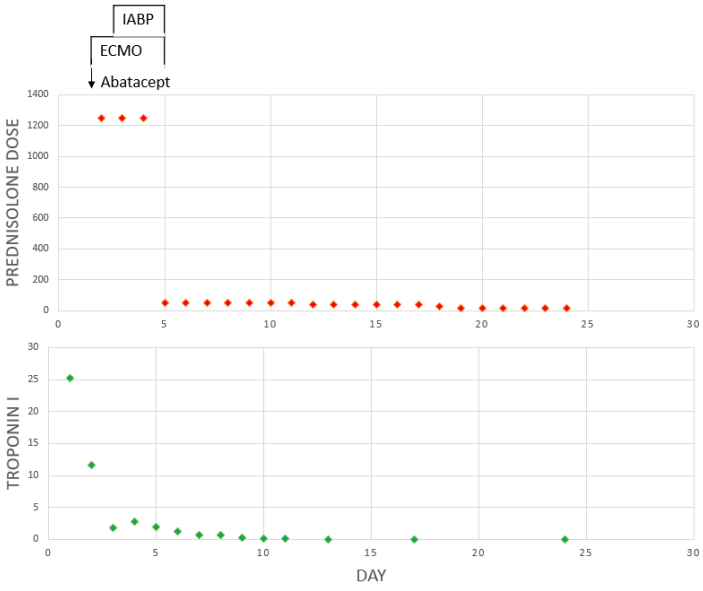


Figure 2 Trponin I level and steroid dose level change
Troponin I level decreased in three days after steroid and Abatacept



pg/mL) were elevated. Coronary angiography showed patent coronary artery. Cardiac echo reported global hypokinesia to akinesia with relative apical sparing and impaired LV contractility. According to the history of Ociperlimab and Tislelizumab injection recently and no significant stenosis of coronary artery, ICI-related myocarditis was suspected. Arrhythmia with ventricular tachycardia developed on the second day of admission. The defibrillation and organ support with veno-arterial membrane oxygenation (VA-ECMO) and intra-aortic balloon pump (IABP) were implanted. Steroid with methylprednisolone pulse therapy was infused for three days (at a dose of 1000mg) and taper to prednisone 1mg/kg/day for 7 days. Intravenous abatacept (at a dose of 500mg) was empirically administered. As the level of troponin I and symptoms of myocarditis progressively decreased (Fig. 2). , ECMO and IABP were removed and the dose of steroid gradually tapered. The patient was discharged six weeks after admission.

Discussion

ICI–related myocarditis is rare but severe complication. The exact mechanism of ICI-related myocarditis remains unclear. Proposed hypothesis include shared antigens between tumors and the heart, T-cells targeting muscle antigens similar to tumor antigens, or T-cells attacking dissimilar antigens[1]. Clinical presentations includes arrhythmias, myocardial infarction, heart failure or cardiogenic shock. Diagnosis includes imaging studies such as echocardiography or cardiac MRI, clinical symptoms, positive biomarker, ECG, pathology of myocarditis or negative angiography for coronary artery disease[2]. Endomyocardial biopsy is the gold standard diagnostic test for myocarditis using the Dallas criteria, which requires inflammatory infiltrate and myocardial necrosis. High-dose corticosteroids are a primary treatment, with additional immunosuppressants if needed for non-responsive cases. Prompt initiation of immunosuppressive therapy is essential to prevent irreversible immune-mediated myocardial damage and subsequent cardiac injury[3].

Abatacept inhibits T-cell activation by specifically targeting CTLA-4, a regulatory protein on T cells. By blocking CTLA-4, Abatacept disrupts the interaction between T cells and antigen-presenting cells (APCs), reducing the production of inflammatory cytokines involved in tissue inflammation and autoimmunity[4]. While not a standard treatment for IRAEs, case reports suggest that Abatacept may be effective, especially in managing ICI-related myocarditis that does not respond adequately to corticosteroids. The use of Abatacept in IRAEs remains largely based on case reports, emphasizing the need for further research and clinical experience to establish its role definitively in managing these complex immune-related complications[5]. Our patient previously had a normal sinus rhythm on ECG. Following nine cycles of ociperlimab and tiselelizumab treatment, she presented with dyspnea and chest tightness. ECG displayed ST elevation in aVR and leads V1-2, alongside diffuse T wave inversion, accompanied by cardiogenic shock and ventricular arrhythmia. Investigations failed to definitively identify infectious, malignant, rheumatologic, or toxic causes. Considering her drug history, we strongly suspected immune-mediated cardiac arrhythmia leading to myocarditis induced by Ociperlimab and Tiselelizumab. Steroid and immunosuppressive drug of abatacept led to a decline in cardiac enzyme levels. Subsequent ECGs revealed no T wave inversion or arrhythmia, confirming the diagnosis of IRAE. Further clinical experience is crucial for accurate management, especially in complex and rare cases.

Conclusion

We report a rare but severe case of ICI-related myocarditis associated with the concurrent use of Ociperlimab and Tiselelizumab. We reversed the patient by using steroid plus abatacept, which may serve as basis for the treatment of ICI-related myocarditis. The clinical presentation of ICI-related myocarditis varies widely, posing challenges for diagnosis. Further research is necessary to determine the accurate diagnosis and optimal management strategies.

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病例報告　112_C 65

登革熱誘發血栓性血小板低下紫斑症:重要的臨床考量及治療案例報告

Dengue Fever-Induced Thrombotic Thrombocytopenic Purpura: A Case Report of Critical Clinical Considerations and Therapeutic Approach

蔡佳妤[1] 陳怡儒[1,2] 洪毓權[1,2] 蘇浤傑[1,4] 鄭孟瑜[1,4] 何茂旺[1,4] 呂思瑩[1,2] 黃歆茹[1,2] 吳秉儒[1,3] 賴彬卿[1,2]
中國醫藥大學附設醫院[1]內科部 [2]內科部腎臟系 [3]內科部胸腔科 [4]內科部感染科

Introduction

Thrombotic thrombocytopenic purpura (TTP) is a form of microangiopathic hemolytic anemia typically marked by a combination of fever, hemolytic anemia, thrombocytopenia, along with renal and neurological abnormalities. The condition arises due to either congenital or acquired deficiency or absence of ADAMTS13, the protease responsible for cleaving von Willebrand factor. Diminished levels of ADAMTS13 activity facilitate the formation of microthrombi, precipitating ischemia and damage to the terminal organs. Acquired TTP, predominantly induced by autoantibodies against ADAMTS13, is more prevalent than the congenital form. Factors like antiplatelet drugs, immunosuppressive medications, HIV, estrogen-based contraceptives, and pregnancy are noted as the primary catalysts for the development of autoantibodies against ADAMTS13, leading to acquired TTP.

The occurrence of acquired TTP, incited by Dengue fever, is exceptionally rare. Here, we present a successfully treated case of a patient who developed TTP as a result of Dengue fever.

Case presentation

A 39-year-old female, with no past medical history, was urgently admitted due to a progressively intensifying lethargy spanning several days. She had been volunteering in Cambodia in the past five months ago before hospitalization, primarily participating in indoor religious activities, without exposure to natural environments or consumption of raw foods. Two weeks prior to admission, she exhibited diminished appetite, accompanied by nausea and vomiting. Due to progressive dyspnea and generalized weakness, she sought medical attention at a local clinic two days before admission, where laboratory findings included: CRP 48 mg/L, positive anti-Dengue IgM and IgG, GPT 29U/L, platelet count 31,000/μL, and Cr 151 μmol/L. She also exhibited fever and multiple petechiae, and Dengue fever was confirmed due to thrombocytopenia and positive Dengue IgM. She immediately returned to Taiwan, initially maintaining consciousness, mobility, and speech but deteriorated to speechlessness and reliance on a wheelchair approximately two hours post-arrival.

One day before admission, a notable decline in consciousness was evident; verbal communication was absent. Emergency department assessment revealed punctate rashes across all limbs. Laboratory analysis disclosed platelet count of 20,000/μL, anemia (Hb: 5.2 g/dL), elevated creatinine (1.27mg/dL), total bilirubin 3.19 mg/dL with direct bilirubin 0.53 mg/dL. LDH was 2311 U/L, Haptoglobin: <5.83 mg/dL, and troponin I 0.3 ng/mL, with normal PT and APTT. Both Direct and Indirect Coombs' Tests were negative. A rapid Dengue fever IgG test returned positive with numerous fragmented RBCs observed on blood smear. A fever peaking at 38.6°C and seizures were observed in the ER. Comprehensive CT scans revealed no discernible abnormalities. The presenting condition, suggestive of thrombotic

microangiopathy (TMA) with concurrent cerebral, cardiac, and renal involvement, necessitated intensive care, instigation of plasma exchange, steroid therapy, and empirical antibiotic administration. Subsequent revelation of 0% ADAMTS13 activity confirmed a diagnosis of TTP. All antiphospholipid syndrome and lupus antibodies were normal, with negative results for CMV, HSV, HIV, HBV, HCV, B19 virus, and EBV. CSF pathogen panel PCR, COVID-19 PCR, and respiratory panel PCR were all negative. Post-plasma exchange and steroid treatment, the patient exhibited considerable improvement, with complete resolution of previous consciousness alterations, and normalization of renal and cardiac function, without sequela. Given the normal ADAMTS13 gene, the diagnosis was confirmed as acquired TTP, precipitated by Dengue fever.

Discussion

Dengue is an arthropod-borne viral disease with a global presence. The vast majority of dengue virus infections manifest as mild symptoms or remain asymptomatic. However, a minor proportion of patients can develop severe conditions including hemorrhagic complications, shock, hepatic damage, cardiomyopathy, encephalopathy, convulsions, meningoencephalitis, and renal failure. TTP is a rare but serious condition associated with TMA, leading to multiple organ failure if diagnosed late. The co-occurrence of TTP with a dengue viral infection is extremely rare and has been documented in only a handful of cases. Given the prevalence of dengue fever in Taiwan during certain times of the year, there might still be a rare instance of dengue fever patients being triggered to develop TTP. If clinical physicians merely diagnose the condition as hemorrhagic dengue fever and adopt supportive care without considering the possibility of TMA, and without confirming ADAMTS13 to rule out TTP, then opportunities for early intervention with plasma exchange and steroid treatment, which can restore patients to normalcy, may be missed.

Conclusion

This case underscores the critical intersection of TTP and Dengue fever, a rare convergence with profound implications. While Dengue predominantly presents with mild or asymptomatic manifestations, its potential to trigger severe complications, including TTP—a grave condition associated with TMA—demands vigilant clinical attention and discernment. The expedited identification of such complications coupled with immediate initiation of tailored interventions such as plasma exchange can significantly ameliorate patient outcomes, preventing irreversible organ damage and ensuring holistic recovery. This instance stresses the imperative for heightened clinical suspicion and decisive intervention in cases where dengue fever might mask the evolution of severe, underlying conditions like TTP, especially in regions with prevalent Dengue occurrences. Further comprehensive studies are pivotal to elucidate the intricate interplay between Dengue virus infections and the onset of TTP, enhancing our understanding and management of these complex medical phenomena.

病例報告　112_C 66

結合射頻燒灼術與 Marshall 靜脈酒精注射成功治療二尖瓣峽部心房撲動-案例報告

Combined Radiofrequency Ablation and Vein of Marshall Ethanol Infusion for Mitral Isthmus Dependent Atrial Flutter

羅翊賓 [1] 黃志勤 [2] 林晏年 [2]
[1] 中國醫藥大學附設醫院內科部 [2] 中國醫藥大學附設醫院內科部心臟血管系

Background

Atrial flutter(AFL) has been defined as a macro-reentrant tachycardia(MRT) around an anatomic obstacle. Mitral isthmus ablation is an established technique used to treat perimetral atrial flutter. Nonetheless, detailed anatomic studies have demonstrated significant variation in the thickness of the myocardium along the mitral isthmus, which results the procedure failure. To complete successful transmual mitral isthmus block, vein of Marshall (VOM) ethanol infusion has emerged as a relatively new therapeutic option[3].

Case presentation

This is a 67-year-old female with history of atrial fibrillation. She underwent pulmonary vein isolation 3 years ago. In the last 3 months, she presented with drug-refractory palpitation despite she took amiodarone 200mg TID, propafenone 150mg BID, diltiazem 30mg TID, propranolol 10mg TID. EKG showed atypical flutter(Figure 1). Under the indication of sustained symptomatic and drug refractoy atrial flutter, she underwent another ablation attempt after exclusion LAA thrombus with TEE. LAT map showed vertical and horizontal re-entrant circuits. The roof and posterior wall were targeted first but did not terminate the tachycardia. Then, we proceeded mitral line ablation. Although aggressive ablation, the tachycardia cycle length only prolonged from 300ms to 330 ms with sequence change. CS and endocardial both showed a conduction gap and missing LAT histogram, epicardial connection is highly suspected. CS venogram showed the presence of Marshall vein.(figure 2.) Persistent atrial flutter was terminated by Vein of Marshall Ethanol infusion (Figure 3.) She remained sinus rhythm after a follow up 41 days.

Figure.1: atypical atrial flutter

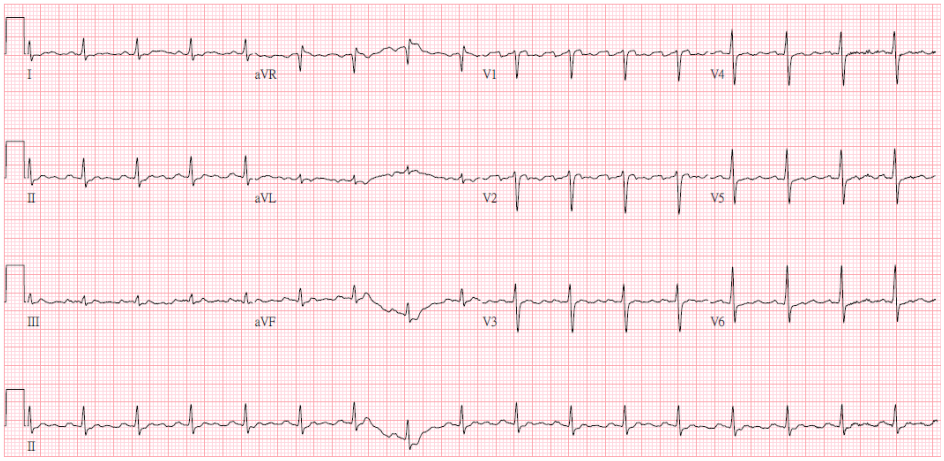
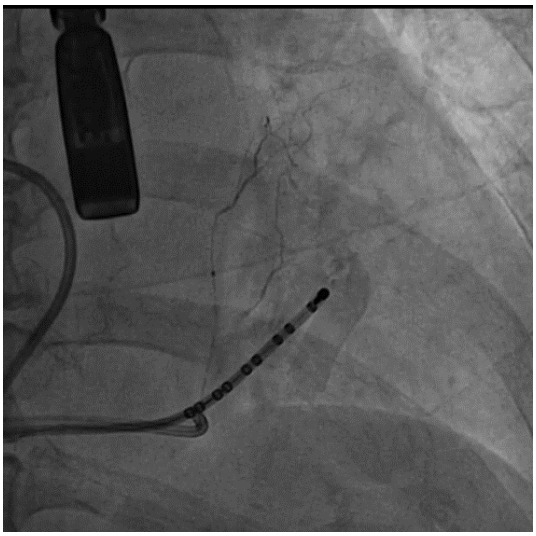


Figure 2. Marshall vein selective venograms showed a medial and lateral branch



Discussion

Figure 3.Termination of atrial flutter after Vein of Marshall ethanol infusion

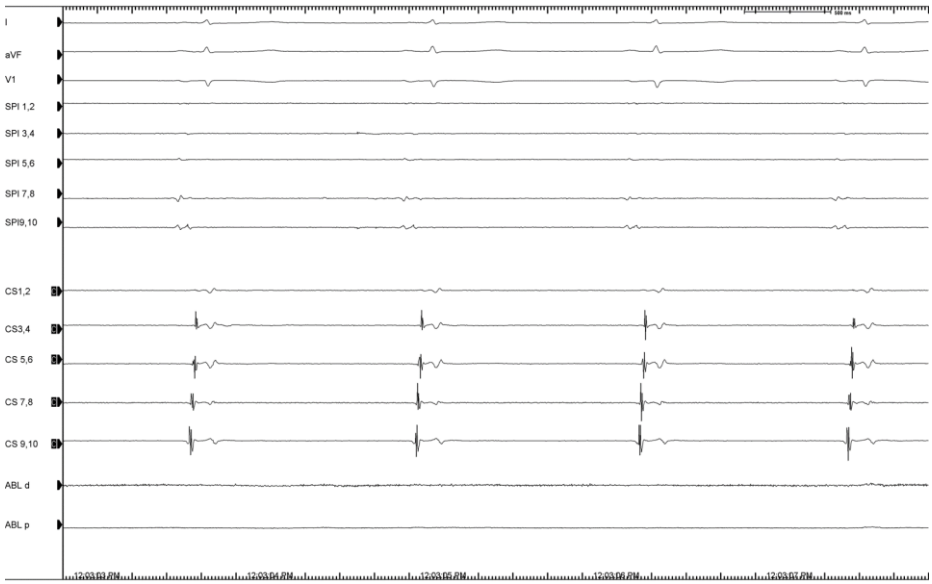
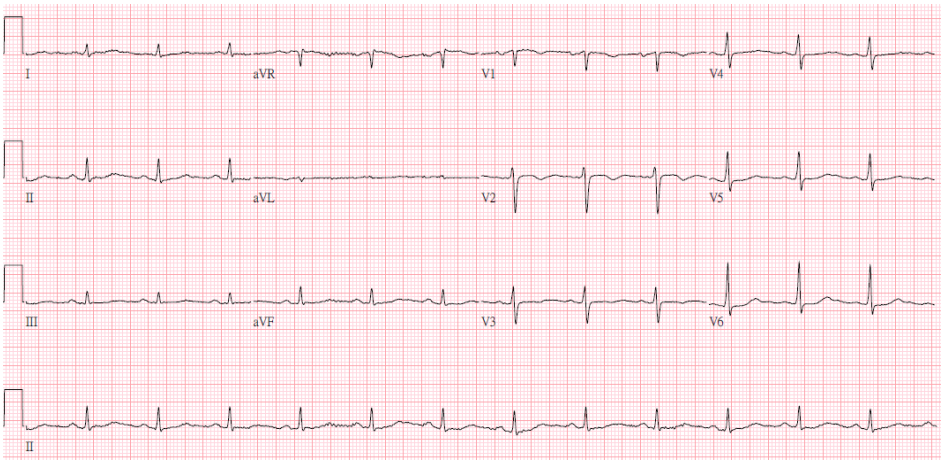


Figure 4. Follow-up EKG report sinus rhythm



The VOM and the ligament of Marshall (LOM) have been the focus of attention of basic and clinical electrophysiologists for several decades. The LOM is a vestigial fold that results from the embryonic obliteration of the left anterior cardinal vein during the transition from a symmetric venous system to the right-sided one. The LOM can be conceived as a connecting pathway between intrathoracic cardiac ganglia and intrinsic cardiac ganglia, specifically the inferior left ganglion, which is located below the left inferior pulmonary vein (LIPV), and would coincide more closely with the VOM as it connects with the CS.Previous studies have shown that the VOM/LOM is a potential cause of AF and a therapeutic target. In patients with persistent AF, the VENUS trial[4] showed that addition of VOM ethanol infusion to catheter ablation, compared with catheter ablation alone, increased the likelihood of remaining free of AF or atrial tachycardia at 6 and 12 months (49.2% vs 38%; P=0.04).

In prior studies, success rates in achieving bidirectional Mitral isthmus block with RFA have been reported to be between 32-92%, and reported ablation times required in previous studies varies around 15±8 minutes, with ablation within the CS needed in 54-91%. José L. Báez-Escudero et al. reported VOM ethanol infusion assists in achieving bidirectional MI block consistently and with minimal RFA times, and it does so in patients with and without prior left atrial ablation[5].

There are following tips for vein of Marshall localization. VOM ostium always sites slightly proximal from the valve of Vieussens, which is distinguished either indirectly by iodine pooling or directly as a translucent structure. A large balloon occluding the coronary sinus is also helpful to visualize the VOM.

Serious complications were also evaluated in 713 consecutive patients treated with VOM ethanol infusion by Tsukasa Kamakura et al.[6] The following adverse events were reported in their study: (1) VOM perforation (2.8%),defined as iodine extravasation into the pericardial

space; (2) pericarditis (1.8%)(3) cardiac tamponade(1.0%); (4) stroke(0.6%); (5) anaphylactic shock (0.15%); (6) high-degree atrioventricular block(0.15%); (7)left atrial appendage isolation(0.15%). In spite of the possible complication, VOM ethanol infusion is highly feasible, with an excellent success rate after the first attempt.
We provided the case with refractory atrial flutter successfully treated with combined technique of radiofrequency ablation and vein of Marshall ethanol infusion without complication.

Conclusion

The evidence regarding the efficacy of Vein of Marshall ethanol infusion for refractory atrial flutter is still evolving. Research studies and case reports have shown promising results in some patients, with successful termination of atrial flutter and improvement in symptoms. However, it's important to note that this technique is considered relatively novel, and more research is needed to establish its long-term effectiveness, safety, and appropriate patient selection criteria.

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病例報告　112_C 67

一位新診斷急性愛滋病毒感染的 31 歲男性伴隨陰性抗體免疫層析確認檢驗法結果

A 31 year old male diagnosed as acute HIV with negative results of HIV 1/ 2 antibody confirmatory test

張傑 [1]　鄭孟瑜 [1,2]

[1] 中國醫藥大學附設醫院內科部　[2] 中國醫藥大學附設醫院感染科

Introduction

We present a 31 year old male with a past history of seizure attack was admitted to CMUH because of intermittent fever and general fatigue for five days. HIV was impressed after lab data disclosed positive of HIV Ag/Ab combo test. While HIV 1/ 2 antibody confirmatory test showed negative and the viral load was >1.0E+7 copies/mL. Improved clinical status and lab data follow-up after Biktarvy used.

This is a 31 year old male with a past history of seizure attack who was admitted to CMUH because of intermittent fever and general fatigue for five days. Intermittent fever with chills accompanied with sore throat, cough with whitish sputum and mild chest tightness with dyspnea. He denied headache, nausea, vomiting, abdominal pain, diarrhea, dysuria, hematuria, skin rash. He also denied contact history of animal, insect or other people with fever. Two days prior to admission, he visited our ER where elevated liver enzymes(ALT 72) and thrombocytopenia(92000) were noted. No specific findings on physical examination (injection wound) or image survey. He then discharged.

Table 1

on admission (2023/6/5)					
WBC	3200 μl	BUN	9 mg/dl	RPR	Non-reactive
Neutrophil	46.8%	Creatinine	0.68 mg/dl	TPHA	<1:80
Lymphocyte	12.1%	Na	135mmol/L	HBsAg	Non-reactive
Monocyte	13.7%	K	3.7mmol/L	HCVAb	Non-reactive
Eosinophil	0%	Ca	9.0 mg/dl	Anti-HBs	190.02
Basophil	0%	Mg	2.7 mg/dl	AntiHBc-IgG	Non-reactive
Hb	14 g/dl	Albumin	3.5 g/dl	Toxoplasma IgM(EIA)	Negative
MCV	82 fl	Lipase	76 U/L	Toxoplasma IgG(EIA)	Negative
Platelet	97000 μl	Amylase	77 U/L	Anti-CMV IgG	Positive
RBC	4.86X10^6 μl	AST	779 U/L	Anti-CMV IgM	Positive
Reticulocyte	0.24 %	ALT	423 U/L	EB VCA IgG	Positive
IgG	1280 mg/dL	T-bilirubin	0.98 mg/dl	EB VCA IgM	Negative
IgA	286 mg/dL	ALP	234 U/L	HIV Ag/Ab Combo test	Reactive
IgM	135 mg/dL	γ-GT	369 U/L	HIV 1/2 Antibody Confirmatory test	Negative
ANA	negative	LDH	815 μU/L	HIV Viral load	>1.0E+7
		TSH	5.0 IU/ml		
		Free-T4	0.82 ng/dl		
		Ferritin	>15000 ng/ml		

Table 2

Lymphocyte surface marker-Infectious disease	
Lymphocyte	1345.9 Cell/μl
CD3 Total T cells	86.5% , 1163.5 Cell/μl
CD19 Total B Cells	3.6% ,48.5 Cell/μl
CD4+ helper/inducer Cells	21.8% 292.9 Cell/μl
CD8+ suppressor/cytotoxic Cells	63.8% 859.3 Cell/μl
CD4/CD8 ratio	0.34

Since new symptoms of hemoptysis and gum bleeding was noted, he visited hema-oncology OPD where worsen of elevated liver enzymes(80) and thrombocytopenia (74000)were noted. He was then admitted to our ward for further survey. While seizure attack once was found on hospitalization day 3,we arrange brain CT to rule out ICH and lumbar to rule out CNS infection. We also survey etiology of fever include infection, inflammation, neoplasm,

miscellaneous cause. Lab data showed positive of HIV Ag/Ab combo test (80.99 S/CO). While HIV 1/ 2 antibody confirmatory test showed negative .We then obtain the blood specimen and the viral load was>1.0E+7 copies/mL. And lumbar puncture showed viral load in CSF specimen was 2.64E＋4 copies/mL. We started antiretroviral treatment with Baktarvy for HIV on hospitalization day 6. Improved clinical status and lab data follow-up after Biktarvy used. Patient was then discharged with OPD follow-up .

Discussion

We performed HIV Ag/Ab combo test first, which disclosed positive. Then we perform HIV 1/ 2 antibody confirmatory test to distinguish neither HIV-1 or HIV-2 be the infection source. However, the finding is negative. Since HIV Ag/Ab combo test detect not only HIV-1 or HIV-2 antibodies, but also HIV-1 p24 antigen. This results raise the possibilities of acute HIV infection. According to the Centers for Disease Control and Prevention (CDC) updates in 2023/5: In situations when the differentiation assay is negative or indeterminate for HIV-1 or HIV-2 antibodies, the laboratories should perform a NAT with a diagnostic claim as a third test [1,2,3].Therefore we performed test for detection of HIV RNA in the blood which showed the viral load was >1.0E+7 copies/mL. Acute HIV-1 infection was diagnosed.

Conclusion

In general, the timing we diagnosed HIV infection often contributed to chronic infection in the past. The reasons are people lack of knowledge and awareness of HIV infection at most. Acute HIV infection is often manifested by acute retroviral syndrome (fever, adenopathy, pharyngitis, rash, myalgia, headache, thrombocytopenia, leukopenia or elevated AST...). As we educate people more about HIV at daily time and people get much more easy access to HIV information on the internet, we believe we will diagnose more acute HIV cases in the future.

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病例報告　112_C 68

少見之反覆上消化道出血原因：一例栓塞後產生之線圈位移

Recurrent Gastrointestinal Bleeding with Unique Etiology: A Case of Coil Migration Post-Transarterial Embolization

邱靖之[1]　張安迪[2]
[1]中國醫藥大學附設醫院內科部　[2]中國醫藥大學附設醫院內科部消化系

Introduction

Upper gastrointestinal bleeding (UGIB) remains a considerable clinical hurdle, especially when confronted with a relatively uncommon underlying cause, which can pose a diagnostic conundrum. Here, we report a patient experienced recurrent UGIB episodes, with primary cause remaining elusive despite undergoing numerous times of endoscopic examinations and computed tomography (CT) examinations.

Case presentation

The patient, a 59-year-old man, with a complex medical history including type 2 diabetes mellitus, hypertension, chronic pancreatitis, diverticulitis of the ascending colon, and a history of gastric ulcer, presented with tarry stool for four days, leading to hypovolemic shock with a hemoglobin level of 6.2 g/dL during an admission in February 2021. An initial esophagogastroduodenoscopy(EGD) revealed reflux esophagitis, LA grade A and subsequent blood transfusion was administered. The hemoglobin level increased to 10.2 g/dL after blood transfusion. However, intermittent bloody stool persisted. Colonoscopy identified diverticulum in the ascending and descending colon but no active bleeding. Symptom of bloody stool improved then with stable hemoglobin level. The patient was thus discharged with outpatient follow-up.

Recurrent Episodes:

The patient returned to the emergency department in March 2021 due to recurrent bloody stool over two days. Mild anemia (Hemoglobin: 10.1 g/dL) was noted, and a repeated EGD revealed gastric mucosal changes, including an ulcer in the antrum and low body of the stomach. Another episode of gastrointestinal bleeding episode with presentation of intermittent tarry stool for one week developed in early-May 2021, and thus presented to our emergency department with severe anemia (Hemoglobin: 4.5 g/dL). However, despite various investigations during the admission, including panendoscopy, colonoscopy, capsule enteroscopy and abdominal CT, which disclosed no contrast extravasation, the source of bleeding remained elusive.

Severe Hemorrhage and Intervention:

In mid-May 2021, the patient experienced a severe episode of massive bloody emesis associated with dyspnea. Hemoglobin levels plummeted to 6.2 g/dL from 8.6 g/dL. Aggressive hydration and blood transfusions were initiated. Due to the extent of the bleeding, a double lumen catheter was inserted for continuous transfusions. Emergent intubation was performed for airway protection during an EGD, which still just revealed a gastric shallow ulcer in the antrum, and incomplete study due to extensive blood clot retention.

Subsequent investigations, including angiography and enteroscopy, but still failed to identify the source of bleeding even of Tc-99m-RBC scan, which disclosed no definite evidence of

active gastrointestinal bleeding.

Suspected Etiology and Surgical Intervention:

Following a period of stability, the patient experienced another bout of massive bleeding with upper left quadrant pain at the end of May 2021. Tracking his medical history, he had ever received transcatheter arterial embolization (TAE) for splenic artery pseudoaneurysm. An EGD identified a deep ulcer near the cardia with a suspected metallic coil, likely originated from a previous coil embolization of the splenic artery pseudoaneurysm (Fig.1). Abdominal CT confirmed the presence of three metallic materials corresponding to the TAE sites. (Fig.2 ; Fig.3)

Follow-Up and Management:

Post-discharge, the patient underwent further percutaneous abscess drainage insertion due to persistent anemia and hematoma formation found on abdominal CT (Fig.6) with presentation of severe left upper quadrant pain and fever. A pseudoaneurysm over the splenic artery was suspected and successfully embolized (Fig.7). With stabilized conditions, the patient was discharged with ongoing percutaneous abscess drainage revisions for hematoma management. After further angiographic evaluations and subsequent percutaneous abscess drainage revisions, the patient's condition improved with percutaneous abscess drainage removed in September 2021.

Fig.1

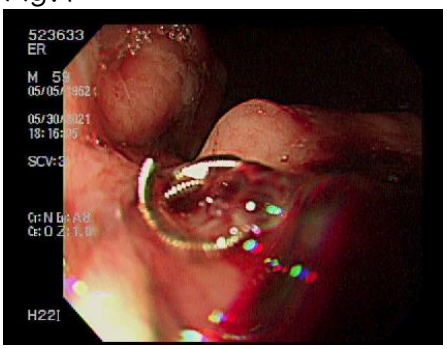


Fig.2

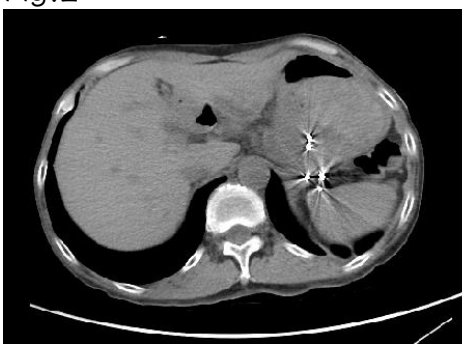


Fig.3

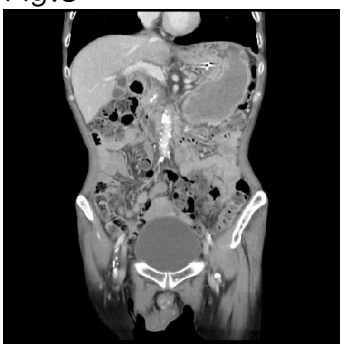


Fig.4

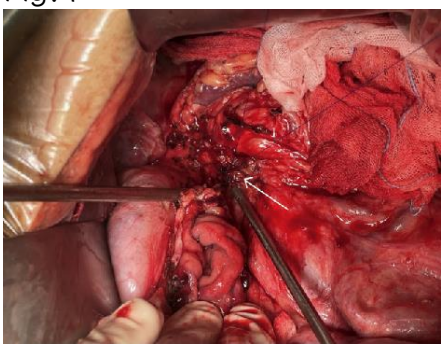


Fig.5

Fig.6

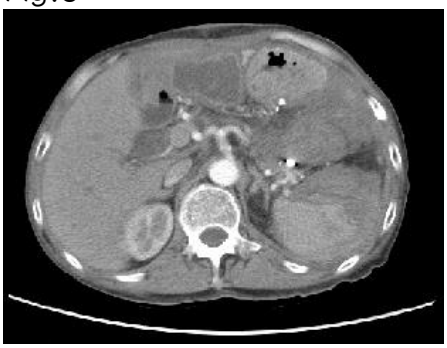
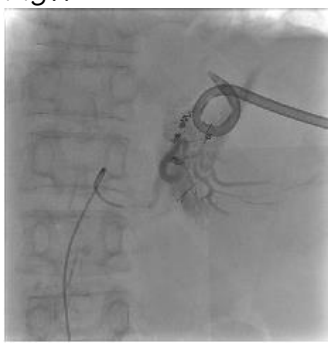


Fig.7



Discussion

Upper gastrointestinal bleeding (UGIB) continues to present a significant clinical challenge, associated with substantial morbidity and mortality rates. The recommended initial approach for treatment is endoscopic hemostatic intervention.

While UGIB can be caused from various etiologies, such as peptic ulcers (47.1%), gastritis(18.1%), esophagitis(15.2%), Mallory – Weiss tears(6.9%), and several other contributing factors[1], coil migration is an exceedingly rare occurrence among these etiologies, with only sixteen cases documented in a literature review[2]. Only in 7 of these cases, the coil migrated into the stomach, which were similar as our case. However, this occurrence can manifest either shortly after the procedure or several years later, ranging from 2 months to 10 years[3], and may lead to severe bleeding due to the development of aorto-enteric fistulas and infections, potentially resulting in fatality. Although the underlying cause of coil migration remained unclear, there was the hypothesis positing that embolization of the feeding artery may induces ischemia, creating conditions conducive to coil migration through the bowel wall[5].

The initial failure to identify coil migration can be attributed to several factors. Firstly, the coil may have become encased within the muscle layers of the gastric wall, resulting in intermittent bleeding episodes that were not readily apparent during initial endoscopic examinations. Secondly, the gasdilation and expansion during EGD may have been inadequate to reveal the coil, potentially being obscured by gastric folds. This limitation in visualization could have contributed to the diagnostic challenge. Lastly, the presence of extensive blood clots within the stomach could have compromised the examination field, further hindering the identification of the migrated coil.

Conclusion

This case underscores the challenging nature of recurrent gastrointestinal bleeding secondary to embolization coil migration. This case report aims to draw attention to the possibility of GI bleeding caused by coil migration. When dealing with a case of chronic pancreatitis accompanied by recurrent UGIB, it is crucial to keep coil migration in mind, particularly if there has been previous TAE treatment.

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病例報告　112_C 69

一個痛風性關節炎和 A 型鏈球菌感染性關節炎同時發生的案例

Concurrent Acute Gouty Arthritis and Group A Streptococcus-related Septic Arthritis: a Case Report

余侑達[1] 周家卉[2] 蘇浤傑[2] 何茂旺[2,3] 王鍵元[4]
[1]中國醫藥大學附設醫院內科部 [2]中國醫藥大學附設醫院內科部感染科 [3]中國醫藥大學醫學院
[4]中國醫藥大學新竹附設分院

Introduction

Concomitant gouty arthritis and septic arthritis is a rare event, but it can happen – many cases had been reported. Aspiration of joint fluid is part of the standard protocol to manage arthritis, and it is promptly ordered for both gouty arthritis or septic arthritis; however, when both conditions co-exist, features of gouty arthritis might mask the presence of septic arthritis, especially when important diagnostic tests such as gram-staining and culture of synovial fluid return false-negative results. Clinical pictures and results of laboratory investigations should be vigilantly combined to guide further plans of management.

Case presentation

A 38-year-old male businessman without any particular chronic disease experienced a sudden onset of fever with arthralgia in his left ankle. He was brought to the emergency department for management. During the clinical encounter, the left ankle seemed swollen. Range of motion was limited and the area of redness was about 6x7 cm over the left ankle; it was painful to touch. Blood work showed leukocytosis with neutrophilia; C-reactive protein was elevated in serum.

Aspiration of synovial fluid was arranged at the emergency department. Content of the synovial fluid showed extreme leukocytosis (332,800/uL) with neutrophilia (95%); monosodium urate crystals were present both intracellularly and extracellularly. The patient was therefore treated as a case of gouty arthritis combined with septic arthritis; oxacillin and ceftriaxone were empirically prescribed. Computed tomography of lower limbs revealed presence of articular effusion in ankle joints bilaterally; the left side seemed more prominent. Department of orthopedics was contacted and arthrotomy was performed at left ankle joint from anterior approach; after irrigation, Hemovac® drainage was deployed for drainage, and then the wound was sutured layer by layer. Culture of synovial fluid and culture of blood both identified *Streptococcus pyogenes* sensitive to penicillin; combination of oxacillin and ceftriaxone was therefore de-escalated to penicillin G. Administration of penicillin G continued for about one week as fever recurred, and then antibiotic was switched to ceftriaxone for another two weeks. Hemovac® drainage remained in place until the drainage became clear. After the patient became ambulatory again, he was discharged under prescription of oral clindamycin for another 9 weeks. He had cellulitis on the same limb for the next 5 years, but no sequela involving the joint had been detected.

Discussion

Gouty arthritis and septic arthritis are different kinds of arthritis; while gouty arthritis is more common, septic arthritis is relatively infrequent. Concurrence of gouty arthritis and

septic arthritis is, therefore, a rare condition. The septic component could be caused by Staphylococcus aureus and species of Streptococcus, Salmonella, Proteus, Pseudomonas, etc. The joint involved is mostly knee. Clinical symptoms such as fever, arthralgia, swelling of joint, limited range of motion could be present. However, laboratory investigation might not always return positive results; leukocytosis in blood, leukocytosis in synovial fluid, meaningful gram-stain and microbes in blood culture might not always be consistent. False negative results could lead to delay of proper treatment, and previous study had shown that negative results in gram-stain and culture of synovial fluid would not rule-out septic arthritis. As a result, multiple entities should be utilized for diagnostic purposes; the overall clinical picture should prompt blood work, and aspiration of synovial fluid for analysis should be timely, and then the results should be combined with the clinical picture to guide further management. When suspecting presence of the septic component, early diagnosis by joint fluid analysis and surgical drainage should also be arranged whenever necessary in addition to treatment using empirical antibiotics.

Conclusion

While gouty arthritis is usually a common condition, septic arthritis is highly destructive and potentially life-threatening. However, despite that concurrent acute-on-chronic condition could definitely exist, overlapping clinical picture could lead to confusion when formulating the working diagnosis upon acquiring false negative results. Timely aspiration of joint fluid and completing analysis of synovial fluid is definitely necessary, but the overall clinical picture should still be considered for judgment of situation, which would then allow arrangement of empirical treatments. A solid protocol of diagnostic framework is the key to timely diagnosis, which would then prompt proper treatment to ensure safety of the patient.

病例報告　112_C 70

腎臟移植後出現腔室症候群的案例分析

Insightful Exploration: A Case of Renal Allograft Compartment Syndrome

涂承佑[1] 陳怡儒[1,2] 蕭博任[3] 洪毓權[1,2] 黃志平[3] 賴彬卿[1,2] 黃秋錦[1,2]
[1]中國醫藥大學附設醫院內科部 [2]中國醫藥大學附設醫院內科部腎臟系 [3]中國醫藥大學附設醫院泌尿部

Introduction

Renal allograft compartment syndrome (RACS) arises due to external compression, leading to graft dysfunction and loss secondary to ischemia. If such a possibility is not contemplated by the clinician, the transplanted kidney may unfortunately succumb to functional loss. We discuss a case involving a 51-year-old male suffering from Compartment syndrome of the renal allograft, including instances where successful intervention was achieved.

Case presentation

A 51-year-old male, with a history of hypertension associated, end-stage renal disease, has been undergoing hemodialysis for a decade. He has a stature of 178cm, a weight of 99kg, and a body mass index of 31.2. HLA matching displayed a solitary 1A1B mismatch, with both B and T cell crossmatches returning negative results. PRA class I was at 3.5 and class II at 0.2. The cadaveric donor, a 59-year-old male, measuring 172 cm and weighing 55kg, had no systemic diseases and was brought to our Emergency Room with an initial Cr level of 1.39 mg/dL, experiencing an Intracranial Hemorrhage during work. The donor's final 24-hour urine volume prior to kidney donation was 3430ml, with a Cr level of 2.2 mg/dL. The warm ischemia time documented was 76 minutes and the cold ischemia time was 8 hours and 13 minutes, with urine output commencing 30 minutes from the graft kidney; the recipient had been anuric for several years post-hemodialysis. Following a seamless cadaveric kidney transplantation, the patient remained in the Post-Operative Room (POR) for ventilator weaning, and upon stabilization with a smooth respiratory pattern, was transitioned to the Intensive Care Unit (ICU). However, upon arrival to the ICU, an ultrasound performed by the nephrologist to monitor graft blood flow disclosed an absence of detectable blood flow in Doppler mode, despite the patient's normotensive state and the absence of acute anemia, hematuria, or substantial bleeding from the Jackson-Pratt drain. Consequently, an emergent exploratory laparotomy was promptly executed. Nevertheless, inspection by the urologist confirmed the integrity of the anastomosis of both the renal vein and artery. A potential small thrombus was overlooked as there was no obvious indication of one. A minor incision was made to the renal vein, revealing a consistent blood flow. Additionally, intra-operative ultrasonography showed gradual improvement in graft blood flow. Suspecting renal allograft compartment syndrome, the abdominal wall was sealed with a Bogota bag to alleviate tension. Post successful weaning, the patient was relocated to the ICU, where improved graft blood flow was noted by the nephrologist through ultrasonography, compared to prior operating room images. Regular immunosuppressants and empirical antibiotics were administered, allowing for direct monitoring of the graft kidney's appearance via the Bogota bag. The patient's urine volume showed progressive improvement, and subsequent color Doppler ultrasound showed effective perfusion to the graft kidney. Post wound closure, by the fourth day, urine output had incrementally risen to approximately 4000ml daily.

Discussion

An elevation in intra-abdominal pressure (IAP) is a prevalent condition among patients post-operatively and has the potential to induce organ dysfunction. However, the implications of increased IAP on complications and graft recuperation subsequent to kidney transplantation are not thoroughly studied or understood. Typically, a regime of moderate hyperhydration is administered during conventional renal transplants, and there is an ongoing inquiry regarding whether this strategy induces the evolution of intra-abdominal hypertension (IAH).

Referencing a study by Dupont V et al., out of 107 enrolled patients, 55 were incorporated in the study, and 74.5% were found to have developed IAH. A Body Mass Index (BMI) >25 kg/m² was associated with the occurrence of IAH {Odds Ratio [OR] 10.4 [95% Confidence Interval (CI) 2.0–52.9]; P = 0.005}. Additionally, a study by Coca A et al. disclosed that 78% of subjects manifested intra-abdominal hypertension within the initial 72 hours post-operatively. Increased IAP was predominantly observed post-transplantation and was independently correlated with delayed graft functionality, complications post-surgery, and non-recovery of graft functionality. Interestingly, not only the overweight recipients appear to be at risk; recipients with a BMI <18, according to Tang L et al.'s study, are speculated to experience vascular compression leading to technical graft loss and consequently, reduced graft survival.

The therapeutic approach to Renal Allograft Compartment Syndrome (RACS) emphasizes early detection, prompt surgical re-exploration, and decompression; if detected late, the functionality of the kidney can significantly degrade, leading potentially to graft failure.

We present a case involving a patient who experienced decreased renal blood flow post-cadaveric kidney transplantation, necessitating an urgent laparotomy to rule out vascular complications. All vessel-related complications were excluded intraoperatively, leading to a consideration of Renal Allograft Compartment Syndrome (RACS) as a probable cause of impaired graft perfusion. The patient had several risk factors for Acute Compartment Syndrome (ACS), including obesity, a tight incision site closure, and resultant bowel swelling. A Bogota bag was utilized temporarily postoperatively to alleviate tension and prevent increased Intra-Abdominal Pressure (IAP). Once the swelling subsided, the wound was closed, and subsequent evaluations confirmed consistent graft perfusion, validating the RACS hypothesis for the observed perfusion impairment.

Conclusion

Immediate identification and intervention are imperative for both IAH and RACS. This case emphasizes the necessity to contemplate RACS as a plausible origin of graft kidney perfusion complications in patients post-transplant, particularly those presenting with risk factors such as obesity and previous abdominal surgeries. Prompt measures, like temporary wound closure utilizing a Bogota bag, have proven effective in mitigating abdominal pressure and maintaining graft functionality. Recognizing RACS is of paramount importance in such patients, where expedited detection and treatment are crucial in averting organ dysfunction and optimizing patient outcomes.

病例報告　112_C 71

漢他病毒感染相關的噬血症候群: 臺灣首例病例報告

Hemophagocytic Lymphohistiocytosis Associated with Hantavirus Infection: First Case Report from Taiwan

林以仁[1] 蘇浤傑[2,3] 施文心[2,3] 何茂旺[2,3]

[1]中國醫藥大學附設醫院內科部 [2]中國醫藥大學附設醫院內科部感染科 [3]中國醫藥大學醫學院內科學科

Introduction

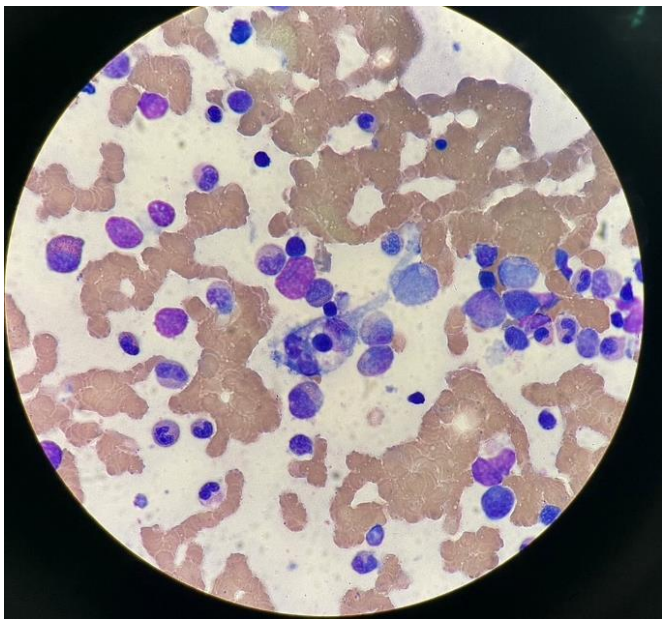
Hantavirus infection is a rare zoonotic disease that has been infrequently reported in Taiwan and is typically transmitted to humans by rodents. Patients may initially present with non-specific symptoms such as fever, headache, and flu-like symptoms, but it can still lead to severe complications such as respiratory failure and renal failure[1]. Hemophagocytic lymphohistiocytosis (HLH) is a severe and life-threatening disorder marked by dysregulated activation of lymphocytes and macrophages, leading to the excessive release of cytokines[2]. Notably, HLH can be secondary to infections, a condition wherein cases related to Hantavirus infection have been sparsely documented in the world. Hence, we are presenting a rare and severe case of Hantavirus infection complicated with hemophagocytic lymphohistiocytosis in Taiwan.

Case presentation

A 34-year-old male without systemic disease was admitted to our Infection ward due to intermittent fever with rigors for 4 days. In the initial presentation, he experienced acute high fever, shaking chills, and muscle soreness. No evidence of COVID-19 or influenza was detected in the rapid tests. He also denied any travel history, contact with individuals exhibiting fever, or cluster history. Additionally, due to occupation as a car mechanic, his exposure to rodents was evident in a factory environment characterized by untidiness and the presence of mice. After initially being treated as a common cold and monitored for 3 days, his symptoms subsequently worsened, characterized by poor appetite, nausea, vomiting, and watery diarrhea. The initial vital signs showed a heart rate of 102 beats per minute, blood pressure at 111/75 mmHg, a respiratory rate of 18 breaths per minute, no desaturation without supplemental oxygen, and a body temperature of 36.3°C. The physical examination revealed multiple petechiae on the face, neck, and lower extremities, as well as conjunctival injection. Laboratory data showed leukocytosis (12700 /ul) with neutrophil predominant (82.7%), thrombocytopenia (Platelet: 57000 /ul), elevated high sensitive C-reactive protein (17.81 mg/dL) and Procalcitonin (17 ng/mL), hyperferritinemia (>15000 ng/ml), impaired renal function (BUN: 45 mg/dL, Creatinine: 4.86 mg/dL) and elevated liver enzyme (Total bilirubin: 3.91 mg/dL, Direct bilirubin: 2.77 mg/dL, ALT/AST: 795 U/L/1050 U/L), Triglycerides (324 mg/dL). The chest X-ray did not reveal any active lung lesions. Abdominal computed tomography revealed only splenomegaly. Based on the presentation and mouse contact, there is a high suspicion of hantavirus syndrome or leptospirosis. Furthermore, in cases of persistent fever accompanied by hyperferritinemia and bicytopenia, it is highly advisable to consider hantavirus syndrome or leptospirosis-associated hemophagocytic lymphohistiocytosis as potential diagnoses. Bone marrow biopsy confirmed the presence of hemophagocytosis (Figure 1). Our surveillance encompassed various potential trigger factors,

namely Epstein-Barr virus (EBV), cytomegalovirus (CMV), HIV, Hepatitis B, Hepatitis C, mycobacterium, autoimmune profiles, and tumor markers. All of these tests yielded negative results. Minocycline and Cefotaxime were empirically administered from Day 1 to Day 12 to cover atypical infections and gastrointestinal tract translocation. Subsequently, the treatment was switched to oral Doxycycline and Cefixime. A systemic corticosteroid, Methylprednisolone, was initially prescribed at a dosage of 40mg per day to manage the Jarisch-Herxheimer reaction and then gradually tapered as necessary. Due to HLH with a catastrophic hyperinflammatory status, intravenous immunoglobulin (IVIG) was administered at a dosage of 2 g/kg over a 5-day treatment course for immunomodulation. His renal function and thrombocytopenia significantly improved, and with his overall good clinical progress. Finally, Hantavirus syndrome-associated hemophagocytic lymphohistiocytosis (HLH) was diagnosed.

Figure 1. Bone marrow biopsy present hemophagocytosis



Discussion

Hantavirus infections cause clinical illness of varying severity, which are borne by rodents. This disease can present with mild symptoms such as fever, headache, muscle soreness; but it can also lead to fatal complications such as respiratory distress or renal impairment, sometimes necessitating hemodialysis support. The virus targets endothelial cells and macrophages, triggering a dysregulated immune response due to excessive cytokine release. This leads to a significant increase in vascular permeability, resulting in marked vascular leakage, contributing to noncardiogenic pulmonary edema and cardiovascular complications, and acute tubulointerstitial nephritis[1]. Hemophagocytic lymphohistiocytosis(HLH) is a severe syndrome that is characterized by hyperinflammatory immune response related to macrophage- and lymphocyte-mediated inflammation. HLH can develop as primarily due to genetic, but more commonly, it occurs secondary to infection, malignancy, and autoimmune disease. Infection-related HLH might be caused by viruses, bacteria, fungi, or parasites. Viral infections, such as Epstein-Barr virus, cytomegalovirus, influenza, and HIV, are well known trigger factors of HLH. Diagnosis of HLH can be established according to the HLH-2004 criteria, which require the presence of at least five of the following presentations: fever, splenomegaly, cytopenia (including at least bicytopenia with hemoglobin <9 g/dL, platelets < 100,000/μL, and absolute neutrophil count < 1000/μL), hypertriglyceridemia ≥265 mg/dL and/or hypofibrinogenemia ≤ 150 mg/dL, evidence of hemophagocytosis, low or absent NK cell activity, ferritin ≥ 500 ng/mL, and elevated sCD25 ≥ 2400 U/mL[2]. Main therapy for HLH is empiric treatment for the suspected underlying condition. Additionally, systemic corticosteroids, IVIG, etoposide, cyclosporin, or other biologics can be considered in severe cases. However, Hantavirus infections are a rare etiology realized associated with HLH, and there have been only a few reported cases with limited treatment experiences. Except for

supportive care, corticosteroid, IVIG and etoposide have been reported to be used successfully in past cases[3,4,5,6]. In our case, we promptly initiated a survey of potential causative pathogens at emergency department due to impression of an atypical infection and the risk of HLH based on the patient's contact history and laboratory data. HLH could be diagnosed with fever, splenomegaly, hypertriglyceridemia, hemophagocytosis in bone marrow, and ferritin ≥ 500 ng/mL. We also initiated early broad-spectrum antibiotic treatment and administered systemic steroid for anti-inflammatory therapy. IVIG was prescribed after the diagnosis of HLH. The patient tolerated the treatment well and was finally discharge with an improved clinical condition.

Conclusion

Hantavirus infection is an uncommon rodent-borne disease that has become increasingly rare in Taiwan in recent years due to improved environmental conditions. We reported the first case of Hantavirus-induced hemophagocytic lymphohistiocytosis successfully treated with systemic steroid and IVIG. Until now, the limited experience for HLH related to Hantavirus infection has restricted our choice of therapy. In conclusion, while basic supportive care and empirical treatment have been administered, further research is needed to determine the indications and roles of IVIG and biological agents in severe cases.

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病例報告　112_C 72

不可被忽視的腹水-一位 Pseudo-pseudo Meigs' syndrome 之案例報告

Pseudo-pseudo Meigs' syndrome: The ascites that should not be neglected

王予賢[1] 楊凱介[1,2] 林武周[3]

[1]中國醫藥大學附設醫院內科部 [2]中國醫藥大學附設醫院風濕免疫科 [3]中國醫藥大學附設醫院婦產部

Abstract

Pseudo-pseudo Meigs' syndrome (PPMS) or Tjalma syndrome is a clinical condition characterized by pleural effusion, massive ascites and elevated CA-125 without benign or malignant ovarian tumor in a patient with systemic lupus erythematosus (SLE).

Case presentation

A 51-year-old woman with a history of lupus nephritis and end stage renal disease under hemodialysis, who was admitted via emergency department due to painless progressive abdominal distension for 2 weeks. She denied fever, chills, cough, abdominal pain, or body weight lost. Physical examination showed distant heart sound, decreased breathing sound over right lower lung field, and with shifting dullness over abdomen without peritoneal signs. Chest X-ray showed cardiomegaly, pleural effusion, and cardiac sonography showed large amount of pericardial effusion with right ventricle (RV) diastolic collapse sign.

She was admitted for thoracentesis and pericardial-pleural window procedure under service of cardiovascular surgeon. Jackson-Pratt (JP) drainage tube was inserted to the pericardium and left pleural space. The ascites examination revealed straw color, slight turbid, non-chylous, and with low serum ascites albumin gradient (SAAG) 0.9 g/dL, which indicated non-portal hypertension related. The ascites showed negative of bacteria, tuberculosis, and malignancy. She had high titer of serum CA-125 (1630 U/mL) (normal value: < 35 U/mL) and gynecologic malignancy was excluded after consulting a gynecologist. The abdominal computer tomography (CT) scan (Figure 1.) and positron emission tomography

Figure 1. Abdominal CT revealed massive ascites and pericardial effusion

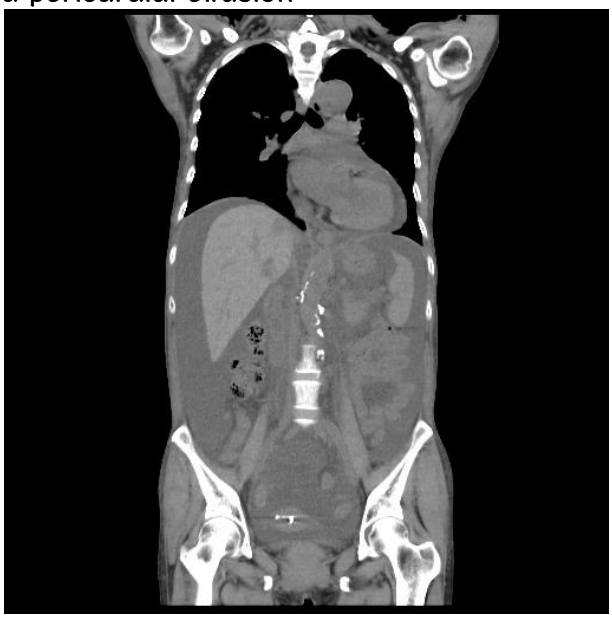
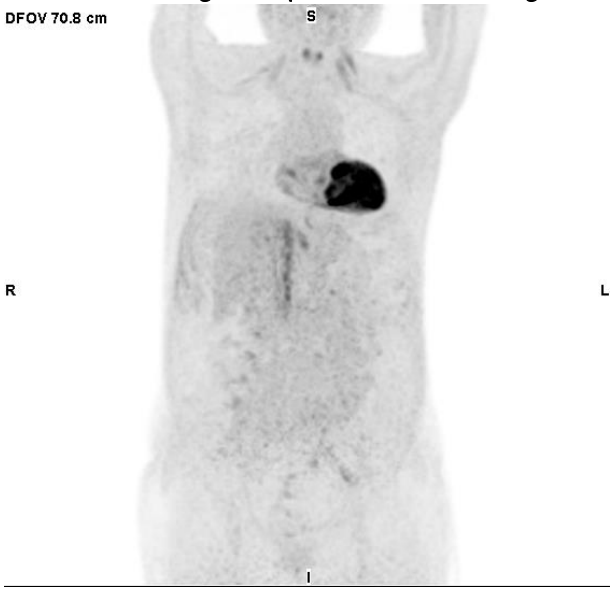


Figure 2. Positron emission tomography (PET) revealed no malignant peritoneal seeding



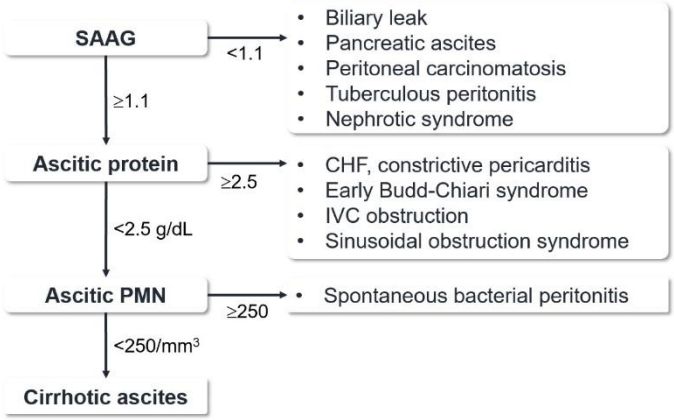
(PET) scan (Figure 2.) revealed no peritoneal seeding, liver cirrhosis, portal thrombosis, para-aortic lymphadenopathy, or ovarian/uterus tumor. Thus, given the absence of malignancy or an infectious process, a presumptive diagnosis of pseudo-pseudo Meigs' syndrome was confirmed by exclusion. She received intravenous methylprednisolone 250 mg for consecutive 3 days and with oral form prednisolone 20 mg/day subsequently. Mycophenolic acid (MPA) 360 mg twice daily was prescribed as for disease modifying anti-rheumatic drugs (DMARDs) and steroid sparing agent. The amount of pericardial effusion and pleural effusion in JP drain gradually decreased before she was discharged from hospital.

Discussion

Meigs' syndrome is diagnosed based on a triad of an ovarian fibroma, pleural effusion, and ascites. It resolves spontaneously after the resection of the fibroma. Other benign cysts of the ovary (such as struma ovarii, mucinous cystadenoma and teratomas), leiomyoma of the uterus, and secondary metastatic tumors to ovary if associated with hydrothorax are referred to as pseudo-Meigs' syndrome.

Tjalma described the first case report of a lupus patient with ascites, hydrothorax and elevated CA-125[1]. Given the patient's clinical and radiographic findings, as well as an elevated serum CA-125 level, there was concern initially for gynecologic malignancy. However, CA-125 has both poor specificity and sensitivity, and is elevated in non-malignant disease states including tuberculosis and connective-tissue diseases, including SLE[2,3]. The differential diagnosis of the ascites SAAG < 1.1 (Figure 3.) includes malignancy (peritoneal carcinomatosis, chylous ascites from malignant lymphoma), nephrotic syndrome, biliary leak, pancreatic ascites, TB, pancreatitis, ruptured pancreatic/biliary/lymph duct, Meigs' syndrome/pseudo-Meigs' syndrome, and pseudo-pseudo Meigs' syndrome such as our case. A kind of ascites that should not be neglected.

Figure 3. The differential diagnosis of the ascites
The Korean Journal of Gastroenterology 2018;72:179~187



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病例報告　112_C 73

半相合造血幹細胞移植對復發或難治性何杰金氏淋巴瘤病人可能是更好的選擇

Haploidentical hematopoietic stem cell transplantation might be a better choice for patient with relapsed/refractory Hodgkin's lymphoma

郭晉廷 [1] 葉士芃 [1,2] 陳姿廷 [1,2] 王幸婷 [1,2] 陳其敬 [1,2]
[1] 中國醫藥大學附設醫院內科部 [2] 中國醫藥大學附設醫院血液腫瘤科

Introduction

Hodgkin lymphoma (HL) accounts for approximately 10 percent of all lymphomas, and Classic HL (cHL) constitutes the large majority of HL. It has two incidence peaks, which most commonly affects adolescents and young adults aged 15-35 years, and less commonly adults ≥ 55 years old. The cure rate of HL is generally satisfactory, which is more than 90% for early-stage disease. Given that the young age and the prognosis, the mean residual live expectancy is thence promising. Most relapses of HL occur within the first two years after diagnosis, and the risk of relapse declines thereafter. However, in relapsed/refractory Hodgkin lymphoma(RRHL) patients, the rescue rate of standard high-dose chemotherapy and autologous hematopoietic stem cell transplantation(HSCT) is less than 50%. Hence, novel agents, such as brentuximab vedotin (BV), anti-CD30 antibody-drug conjugate, nivolumab and pembrolizumab, the anti-PD1 inhibitor, and allogeneic-HSCT stand out for alternative treatment options. Herein we report a case of cHL, who had been treated with 3 lines of therapy, who had confronted 2nd relapse of disease, successfully treated with haploidentical HSCT over a 42-month follow-up period.

Case presentation

A 27-year-old female without the history of chronic disease before had accidental found mediastinum mass around 8cm during regular health checkup and cHL, nodular sclerosis, initial stage IIa, was diagnosed according to the report of biopsy which showed IHC stains for CD30(+), CD15(-), CD20(weak and focal+). Bone marrow biopsy showed moderately to markedly myeloid hyperplasia. Positron Emission Tomography/ Computed tomography (PET/CT) scan disclosed malignant lesions at left anterior middle mediastinum and left supraclavicular region. After chemotherapy of four courses of ABVD + 2 courses of R-ABVD in Taichung Veterans General Hospital, which achieved 1st complete remission in May. 2012. Followed PET/CT scan showed residual enlarged lymph nodes at

Figure 1

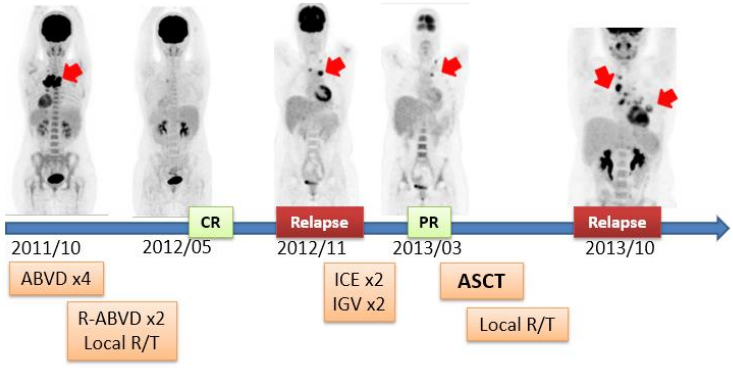
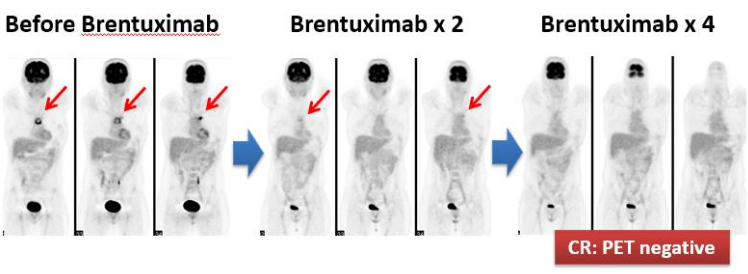


Figure 2



mediastinal region in Nov. 2012, and she received salvage chemotherapy regimen with 2 courses of ICE and 2 courses of IGV(Ifosfamide, Gemcitabine, Vinorelbine), and conditioning chemotherapy with BEAM and autologous HSCT in March 2013 because of persisted residual disease, and then subsequent adjuvant radiotherapy over mediastinal lymph node and left lower lung. 2nd relapse of left lower lung cavity and mediastinum lesion (figure 1) was proven according to pathology of thoracoscopic wedge resection performed in Oct 2013. Allogeneic HSCT was planned in 1 month after 4 doses of BV (figure 2), and human leukocyte antigen(HLA) fully matched sibling was available, but she chose haploidentical-HSCT from mother due to personal reason, which resulted in complete remission of the disease (figure 3) over a 42-month follow-up period, and only grade 1 chronic graft versus host disease(GVHD) of skin rash over face (figure 4) was complained.

Figure 3

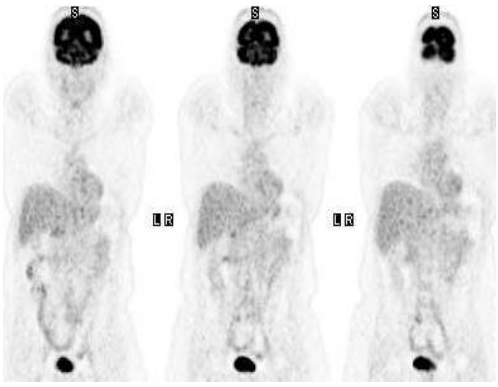
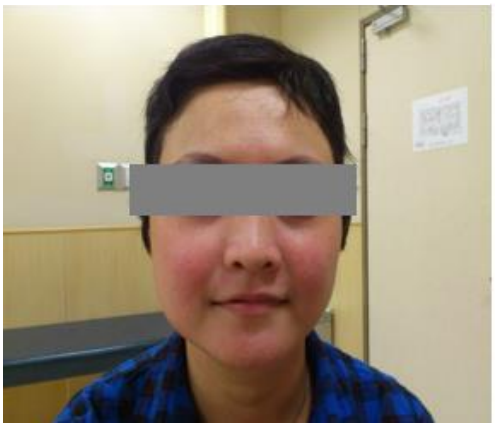


Figure 4



Discussion

Despite the prosperous development of the novel agents these years, RRHL remains a challenging disease. The median duration of response of Nivolumab in patient with RRHL is 18.2 months in all responders [1], and the median progression free survival of Pembrolizumab is 56.5 months in the CR subset [2]. Overall, the median time of disease control under the checkpoint inhibitor not only less than the life expectancy of health people under the same age, but also less than 5 years.

MS Faisal et al. presented a time-trend analysis of RRHL patients who received allogeneic HSCT from 2001-2017. [3] The study demonstrated encouraging results in overall survival (OS) and the progression-free survival (PFS), which was significantly increased in the era of novel agents. However, though the incidence of acute GVHD was similar in both eras ($p = 0.50$), and the incidence of chronic GVHD was higher in era of novel agents(55% vs. 21%, $p = 0.03$). Here we compare the two study both publish in 2017. One is haploidentical HSCT for RRHL, a study from European Society for Blood and Marrow Transplantation (EBMT) [4], and the other one is matched sibling donor/ matched unrelated donor(MSD/MUD)-HSCT for RRHL, a retrospective analysis by Giaccone et al.(2017), [5] respectively. The EBMT reported the non-relapse mortality rate in 1 year is 17%, while 18% of 1 years in the Giaccone team. As for the OS and PFS, the MSD/MUD data is 51%/39%, which is slightly inferior to the Haplo data of 67%/43%. When it comes to the GVHD prophylaxis, calcineurin inhibitor(CNI)/ Methotrexate were used in the MSD/MUD-HSCT group, and post-transplant cyclophosphamide (PTCy)/CNI/Mycophenolate mofetil in the Haplo-HSCT group. Of note, grade 2-4 acute GVHD is found in 33% of Haplo data and 37% of MSD/MUD data, as the incidence of chronic GVHD in 2 years is 26% in the Haplo subset and 46% in the MSD/MUD subset.

A retrospective study of 90 patients who received non-myeloablative allogeneic HSCT revealed that the non-relapse mortality (NRM) was significantly lower for HLA-haploidentical

related (P=.02) recipients compared to HLA-matched related recipients. [6] The author also indicates significantly decreased risks of relapse for HLA-haploidentical related recipients, compared to MSD(P=.01) and MUD (P=.03) recipients.

Conclusions

Our patient is disease free from RRHL after haploidentical HSCT for at least 42 months and only grade 1 chronic GVHD of skin rash over face is complained. Allogeneic HSCT could offer a chance of cure for patients with RRHL. Haplo-HSCT with PTCy GVHD prophylaxis had shown not only to lower chronic GVHD rate but also comparable survival/relapse outcome to MSD/MUD. In the era of novel agents, Haplo-HSCT with PTCy GVHD prophylaxis might be a solution of higher the risk of chronic GVHD.

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病例報告　112_C 74

同時出現肺栓塞和左心耳血塊：巧合還是有關連？
When left atrial appendage mass meets pulmonary embolism, is it coincidental or causal?

黃志勤[1] 梁馨月[1,2]
[1]中國醫藥大學附設醫院內科部心臟血管系 [2]中國醫藥大學生物醫學影像暨放射科學學系

Introduction
The detection of intracardiac mass is often incidental. Patients were usually without symptoms. The diagnosis of thrombus, vegetation or malignancy pointed towards different treatment plan. The workup of intracardiac mass is mainly supported by cardiac MRI and Transesophageal cardiacechography. Here, we presented a case with co-existence of pulmonary embolism and left appendage mass with focus on cardiacechography technical and clinical evaluation.

Case presentation
This is a 73-year-old male under hormonal therapy for prostate cancer. He was presented to emergency department due to bloody sputum for a week. The initial EKG showed atrial fibrillation. Chest CT revealed sub-massive pulmonary embolism and left atrium mass. There was no sign of pulmonary infarction. Without the availability of cardiac MRI, Transesophageal Echography (TEE) was done. The left atrium intracardiac mass was located within the left atrial appendage. No blood flow was detected by color doppler within the intracardiac mass. There is sign of spontaneous echo contrast in left atrium. Doppler revealed a low atrial appendage-emptying velocity of < 20 cm/s. 4D image shows rotational motion of the mass. No stalk was detected. Bicaval view color doppler revealed no sign of atrial septal defect. The diagnosis is acute pulmonary embolism and left atrial appendage thrombus. The patient was started on heparin pump and later crossed over to apixaban 5m BID. The plan is to perform a cardiac imaging follow up 3 months later. The result will be available by November 2023.

Discussion
Echography remains the primary imaging tool for assessment of intracardiac mass. Cardiacechography has limitations of poor penetration as compared to cardiac MRI. Cardiac MRI is an excellent tool for intracardiac mass inner content evaluation especially on scar tissue, fluidity, lipomatous and vascularity. It could offer diagnosis with a higher level of confidence. Nevertheless, cardiac MRI is also time consuming, expensive, often requires huge space for set up and not readily available. There is value in advancing the cardiacechography evaluation skill on intracardiac mass.
The differential diagnosis of intracardiac mass includes benign or malignancy tumor, thrombi, vegetations, and congenital anomalies. Cardiacechography characterizes the size, morphology, and location of intracardiac mass. It also provides peri-area information. Evidence of peri-area stasis such as spontaneous echo contrast in left atrium, right atrium or left ventricular apex marks the risk of thrombus formation. The most common location for thrombus formation includes left ventricular apex with sign of akinesis or dyskinesis, left atrial appendage and right atrial appendage. Conditions that lead to stasis of blood

predisposes the risk of thrombus formation. Mitral valve stenosis, prosthetic valves, atrial fibrillation, dilated and restrictive cardiomyopathy increases the risk of thrombus formation in left atrium. To optimize the sensitivity of thrombus formation, a high frequency transducer (with 5 MHz) and short focal length can be set. Contrast injection or agitate saline injection could also increase sensitivity of thrombus formation by presence of contrast opaque space occupying lesion. Contrast enhancement within intracardiac mass marks the neovascularized nature of tumor and especially pointing towards malignancy. Transthoracic cardiacechography (TTE) has limitation on visualization of left or right atrial appendage. Transesophageal cardiacechography (TEE) offers a better chances of emboli detection. Doppler image is used to assess flow velocity within the appendage. A low atrial appendage-emptying velocity (<20cm/s) has been reported to significantly increase the embolic risk. 4D echography better illustrate the overall size, shape, rotational motion, and attachments of the intracardiac mass. As it is showed in this case, an intracardiac mass was detected in left atrial appendage with no stalk, but there is rotational motion with left atrium spontaneous echo contrast. A diagnosis of thrombus is made.

The case is also presented with sub-massive pulmonary embolism and newly diagnosed atrial fibrillation. Hence, it raises the question of the presence of atrial septal defect (ASD) or patent foreman ovale (PFO). A PFO is demonstrated with atrial shunting by in the absence of anatomic defect such as ASD. With the injection of contrast of agitated saline, the presence of more than 10 microbubbles in the left atrium within 3 cardiac cycles is consistent with PFO. Color doppler is used to detected atrial shunting. To detect of low velocity shunting, velocity scale should be set to wider range. TEE offers a more flexible maneuver and complete visualization on atrial septum. Hence, it is a preferred tool over TTE. No atrial shunting was detected in this case. Hence, the left atrial appendage thrombus is independent from the formation of pulmonary embolism.

Conclusion

Although cardiac echography does not provide much information on inner content or texture of intracardiac mass, it provides real time information on the location, shape, and rotational movement, and mostly importantly the interaction of the mass with peri-area tissues. In this case, we treat the patient as sub-massive pulmonary embolism and left atrial appendage thrombus with apixaban. Cardiac echography is readily available for follow up of the condition.

病例報告　112_C 75

硫代硫酸鈉短期治療應用於一例鈣化防禦症的成功案例

Successful Application of Short-term Sodium Thiosulfate Treatment in a Case of Calciphylaxis

石硯文[1] 陳怡儒[1,2] 陳宏基[3] 張廖年峰[4] 洪毓權[1,2] 謝松霖[1,2] 郭慧亮[1,2] 王怡寬[1,2] 賴彬卿[1,2]
[1]中國醫藥大學附設醫院內科部 [2]中國醫藥大學附設醫院內科部腎臟系 [3]中國醫藥大學附設醫院外科部整型外科 [4]中國醫藥大學附設醫院皮膚科

Introduction

Calciphylaxis, a severe complication predominantly linked to chronic kidney disease, is characterized by calcium deposits in the small blood vessels of the skin and fatty tissue, and can also manifest in patients suffering from acute kidney injury. The substantial morbidity and fatality rates that accompany calciphylaxis emphasize the critical need for accurate diagnosis and appropriate treatment. Nonetheless, achieving a clinical diagnosis of calciphylaxis can be exceptionally challenging. In this instance, we showcase a case of calciphylaxis that has been successfully treated.

Case Presentation

A 37-year-old female patient with a medical history of chronic glomerulonephritis-related end-stage renal disease was undergoing peritoneal dialysis. She had tertiary hyperparathyroidism post-parathyroidectomy and persistent hyperphosphatemia due to long-term poor diet control, despite treatment with Lanthanum Carbonate, Calcium Acetate, and Cinacalcet. Two months before admission, the patient sustained a burn injury to her buttock and left thigh during far-infrared therapy. She self-treated the wound with topical honey which leading to wound progression. Subsequent debridements were performed at an outpatient Plastic Surgery department, but the patient refused hospitalization and continued self-treatment with various brands of honey. Due to unbearable wound progression and pain, the patient was admitted for infection and pain control. However, despite antibiotic therapy, wound care, and pain management with morphine, the wound still progressed even after undergoing several debridements. Autoimmune markers and HbA1c were all within normal limits. Eventually, the patient agreed to have a skin biopsy, and the results confirmed intraluminal vessel calcification with fibrinoid necrosis of the vascular wall, epidermal necrosis, dermal necrosis, and fat necrosis with adjacent mixed lymphocyte, neutrophil, and histiocytic infiltration, indicative of Calciphylaxis. To address the risk factors of Calciphylaxis, we adjusted the patient's peritoneal dialysis to hemodialysis for phosphate removal. Multiple debridements were performed, and a Kerecis skin graft was transplanted to the lower thigh. Sodium Thiosulfate(STS) was administered three times a week for 6 weeks, resulting in significant wound healing. Moreover, the patient's pain completely subsided, allowing for the withdrawal of morphine three months after the diagnosis of calciphylaxis. The wound continued to steadily improve, and six months post-diagnosis of calciphylaxis, the patient was transitioned back to peritoneal dialysis.

Discussion

Calciphylaxis is a complex condition characterized by microvascular calcification, typically

manifesting as painful cutaneous lesions with a poor prognosis due to reduced arteriolar blood flow from calcification, fibrosis, and thrombosis, mainly impacting dermo-hypodermic arterioles. STS acts to alleviate both intravascular and extravascular calcifications by chelating calcium salts to form soluble calcium thiosulfate, reducing the calcification burden on adipocytes and vascular smooth muscle cells and decreasing reactive oxygen species. The dosage of intravenous STS is variable; an initial 12.5g dose may be followed by 25g three times weekly, with alternative schedules also documented, and it can be administered during hemodialysis where applicable. The optimal duration for STS treatment is still undetermined. In studies, it showed complete resolution in 26-52% of patients and significant improvement in 19% with differing treatment durations. In this case, a shorter STS therapy duration of approximately 6 weeks showed significant clinical improvement. The treatment duration must be balanced against increased risks such as skeletal fractures seen in long-term STS treatment.

The definitive treatment for calciphylaxis, especially regarding STS, remains elusive due to a scarcity of high-quality studies. However, existing evidence does indicate that short-term administration of STS can offer substantial therapeutic benefits in certain scenarios. Further rigorous research is essential to establish definitive treatment guidelines for calciphylaxis, focusing on the potential role of STS.

Conclusion

Calciphylaxis, majorly associated with chronic kidney disease, emerges as a grave and fatal condition, characterized by calcification in the small blood vessels of the skin. This condition poses significant diagnostic and therapeutic challenges due to its intricate nature and the considerable rates of morbidity and mortality associated with it. In this context, we have outlined a successful intervention strategy in a patient with a complex medical background, utilizing STS. This approach showed substantial improvements in wound healing and pain management over a treatment period of six weeks. Given that STS is currently not covered by insurance in Taiwan and comes with high costs, our successful short-term application of STS, complemented by debridement, can serve as a reference for clinicians and patients alike, potentially mitigating concerns over financial constraints. Early intervention with STS might accelerate recovery; however, this necessitates more comprehensive studies to fortify the evidence base.

病例報告　112_C 76

上帝為腦開了扇後門－孕婦發生隱源性腦中風的案例報告

A Back Door to the Brain: A Case report of Cryptogenic Stroke in Pregnancy

邱于嘉[1] 李穎超[2] 蕭文智[2]
[1]中國醫藥大學附設醫院教學部一般科內科組 [2]中山醫學大學附設醫院內科部心臟內科

Introduction

Patent foramen ovale (PFO) is a congenital cardiac abnormality, reported to occur in 20–30% of the general population. It primarily facilitates right-to-left shunting from the venous to the arterial circulation and is often asymptomatic. Typically, it remains undetected until a change in coagulation status occurs, such as during pregnancy.

Previous studies have suggested that PFO may be associated with a heightened risk of various pathological conditions, including cryptogenic stroke. Potential mechanisms underlying strokes associated with PFO include paradoxical embolism, wherein a venous clot traverses the PFO, in situ clot formation within the PFO, and atrial arrhythmias due to disruptions in electrical signaling. Various risk factors for PFO-attributable strokes have been investigated. These factors include the patient's age, the size and morphology of the PFO, the degree of shunting, the presence of atrial septal aneurysm, and imbalances within the coagulation-anticoagulation systems.

This case report provides a detailed account of a 39-year-old pregnant female who experienced a cryptogenic stroke.

Case presentation

A 39-year-old female with a medical history of dyslipidemia and no recent medication use. Furthermore, she was in the eighth week of pregnancy at the time of presentation.

Prior to the incident, the patient was entirely independent in her activities of daily living and exhibited normal functioning, and she went to sleep at 10:00 PM on August 15th, 2022. On August 16th, her family found her with no verbal response, accompanied with weakness over her right limbs and a fixed horizontal gaze to the left side. Consequently, she was brought to the emergency department of Chung Shan Medical University Hospital at 7:00 PM.

Upon her arrival, her Glasgow Coma Scale score was E3-4M5-6V1. A neurological examination indicated that she was alert but unresponsive in terms of verbal output. Notably, she displayed restricted extraocular movement towards the right side, with a negative response to right-sided threatening stimuli. Furthermore, she presented with right hemiplegia and right central facial palsy. Laboratory data revealed no remarkable findings except for leukocytosis. The electrocardiogram showed sinus rhythm without obvious ST-T changes. Chest radiography showed no apparent pneumonia patch and no mediastinal widening. Brain computed tomography perfusion and computed tomography angiography disclosed no intracranial hemorrhage but revealed left M1 total occlusion with penumbra. With the impression of acute ischemic stroke, endovascular thrombectomy was performed on August 16th.

During hospital care, a survey of risk factors for cryptogenic stroke was conducted. Brain magnetic resonance imaging on August 17th revealed infarction in the left middle cerebral artery (MCA) territory and susceptibility microhemorrhage in the left corpus striatum. As a

treatment, antiplatelet therapy with Aspirin was initiated. A follow-up computed tomography scan on August 19th indicated infarction in the left MCA territory with focal hemorrhagic transformation and minimal intraventricular hemorrhage within the left lateral ventricle. Subsequently, the patient's antiplatelet therapy was switched to Clopidogrel.
Echocardiography, conducted on August 18th, revealed the presence of a PFO with excess interatrial septum motion and left-to-right shunting. Additionally, a string-like thrombus was identified in the left common femoral vein. No abnormal finding was found in Holter EKG examination. Given the presence of PFO and suspicion of deep vein thrombosis, anticoagulant therapy with Apixaban was prescribed (August 20th-29th). Phleborheograph performed on August 24th still confirmed the presence of a thrombus in the left common femoral vein. Subsequently, catheterization was performed on September 2nd, and PFO transcatheter closure was successfully completed using the Amplatzer septal occluder.
In addition to her cardiovascular events, the patient also experienced intrauterine embryo demise and suspected septic abortion during the course of her treatment. As a result, she received antibiotic therapy with Tazocin and uterotonic therapy with Misoprostol. Following stabilization, a comprehensive rehabilitation program was arranged to facilitate her recovery.

Discussion

Cryptogenic stroke accounts for 15–40% of all ischemic strokes, and PFO is found in 40–56% of patients under 55 years old with cryptogenic stroke or transient ischemic attack (TIA). Previous studies have also shown that PFO-related strokes are associated with young age. In addition to traditional stroke risk factors such as hypertension, dyslipidemia, and smoking, PFO has been established as an independent risk factor for cryptogenic stroke.
Previous studies have also found that pregnant women are at a higher risk of both ischemic and hemorrhagic strokes. Additionally, pregnancy is considered one of the major risk factors for the development of venous thromboembolism, potentially attributed to thrombophilia. The heightened thrombogenicity in the peripartum period is mainly due to pregnancy-induced physiological changes. Hormonal shifts elevate clotting factors. Furthermore, physical changes, such as increased pressure on pelvic veins due to the gravid uterus and reduced lower extremity blood flow, may enhance the thrombotic state. Additionally, the left iliac vein may be compressed by the right iliac artery, further raising the risk of clot formation in the left iliac vein. Acting as a 'back door to the brain,' PFO can allow venous clots to enter arterial circulation via interatrial right-to-left shunting, potentially resulting in ischemic stroke.
According to recent international guidelines, PFO closure and long-term antiplatelet therapy are recommended for patients aged between 18 and 60 years who have experienced a previous stroke or TIA. Previous trials have also indicated that PFO closure is associated with a lower rate of recurrent ischemic strokes than medical therapy alone during extended follow-up, although it may carry a higher risk of device complications and atrial fibrillation.

Conclusion

The case highlights the intricate interplay between pregnancy, PFO, and cryptogenic stroke. Understanding these relationships is crucial for risk assessment and appropriate interventions in patients with similar clinical presentations. Early recognition and management, including PFO closure, can potentially mitigate the risk of recurrent cryptogenic strokes.

病例報告　112_C 77

快樂農場未知的一面：腎移植患者梨型鞭毛蟲感染案例報告

The Unforeseen Risks of Joyful Farms: A Case Report of Giardia lamblia Infection in Renal Transplant Patients

許偉權 [1] 陳怡儒 [2,3] 洪毓權 [2,3] 周佳卉 [2,4] 賴彬卿 [1,2]

[1] 中國醫藥大學附設醫院教學部一般科 [2] 中國醫藥大學附設醫院內科部 [3] 中國醫藥大學附設醫院內科部腎臟系 [4] 中國醫藥大學附設醫院內科部感染科

Introduction

Patients undergoing renal transplantation require lifelong administration of immunosuppressive agents, consequently elevating their risk of infections. The sanitary conditions and climate in Taiwan are superior compared to those in both developed and undeveloped countries; thus, the chances of parasitic infections are relatively low and can even be easily overlooked. However, with the ascent of contemporary societal values that embrace a healthy, active lifestyle and harmony with the natural environment, many sources of infection, previously deemed improbable, are subtly becoming more prevalent in the daily lives of transplant patients. In light of this, we present a case report of a renal transplant recipient infected with giardiasis, offering insights into these emerging concerns in kidney transplantation.

Case presentation

A 61-year-old male patient with end-stage renal disease of unknown etiology underwent cadaveric kidney transplantation in 2011. He was diagnosed with Cryptococcus-related pneumonia a year before this admission and has been prescribed fluconazole since then. A month prior to admission, he experienced persistent abdominal distension and poor appetite, which he suspected might be related to fluconazole, leading him to self-discontinue the medication. Following this, he noticed a decrease in urine output, worsening dyspnea on exertion, and peripheral limb edema. During outpatient department monitoring, he developed acute renal failure, likely due to rejection. As a result, his immunosuppressants were adjusted to Mycophenolate mofetil 180mg 3-tab BID, Tacrolimus 0.5mg 1 tab QOD, and Methylprednisolone 16mg/day. However, his poor appetite persisted, and his dyspnea even progressed, necessitating hospitalization for emergency hemodialysis. Despite improvement in uremia and edema, his appetite remained poor, with mild loose stool and bowel distension noted. An EGD confirmed multiple erosions over the antrum but no active gastric ulcer, and appetite did not improve with proton pump inhibitors treatment. Additionally, a low cytomegalovirus (CMV) blood viral load of 668 IU/ml was detectable without RBC positive from stool routine, inadequately explaining it as due to a CMV infection. Due to persistent mild loose stool, gastrointestinal PCR was conducted, surprisingly detecting Giardia lamblia. After several days of metronidazole treatment, the patient's appetite significantly improved. Given the concurrent infections of Cryptococcus and Giardia lamblia, environmental contact was highly suspected as the source. Upon discussion regarding potential exposure to further infections from environmental contact, he disclosed that he owned a farm near his house where he often worked barehanded and barefoot among the plants and crops, frequently coming into contact with contaminated water from the plants and observing doves walking in

the field. We concluded that his Cryptococcus and Giardia lamblia infections might be related to his agricultural practices and lack of self-protection and isolation. After instructing on good hygiene practices, the patient was successfully discharged, did not require dialysis, and maintained a stable condition in stage 5 chronic kidney disease.

Discussion

Giardia lamblia, a flagellated protozoan parasite, predominantly inhabits the upper section of the small intestine, inducing a condition known as giardiasis. This parasitic infection is ubiquitously distributed across the globe, showing a varying incidence rate—20%-30% in developing regions and 3%-7% in developed nations. The organism manifests in two distinct forms: cysts and trophozoites. The host expels cysts through feces, which are then transmitted when ingested via contaminated food or water, through direct oral-fecal contact, or by zoonotic means. Upon entering the initial segment of the proximal small intestine, the cysts undergo transformation into trophozoites and colonize the gastrointestinal tract. The clinical manifestations of Giardia infection are diverse, ranging from asymptomatic cases to acute symptomatic presentations, including abdominal discomfort, flatulence, steatorrhea, and diarrhea. Although Giardia infections are generally self-limiting, they may cause chronic diarrhea in immunocompromised patients. To the best of our knowledge, no research papers or case discussions related to this condition have been reported in Taiwan, making this the inaugural report of Giardia lamblia infection in renal transplant recipients within the region. In this case, the stool analysis of the patient revealed no traces of enterocolitis induced by bacteria, viruses, or other parasites. However, Giardia lamblia were identified through gastrointestinal panel PCR. This revelation underscores the likelihood of unseen infections in renal transplant recipients—conditions that evade detection by conventional fecal examination and parasitic ovum microscopy. Advanced techniques, such as Polymerase Chain Reaction (PCR) technology, offer a more precise identification of potential infectious agents. This breakthrough also suggests that renal transplant recipients might harbor covert infections, often overlooked by medical practitioners. Looking forward, employing PCR to identify potential infection sources in renal transplant patients displaying gastrointestinal symptoms could serve as an efficient approach to resolving clinical conundrums.

Conclusion

In conclusion, this case underscores the critical implications of environmental exposures and the evolving lifestyle norms on the infection risks among renal transplant recipients, particularly in regions with superior sanitary conditions like Taiwan. The unprecedented incidence of giardiasis and Cryptococcus in a patient, potentially contracted from agricultural practices, underscores the need for advanced diagnostic strategies, such as PCR technology, especially when conventional methods fail to detect such infections. This study accentuates the importance of considering environmental interactions in assessing infection risks and the need for meticulous hygienic practices among immunocompromised individuals. It advocates for heightened awareness and the integration of advanced diagnostics to effectively manage and mitigate infection risks in transplant recipients in our continually evolving medical and environmental landscape.

病例報告　112_C 78

成人先天性血栓性血小板低下紫斑症的診斷挑戰與臨床治療

Diagnostic Challenges and Clinical Management of Congenital Thrombotic Thrombocytopenic Purpura in Adults

楊豐旭[1] 陳怡儒[2,3] 洪毓權[2,3] 呂思瑩[2,3] 張芳慈[4] 朱昌宏[5] 呂明桂[4] 賴彬卿[2,3]
[1]中國醫藥大學附設醫院教學部一般科 [2]中國醫藥大學附設醫院內科部 [3]中國醫藥大學內科部腎臟系
[4]中國醫藥大學附設醫院神經部 [5]中國醫藥大學附設醫院急診部

Introduction

Thrombotic thrombocytopenic purpura (TTP) is a rare and perilous thrombotic microangiopahy(TMA) condition characterized by microangiopathic hemolytic anemia(MAHA), consumptive thrombocytopenia, and organ impairment. The pathophysiology of TTP predominantly relates to a deficiency in the protease ADAMTS13, a critical enzyme responsible for cleaving von Willebrand factor multimers. Hence, diminished activity of ADAMTS13 is correlated with the augmentation of von Willebrand factor multimers and a heightened propensity for microvascular thrombosis. Severe ADAMTS13 deficiency can either be congenital, resulting from mutations in the ADAMTS13 gene or acquired, largely attributed to the presence of autoantibodies against ADAMTS13.

Epidemiologically, congenital TTP represents 10% of all TTP occurrences, while acquired TTP comprises the remaining 90%. Notably, the prevalence of congenital TTP is extremely low in adults, approximately 2%, but can escalate to 35% in pediatric populations. Clinical manifestations of TTP commonly include extensive formation of microthrombi, primarily impacting the brain (in 60% of patients, exhibiting symptoms such as headache, confusion, stroke, coma, and seizures), the heart (in 25% of patients, demonstrating electrocardiographic anomalies and myocardial infarction), and the mesenteric vessels (in 35%, leading to abdominal discomfort and diarrhea).

Moreover, a significant correlation exists between congenital TTP and an increased likelihood of transient ischemic attacks (TIAs) and strokes, especially in younger individuals. Thus, clinicians should contemplate a TTP diagnosis when younger patients exhibit TIAs or strokes, particularly when accompanied by thrombocytopenia and microangiopathic hemolytic anemia.

Case presentation

A 53-year-old male with a medical history of benign prostatic hyperplasia managed with tamsulosin, susceptibility to urticaria, and intermittent consumption of Chinese herbs, was admitted to the emergency department (ED) due to right-sided numbness and aphasia. Neurological evaluation in the ED identified aphasia and a reduction in right upper arm muscle strength to grade 4. An urgent brain computed tomography revealed a focal perfusion defect in the left frontal region with a 7ml mismatch on MIStar ® and slight decreased perfusion in the left frontal lobe and posterior periventricular area on RAPID(*Rapid* processing of perfusion and diffusion). Additionally, laboratory findings were significant for a platelet count of 11,000/uL, Hb 9.7 g/dL, fragmented RBCs on blood smear, LDH 693 U/L, GFR 77 mL/min/1.73m², and normal PT and APTT; hypoglobulinemia was observed at <5.83 mg/dL. The patient denied experiencing headache, chest pain, abdominal pain, or hematuria. Given these findings, a working diagnosis of thrombotic microangiopathy was made, and the patient

underwent plasma exchange and received steroid treatment. The ADAMTS13 activity testing confirmed 0% activity, establishing a diagnosis of TTP. Under the treatment, the patient's aphasia, right upper limb weakness, renal function, and hemolysis markers all showed improvement. However, during hospitalization, as plasma exchange was tapered from daily to every other day along with steroid treatment, the patient's hemolysis markers worsened, and platelet count dropped to 14,000/uL; ADAMTS13 activity remained at 0%. Given this refractory TTP, the volume of plasma exchange was increased, returned to daily treatment, and was combined with pulsetherapy methylprednisolone 1g for three days. Subsequently, the patient's hemolysis markers improved, and he was discharged on oral prednisolone 5mg 3#BID with normal renal function and without any residual sequelae from the previous transient ischemic attack.
Genetic testing of the patient's ADAMTS13 gene revealed a heterozygous mutation, ADAMTS13: c.1492C>T(p.Arg498Cys), classified as likely pathogenic in the ClinVar database. Subsequent genetic analysis will be conducted on the patient's family members, and further assessment will be done to evaluate whether they exhibit manifesting TTP.

Discussion

According to the literature, congenital TTP represents 10% of all TTP cases, while the acquired form constitutes the remaining 90%. The prevalence of congenital TTP is notably low in adults, approximately 2%, but can escalate to 35% in pediatric populations. From an epidemiological standpoint, this case falls into a relatively low percentage group.
A middle-aged male presented with neurological manifestations and concurrent thrombocytopenia. The clinical differential diagnosis should encompass other conditions associated with MAHA and thrombocytopenia, including Shiga toxin-mediated hemolytic uremic syndrome, atypical hemolytic uremic syndrome, drug-induced TMA, disseminated intravascular coagulation, systemic rheumatic diseases, systemic malignancy, glucose-6-phosphate dehydrogenase deficiency, and severe vitamin B12 deficiency, among others. In this instance, early detection of reduced ADAMTS13 activity facilitated prompt and appropriate intervention.
However, many physicians might cease plasma exchange once they observe improvement in hemolysis markers following plasma exchange and steroid treatment, a precarious practice given the risk of disease rebound in TTP, as evidenced in our patient. Despite careful tapering of plasma exchange frequency, a rebound still occurred. Thus, it's crucial to emphasize that monitoring of hemolysis markers, including LDH and platelet count, should continue until all are within normal ranges before reducing the frequency of plasma exchange. Continual monitoring of LDH and platelet count is mandatory during tapering, and if stable, steroids can be transitioned to oral. Before discharge, it is recommended to ensure that hemolysis markers remain stable with oral steroids and without plasma exchange for two days.
Taiwan has recently classified congenital TTP as a rare disease, and besides plasma exchange, the introduction of apadamtase Alfa can potentially offer a diverse therapeutic environment for patients with congenital TTP in Taiwan.

Conclusion

Thrombotic Thrombocytopenic Purpura (TTP) is a rare and life-threatening condition. This case involved a middle-aged male who presented with neurological symptoms, microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and was diagnosed with TTP

following the early detection of reduced ADAMTS13 activity, allowing for the commencement of appropriate treatment. Although congenital TTP is extraordinarily rare, predominantly presenting in children, this case illustrates the clinical course and prognosis of congenital TTP in adults.

During the treatment of TTP, meticulous attention is needed to monitor hemolysis markers, as LDH and platelet count are positively correlated with TTP disease activity. Clinicians need not wait for the confluence of the pentad of fever, thrombocytopenia, hemolytic anemia, renal dysfunction, and neurologic dysfunction to consider a differential diagnosis of TTP. When a patient exhibits MAHA and thrombocytopenia with organ damage, it necessitates the initiation of differential diagnosis for TMA. This approach ensures early detection and intervention for TTP.

病例報告　112_C 79

懷孕誘發多重器官衰竭的非典型性溶血性尿毒症症候群：探討其臨床挑戰與診斷重要性

Pregnancy-Induced Atypical Hemolytic Uremic Syndrome Leading to Multi-Organ Failure: Exploring its Clinical Challenges and Diagnostic Significance in Medical Practice

李卓達[1] 陳怡儒[1,2] 洪毓權[1,2] 呂思瑩[1,2] 梁信杰[1,2] 賴彬卿[1,2]
中國醫藥大學附設醫院[1]內科部 [2]內科部腎臟系 [3]內科部胸腔科

Introduction

Atypical Hemolytic Uremic Syndrome (aHUS) is a life-threatening condition, potentially precipitated by autoimmune diseases, pregnancy, infections, and surgical procedures. Preeclampsia is a multisystem progressive disorder, characterized by the new onset of hypertension and proteinuria, or the new onset of hypertension coupled with significant end-organ dysfunction, with or without proteinuria, typically manifesting after 20 weeks of gestation or in the postpartum period. Occasionally, clinicians may misinterpret cases of acute kidney injury in pregnant women as preeclampsia and may opt for induced labor or emergency cesarean section in critical situations. However, both induction and cesarean section can further trigger the complement pathway. If the patient has atypical hemolytic uremic syndrome, it often results in a 'second hit,' leading to potentially fatal multiple organ failure due to extensive thrombotic microangiopathy (TMA).

Case Presentation

The patient, a 42-year-old female, experienced acute renal failure and hypertension following her second pregnancy. She underwent a spontaneous abortion in 2022, and, during her fourth pregnancy in 2023, was referred to another hospital due to escalating hypertension and proteinuria at 23 weeks of gestation; she was diagnosed with severe preeclampsia. A cesarean section was performed at 32 weeks. However, post-discharge, her renal function did not improve, showing rapid and severe deterioration, accompanied by hypertension, hemolytic anemia, and thrombocytopenia. Another institution diagnosed her with refractory hemolytic anemia and highlighted the impending need for dialysis, recommending a low protein diet at home. However, her condition failed to stabilize, and, facing reduced urine output, chest tightness, and hemoptysis, she was transferred to our hospital. Upon admission, severe pulmonary hemorrhage had induced acute respiratory failure, necessitating immediate ventilatory support, and was associated with concurrent heart failure, hepatitis, and pancreatitis. Laboratory findings included Cr 3.96 mg/dL, BUN 125 mg/dL, LDH 687 U/L, Hb 5.1 g/dL, and a platelet count of 83,000/uL. Both direct and indirect Coomb's tests were negative, as were stool O157:H7, antiphospholipid, lupus-related autoimmune markers, CMV, HSV, EBV, COVID-19, and influenza virus. ADAMTS13 activity was normal, and there was no history of drugs that could induce drug-related TMA. Given the impression of aHUS, the patient underwent nine sessions of plasma exchange but demonstrated poor response; hence, anti-complement therapy was initiated, resulting in improvements in hemolytic markers and all affected organs. The patient no longer required supplemental oxygen. Evaluation of the aHUS gene panel revealed mutations in CR1, accompanied by concurrent amino acid alterations. In the future, it is anticipated that anticomplement therapy could be gradually reduced following the stabilization of TMA.

Discussion

Atypical Hemolytic Uremic Syndrome (aHUS) is a rare and severe form of thrombotic microangiopathy (TMA) distinguished by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal impairment. This clinical manifestation is uniquely disparate from thrombotic thrombocytopenic purpura and other diseases associated with TMA. aHUS-induced TMA has the propensity to affect various organ systems, often leading to rapid multi-organ dysfunction and elevated mortality risk. Pregnancy-associated aHUS (p-aHUS) predominantly occurs during pregnancy or the postpartum period, accounting for an estimated 7% of all aHUS instances. It exhibits clinical similarities with other complications linked to pregnancy. Complement mutations associated with aHUS have been detected in 5-15% of cases with preeclampsia and a greater proportion of HELLP syndrome cases. The occurrence of aHUS is not precluded by a normal first pregnancy, as a significant 57% of patients initially demonstrate aHUS manifestations during subsequent pregnancies. Mutations associated with the alternative, lectin, classical, and coagulation pathways have been identified in multiple aHUS research studies. It's crucial to acknowledge that patients may present with polymorphisms in multiple genes instead of a singular gene mutation. Our current analysis of extant literature delineates that genes associated with aHUS exhibit a broad spectrum of variability, including CFH, CD46, CFI, C3, CFB, THBD, CFHR1-5, DGKE, VTR, C2, C3AR1, C8B, C9, C4BPA, CFD, MASP1-2, MMACHC, PLG, WT1, VWF, CR1, CXCL12, C5, TLR4, CXCR4, HASP, KNK, INF2, EXOSC3, TSEN2, CD36, and VTN. Over the past eight years, our institution has diagnosed 31 adults with this condition, of which four manifested CR1 mutations. Genetic analysis in aHUS functions as a pivotal prognostic indicator to evaluate the probability of recurrence, appropriateness of reducing anticomplement therapy, and the viability for renal transplantation. However, due to the intricate and time-intensive nature of genetic analytics coupled with the swift and elevated mortality rate of this uncommon disease, the immediate initiation of therapeutic interventions to facilitate the recovery of the affected organs remains of paramount importance.

Conclusion

In conclusion, Atypical Hemolytic Uremic Syndrome (aHUS) is a grave and frequently misdiagnosed disorder, posing substantial, life-threatening ramifications, especially notable in pregnant individuals. The case in point underscored the detrimental outcomes stemming from erroneous interpretation of aHUS symptoms as manifestations of conditions such as preeclampsia, instigating unsuitable interventions and escalating the disease to catastrophic multi-organ failure. Swift, accurate diagnosis coupled with appropriate therapeutic strategies, such as anti-complement therapy, are crucial for effective management of aHUS and for circumventing irreversible damage to organs. The intricate and diverse genetic components of aHUS call for elevated clinical vigilance, particularly in instances related to pregnancy, to ensure prompt intervention and to realize optimum patient outcomes. Furthermore, in pregnancies presenting with new Microangiopathic Hemolytic Anemia (MAHA), thrombocytopenia, elevated LDH, novel proteinuria or microhematuria or newly identified Acute Kidney Injury (AKI) concurrent with new Hypertension (HTN), it is imperative to meticulously exclude the possibility of aHUS.

病例報告　112_C 80

腎移植誘發非典型性溶血性尿毒症候群的挑戰與對策：一個成功短期使用 Ravulizumab 治療的案例報告

Challenges and Strategies in Managing Kidney Transplant-Induced Atypical Hemolytic Uremic Syndrome: A Case Report on Successful Short-Term Treatment with Ravulizumab

翁翠儀 [1] 陳怡儒 [1,2] 黃柏豪 [1,3] 洪毓權 [1,2] 葉進仲 [4] 黃秋錦 [1,2]
中國醫藥大學附設醫院 [1] 內科部 [2] 內科部腎臟系 [3] 內科部免疫風濕科 [4] 泌尿部

Introduction

Atypical Hemolytic Uremic Syndrome (aHUS) is an ultra-rare thrombotic microangiopathy (TMA) disease, characterized by sudden, progressive damage and is a chronic, genetic, and life-threatening condition. In 35-50% of cases, gene mutations are non-detectable, reflecting the complexity of the disease. It has systemic implications, with 63% of aHUS patients experiencing at least one complication outside of the kidney, affecting neurologic, cardiovascular, and gastrointestinal systems. The syndrome affects both adults and children, with no gender predisposition. Approximately half of the patients are adults. A high clinical suspicion of aHUS is imperative in all patients presenting with TMA. Advancements in treatment options necessitate early diagnosis and intervention. The pathogenesis of aHUS is associated with complement pathways, primarily the alternative pathway, but there are studies showing associations with the lectin and classic pathways as well. Exposure to events that activate complement pathways can precipitate instability in aHUS, increasing the risk of death due to complications from multiple organ involvement in thrombotic microangiopathy. Kidney transplantation, ischemic reperfusion injury, and the use of immune suppressants are common triggers. Therefore, for patients diagnosed with aHUS before kidney transplantation, a meticulous assessment is required to determine whether early use of anti-complement therapy is necessary as a preventive measure. However, many clinicians encounter situations where patients slated for kidney transplantation have no previous records of being aHUS patients, making the management of post-kidney transplantation TMA a significant challenge. We share the first case in Taiwan where a patient developed aHUS during kidney transplantation and was successfully treated with Ravulizumab.

Case presentation

The 45-year-old female patient, with systemic lupus erythematosus (SLE) related end-stage renal disease (ESRD) since 2012, was admitted for cadaveric kidney transplantation. Her SLE was stable and didn't require immunosuppressive therapy. The kidney donor was a 58-year-old male who experienced spontaneous intracranial hemorrhage and required 4 minutes of CPR. His creatinine level was normal at 0.92mg/dl upon arrival at our emergent department but progressed to 4.5 mg/dl on the day he donated his kidney; his last 24-hour urine output was 150 ml/min. The HLA matching between the graft recipient and the donor revealed a 1A1B mismatch. We informed the recipient about the predictable delayed graft function, and she consented to proceed with the transplantation with our usual regiment.

The recipient had cadaveric kidney transplantation smoothly, with adequate graft blood flow and improving urine output from 24 hours post-operation. However, unusually high blood pressure of SBP 180 mmHg combined with thrombocytopenia, microangiopathic hemolytic

anemia, LDH 662 U/L, fragmented RBCs on blood smear, and other symptoms pointed towards the impression of post kidney transplantation TMA. We initiated plasma exchange immediately on day 2 post-transplantation and reduced the tacrolimus dose. Due to persisting hemolysis markers and normal DSA results, antibody-mediated rejection seemed very unlikely, prompting the addition of ravulizumab on post-transplantation day 6. Hemolysis markers finally improved by day 10, allowing for smooth PCN insertion for the graft hydronephrosis. The patient received the second dose of ravulizumab on day 20 and subsequently received it every 8 weeks, completing the third and fourth doses, and has not used any anti-complement therapy since then. One-month post-operation, she experienced instability in aHUS due to Stenotrophomonas related urinary tract infection complicated with bacteremia but stabilized after antibiotic treatment and removal of the double J catheter from the transplanted kidney. To date, 1 year and 10 months post-transplantation, the patient has not used any more anti-complement therapy, and the tacrolimus drug level has been maintained between 5-6 ng/ml, indirectly proving that the patient's TMA was not caused by calcineurin inhibitor.

Discussion

In the management of aHUS, clinicians often encounter dilemmas due to the potential triggering by reperfusion injury, antibody-mediated Rejection (ABMR), and calcineurin inhibitor (CNI) pathways. For those with unidentified aHUS, critical interventions like kidney biopsies and discontinuation of tacrolimus under severe thrombocytopenic conditions are required, posing risks of fatal bleeding and graft rejection. There is substantial variability in the incidence of de novo TMA, ranging from 1.1% to 14%, with CNI-associated TMA marked by acute kidney injury and disturbances in vasoactive peptides, leading to arteriolar vasoconstriction and endothelial damage. Balatacept, although effective in eliminating CNI-induced TMA by preventing T lymphocyte activation, brings forth an increased kidney rejection risk and poses accessibility and cost challenges in regions like Taiwan. Furthermore, cases associated with AMR reveal detrimental outcomes, with ischemia-reperfusion injury being a consequential and inevitable complication, escalating complement-mediated injury. Ravulizumab offers a more stable and long-lasting alternative to Eculizumab for aHUS management, with the possibility of discontinuation in stabilized, low-recurrence type patients.Managing post-transplant TMA presents significant challenges, especially in kidney transplant recipients originally unknown to have aHUS. Here, we present a case of kidney transplantation-induced aHUS successfully treated with Ravulizumab. In circumstances where organ donors are scarce, initiating differential diagnosis for TMA is crucial when the recipient shows signs of MAHA, thrombocytopenia, elevated LDH, and dropping haptoglobin. Additionally, early intervention with anticomplement therapy is vital for the recovery of the transplanted kidney. Relying on genetic reports that can take several weeks or risking renal transplant rejection by discontinuing tacrolimus and conducting kidney biopsies under severe thrombocytopenic conditions leading to uncontrolled bleeding, are indeed unfavorable and impose additional risks on the patients. Once the condition of aHUS patients stabilizes, there is an opportunity to reduce or even discontinue anticomplement therapy.

病例報告　112_C 81

一位肝細胞癌男性患者經動脈化學栓塞術後併發支氣管膽道廔管:案例報告

A 75-year-old Man with Hepatocellular Carcinoma status post Transcatheter Arterial Chemoembolization（TACE） Complicated with Acquired Bronchobiliary Fistula（BBF）: a Case Report

林明憲 [1] 賴學洲 [1,3] 呂庭聿 [4] 鄭文建 [1,2]

[1] 中國醫藥大學附設醫院內科部 [2] 中國醫藥大學附設醫院胸腔暨重症系 [3] 中國醫藥大學附設醫院消化系肝膽科 [4] 中國醫藥大學附設醫院外科部胸腔外科

Introduction

Liver cancer, more specifically hepatocellular carcinoma （HCC）, is the second leading cause of cancer-related death and its incidence is increasing globally[1]. TACE is commonly utilized as an effective treatment for intermediate-stage HCC that cannot be surgically removed. The TACE procedure, while effective against tumors, can potentially cause complications including hepatic artery injury, nontarget embolization, pulmonary embolism, hepatic abscess, biliary strictures, hepatic failure, and intrahepatic biloma formation[2]. Peacock first reported Bronchobiliary fistula (BBF), a rare disorder characterized by an abnormal interconnection between the biliary tract and bronchial trees, in 1850[3]. The therapeutic choice of bronchobiliary fistula included surgical and non-surgical procedures[4]. Herein, we present a case report with a HCC status post TACE complicated with bronchobiliary fistula and under surgical repair.

Case Presentation

This 75-year-old retired married male with history of type 2 diabetes mellitus, hypertension, hepatocellular carcinoma induced by chronic hepatitis C, and complete staging revealing AJCC staging IIIb （T4N0M0）, Barcelona clinic liver cancer stage C, and status post transcatheter arterial chemoembolization, radiofrequency ablation, S5 and S1-3 segmentectomy decades ago, and chronic kidney disease stage 3a, presented to emergency department due to fever and chillness for 1 day.

He had diarrhea for 2 days with mild right upper quadrant pain with visual analog scale 3 of 10, dark yellowish urine color, and decreased skin turgor. He denied tarry stool, clay stool, nor coffee ground. He had bright-yellowish phlegm （Figure 1） with no respiratory distress. Physical examination showed blood pressure 100/60 mmHg, heart rate 120 per minute, respiratory rate 22 rate

Figure 1 Bright-yellowish sputum from this patient

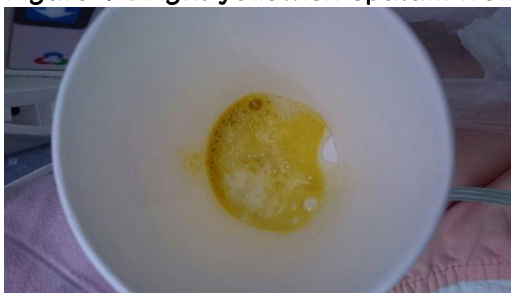
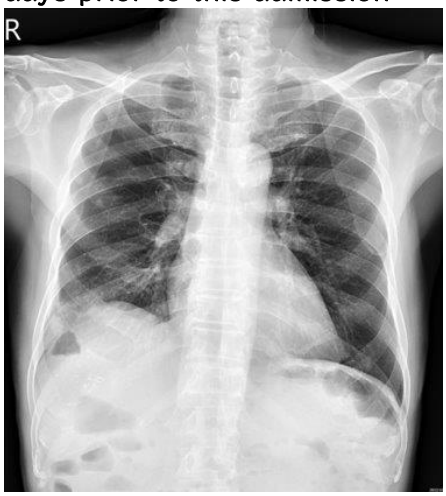


Figure 2. An air-fluid level lesion in the liver 4 days prior to this admission



120 per minute, respiratory rate 22 per minute, body temperature 38.5 ℃, and SpO2 94% under room air. Lab data revealed white blood cell 4500 per micro liter with neutrophilic segment 81.7%, Hemoglobin 14.9 g per dL, platelet 110000 per micro liter, Blood urea nitrogen 37 mg/dL, creatinine 1.46 mg/dL, GFR 47 mL/min/1.73m^2, total bilirubin 1.78 mg/dL, direct bilirubin 0.67 mg/dL, hsCRP 4.84 mg/dL. Chest x-ray showed right lower lung increasing infiltration and he was treated with pneumonia initially with Amoxicillin/ Clavulanic (soonmelt) for one day, but no improvement was noted. Compared with previous chest plain film (Figure 2), he had one air-fluid level lesion in his liver four days prior to this admission, which was considered biloma or liver abscess. Abdominal echo showed a 6.87 x 7.03 cm heterogenous mix-echoic lesion at S5/8, favor of abscess or biloma. We shifted antibiotics to ertapenem, and then contrast abdominal CT showed rule out bronchobiliary fistula at right lung (Figure 3). Liver culture obtained from echo-guided biopsy showed no growth of bacteria.

Figure 3. Fistula between S8 of liver and the right lower lung

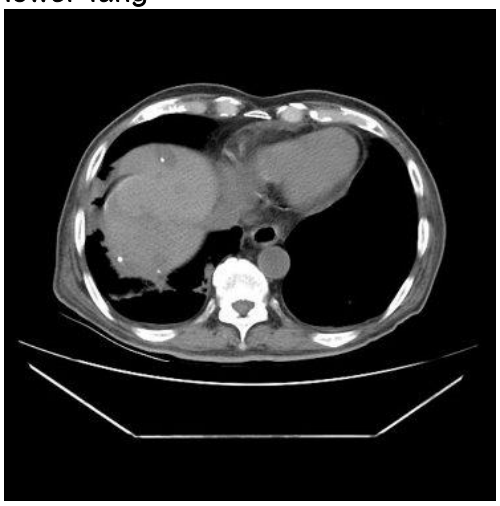
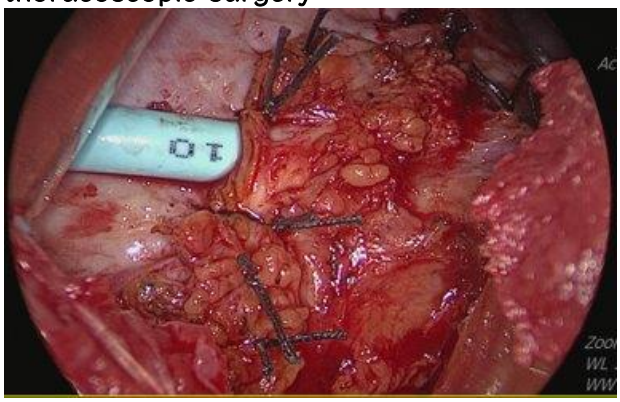


Figure 4. A pigtail was inserted into subphrenic area from the view of video-assisted thoracoscopic surgery



We consulted the thoracic surgeon and under careful discussion with the patient and his family, this patient received thoracoscopic wedge resection of right lower lung and repair of diaphragm. A 24 French chest tube was placed at chest and the adhesion between S8 of the liver, right lower lung, and the defect of the diaphragm was noted while entering pleural cavity. Pneumonolysis was done. Wedge resection of the right lower lung was performed to close the fistula. Primary suture repair of diaphragm with 1-0 silk, and a 14 French pigtail was placed at subphrenic area(Figure 4). He had no bright-yellowish sputum after the surgery. The chest tube was removed on post operation day 10, and he can go home on post operation day 11 with the pigtail left for delayed removal 8 weeks later. He finally passed away 10.5 months later due to the terminal stage of hepatocellular carcinoma, which was complicated by massive bilateral pleural effusion and massive ascites.

Discussion

Biloma is a common complication after Transarterial Chemoembolization (TACE), characterized by a distinct bile collection in areas outside the biliary regions. Additionally, a bronchobiliary fistula refers to an unusual connection between the biliary system and the bronchial tree via the diaphragm[5]. The article discussed the diagnosis of BBF, which is typically based on clinical symptoms, including bilioptysis, pleural effusion, atelectasis, liver abscess, and intrahepatic bile duct dilatation. Bilioptysis is identified as the most common symptom among BBF patients[4,5]. Returning to our case, who had his last TACE over a year

ago, was admitted due to a new episode of diarrhea and right upper quadrant pain, which likely exacerbated his biloma. His previous chest x-ray showed no biloma. The increased intraabdominal pressure may have accelerated the formation of a bronchobiliary fistula. To address potential bile tract infection, his medication was switched to ertapenem from soonmelt, and he remained fever-free throughout his hospital stay. Given his previous independent lifestyle, surgical intervention was performed, including right lower lung wedge resection, diaphragm repair, and the insertion of a chest tube and a pigtail for drainage. He was discharged on the 11th post-operation day. However, 10.5 months later, due to the terminal stage of his HCC, his family decided on a do not resuscitate order and he passed away. The surgical intervention proved valuable in managing the bronchobiliary fistula.

Conclusion

We presented a patient with bronchobiliary fistula caused by hepatocellular carcinoma (HCC) after transcatheter arterial chemoembolization (TACE) and suffering from diarrhea underwent a successful surgical repair procedure.

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病例報告　112_C 82

卡介苗誘發的反應性關節炎：診斷和治療難題

BCG-Induced Reactive Arthritis: A Diagnostic and Therapeutic Conundrum

陳國鈺[1]　楊凱介[2]

[1]中國醫藥大學附設醫院內科部　[2]中國醫藥大學附設醫院風溼免疫科

Abstract

A 51-year-old man with a medical history of chronic hepatitis B, a past transient ischemic attack, and high-grade urothelial carcinoma presented with ongoing fever and widespread joint pain after undergoing Bacillus Calmette-Guérin (BCG) intravesical treatment for his bladder cancer. Initially thought to have a urinary tract infection and BCG-induced arthritis, his symptoms persisted even after receiving celecoxib and hydrocortisone. Subsequent tests showed increased levels of white blood cells, high-sensitivity C-reactive protein, and ferritin. Additionally, specific HLA types were identified, hinting at a multifaceted etiology for his BCG-related reactive arthritis[1-11]. The patient's condition improved with intravenous methylprednisolone, highlighting the importance of a comprehensive, team-based approach to treating this uncommon yet serious side effect of BCG therapy.

Introduction

Bacillus Calmette-Guérin (BCG) is a standard intravesical treatment for non-invasive high-grade papillary urothelial carcinoma, known for its efficacy in reducing bladder cancer recurrence[11]. However, one of side effects is the BCG-induced reactive arthritis[10]. This condition occurs in only 0.5% to 1% of patients undergoing BCG therapy and presents a diagnostic puzzle, often featuring a mix of arthritis, urethritis, and conjunctivitis [8, 9]. While the exact cause remains elusive, it's generally considered an autoimmune response to the mycobacterial elements in intravesical BCG therapy[7]. Diagnosis becomes even more complex when other medical conditions are involved, as was the case with our patient, who had a medical history that included chronic HBV, a previous transient ischemic attack, and ongoing treatment for urothelial carcinoma[5]. This case report delves into the intricate diagnosis and management of BCG-induced reactive arthritis, with a special focus on the role of co-morbidities and potential genetic factors, such as specific HLA types, in influencing the disease course[6]. By examining a patient with multiple co-morbidities, we aim to shed light on the multifaceted challenges of treating this uncommon yet serious BCG therapy complication.

Case report

A 51-year-old male with a history of chronic HBV carrier, transient ischemic attack in 2015, and non-invasive high-grade papillary urothelial carcinoma (treated with transurethral resection of bladder tumor on April 4, 2023) and subsequent BCG therapy was admitted to the emergency department (ED) on June 29,2023 due to persistent fever and multiple joints pain since June 20, 2023.

On March 22, 2023, he received fiberoptic cystoscopy at urologist department with initial presentation of urinary hesitancy and terminal dribbling for two months, hematuria (urine RBC:240/HPF), and three hyperechoic masses were identified by sonography. Fiberoptic cystoscopy revealed multiple bladder tumors at various sites, including the posterior and

anterior walls, bladder neck at the 10 and 2 o'clock positions. On April 4, 2023, he received transurethral resection of bladder tumor (TURBT), with pathology confirming non-invasive high-grade papillary urothelial carcinoma. Subsequently, he received weekly BCG bladder treatments for a total of six sessions, with the final instillation occurring on June 7, 2023. However, following the final BCG dose, the patient developed fever up to 38°C, and experienced multiple joints pain affecting bilateral shoulders, elbows, wrists, hips, knees, ankles, and the cervical spine, along with morning stiffness more than 2 hours. Rheumatologist was consulted and musculoskeletal (MSK) ultrasound revealed mild synovitis with effusion over bilateral wrists, knees and right tibial-talar joint. Synovial effusion analysis did not yield pleocytosis or any microorganism upon culture. BCG related reactive arthritis was highly suspected. He experienced improvement after starting celecoxib 200mg twice daily and hydrocortisone 100mg thrice daily and was subsequently discharged home.

On 29 Jun, 2023, he was admitted to rheumatologist ward via emergency department(ED) because of recurrent of fever up to 38°C and polyarthritis. He denied trauma, symptoms of respiratory tract infection, diarrhea, animal contact, or high risk sexual exposure history. COVID-19 nasal swab PCR was negative. MSK ultrasound revealed grade 1 synovial hypertrophy with peri-articular inflammation and effusion over right wrist, 2nd PIP joint of toe, left elbow, tibial-talar, and 3rd PIP joint of toe. Additionally, he exhibited tenosynovitis over right extensor digitorum tendons, 2nd and 4th flexor tendons (dactylitis pattern), left tibialis posterior and flexor digitorum longus tendon. Synovial effusion from left tibial-talar joint revealed white blood cells:350/cumm (normal <200/cumm), without evidence of microorganisms or crystals. Laboratory blood tests revealed elevated C-reactive protein (CRP:25.14mg/dl; normal <1.0mg/dl), erythrocyte sedimentation rate (ESR:88 mm/1 hr; normal:<20 mm/1 hr) and rheumatoid factor (RF:224 IU/ml; normal <20 IU/ml). However, tests for anti-cyclic citrullinated peptide antibody(anti-CCP), Antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), Syphilis-Rapid plasma (RPR), serum Quantiferon-Gold test (QFT), and urine chlamydia/gonorrhea PCR were all negative. The human leukocyte antigen (HLA) typing revealed HLA-B 40(60) and C-07, which could compatible with peripheral spondyloarthropathy[12]. No evidence of sacroiliitis or spinal spondyloarthritis features observed on X-ray. Thus, *BCG-related reactive arthritis and tenosynovitis was confirmed. Intra*venous methylprednisolone and Celebrex 200mg twice daily were prescribed with improvement of all symptoms. He was discharged home with oral prednisolone and Celebrex.

Discussion

BCG therapy, a cornerstone in treating non-invasive high-grade papillary urothelial carcinoma, is generally well-tolerated but not without its share of complications. One rare but clinically significant adverse effect is BCG-induced reactive arthritis[10,11]. The co-existence of these conditions raises questions about their potential synergistic effects with BCG therapy in triggering or exacerbating reactive arthritis, a notion supported by some literature[8].

The immunological underpinnings of BCG-induced arthritis remain elusive. However, there's speculation that antigenic overlap between mycobacterial components and human tissue could be a contributing factor[1]. This theory could shed light on the autoantibody production observed in our patient. The initial diagnosis was a blend of UTI and BCG-related arthritis, which complicated the clinical picture. The role of comprehensive differential diagnosis is paramount, especially when polyarthritis manifests after BCG therapy[5].

Treatment-wise, our patient initially received celecoxib and hydrocortisone but eventually required intravenous methylprednisolone. This aligns with literature suggesting that NSAIDs often fall short in symptom control, making corticosteroids a more effective alternative[4,6]. The recurrence of symptoms in our patient is noteworthy and echoes similar cases where symptoms either abated or persisted, emphasizing the need for vigilant long-term follow-up[3]. Diagnostic markers like leukocytosis, hs-CRP, and ferritin were elevated in our patient, corroborating their utility in both diagnosis and disease monitoring, as previously documented[2]. The presence of specific HLA types in our patient hints at a genetic predisposition, an area still under active investigation[1]. HLA-B40(60) has been shown to be related to B27 negative ankylosing spondylitis or spondyloarthropathy in Taiwan13. The HLA-B40(60) typing in our patient was one of the predisposing risk factors for developing reactive arthritis. Given the multifaceted nature of this condition and the potential for symptom recurrence, long-term monitoring is indispensable, especially for patients with multiple co-morbidities undergoing BCG therapy[10]. In summary, BCG-induced reactive arthritis is a multifaceted condition requiring a multidisciplinary approach for optimal management. Our case contributes to the existing literature and underscores the need for further research, particularly in patients with multiple co-morbidities.

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病例報告　112_C 83

第四型免疫球蛋白 G 相關疾病于不尋常表現: 心包膜及肋膜積液!

Another show for IgG4-RD; rare presentation with pericardial and pleural effusion!

張家寧[1] 吳宏彬[1,3] 何茂旺[1,2] 蘇浤傑[1,2] 洪偉哲[1,4] 許登傑[1,4] 吳青峰[5] 張菡[6]
中國醫藥大學附設醫院[1]內科部 [2]感染科 [3]心臟血管系科 [4]風濕免疫科 [5]心臟血管外科 [6]病理科

Introduction

IgG4 related disease(IgG4-RD) which is still immature topics in clinical medicine, is one that any organ could be involved with. Its systemic nature with disease spectrum fools clinicians with similar but totally different clinical diagnosis. IgG4-RD might become an upcoming hot issue in immune-related diseases. Of course, there remains much more to explore with this condition. This case was reported for the purpose to record rare presentation of IgG4-RD and sharing experience.

Case presentation

62-year-old Taiwanese lady presented with progressive breathlessness for about one week with associated intermittent low grade fever of about 38'C for about 10 days. Serositis involving pleural and pericardial effusion was noted. After serial survey including work up for fever of unknown origin, no focus was found. Pericardiectomy was done and pathology report of which showed mild lymphoplasmacytic infiltration, rare neutrophilia and marked fibrosis without granuloma, increased ratio of IgG4/IgG of 60% with predominant CD-3 positive lymphocytes (predominantly T cells more than B cells). Serum IgG subclasses showed elevated IgG4 151.9 mg/dl was noted. IgG4-RD was highly suspected.
This case was reported in the purpose that if any other patient presenting with similar symptoms or medical personnels dealling patients with similar symptoms can have some consideration as differential diagnosis in patients with serositis of unknown focus and fever of undetermined focus. Although some literature mentioned fever is uncommon, our patient did have fever.

Conclusion

Any organ could be involved in IgG4-RD and not to forget this condition if other possible etiology has been excluded. The reference literature regarding IgG4-RD needs more information to be evoluted to catch the gap. Any organ could be involved in IgG4-RD as its systemic nature with disease spectrum and not to forget this condition if other possible etiology has been excluded.

病例報告　112_C 84

關注新型冠狀病毒相關甲狀腺機能失調; 時間會證明!

Pay attention for COVID-19 related thyroid dysfunction; time will show!

張家寧[1] 曾盈瑜[1,2] 陳韋成[1,3]
中國醫藥大學附設醫院[1]內科部 [2]新陳代謝科 [3]胸腔內科

Introduction

Coronavirus disease 2019(COVID-19) infection which has unpredictable destination in patients so far has caused variable systemic involvement, as angiotensin-converting enzyme-2 (ACE2) receptors express in almost everywhere with variable densities. Being a viral infection, it is not surprising COVID-19 causes autoimmune conditions, and why we mentioned the case is to remind not to forget COVID-19 attacks not only lungs. Emerging case reports and analysis also emphasize on post-COVID-19 status and related illness. It might be wise to monitor patients with COVID-19 infection for new thyroid disease or progression of preexisting thyroid disease.

Case presentation

47 years old Taiwanese lady who is married and works as an office-lady, presented with progressive palpitation with chest tightness for about one month. Her endocrinology status and renal function were checked in 2020 June as she was diagnosed with hypertension for which survey showed no obvious cause of secondary hypertension. During COVID-19 era, she had Moderna vaccination for 3 doses. She had COVID-19 infection in 2022 June for the 1st time. Graves' disease was diagnosed after 5 months of COVID-19 infection which was well controlled till March 2023. She got second time COVID-19 infection in May 30, 2023 and thyroid storm occurred in June 2023.

病例報告　112_C 85

黏液玫瑰單細胞菌於人體免疫缺乏病毒個案所造成之心內膜炎

Infective endocarditis caused by *Roseomonas mucosa* in a HIV-infected man

林羅威[1] 李鑒峰[1,2,3] 王唯堯[1,2,3] 曹世明[1,2,3] 李育霖[1,2,3] 李原地[1,2,3]

[1]中山醫學大學附設醫院內科部 [2]中山醫學大學附設醫院感染科 [3]中山醫學大學醫學院醫學系

Introduction

The genus Roseomonas, of pink-pigmented glucose non-fermentative bacteria, were described in 1993 in clinical samples. Opportunistic infections due to this species are related to the patient skin microbiota[1]. There are no large trial investigated this pathogen, but a few cases have been reported in the past decades, including infectious spondylitis, peritonitis with HIV, and acute lymphoblastic leukemia[2]. We presented a case lived with HIV, diagnosed with *Roseomonas mucosa* related infective endocarditis.

Case presentation

A 24-year-old indigenous man, working as a service worker, presented with rapidly progressive shortness of breath for a month, accompanied with fever, chills, palpitation, orthopnea, and chest tightness in recent 5 days. On physical examination, we found a high-pitched, Grade IV early diastolic decrescendo murmur at Erb's point, jugular vein engorgement, rales over bilateral lung field. The initial laboratory data revealed leukocytosis (15970/ul) with segment predominant (96.7%), elevation of d-dimer (3460.50 ng/ml), high-sensitive C-reactive protein (1.687 mg/dl), acute liver injury (ALT: 526 U/L, AST: 654 U/L), and mildly elevated cardiac enzyme (High sensitive Troponin I: 54.0 pg/ml). The chest X ray reported an increased alveolar pattern of bilateral lungs and cardiomegaly. The transthoracic echocardiography (TTE) revealed severe grade aortic regurgitation and suggested tearing or rupture of the aortic valve. The transesophageal echocardiography (TEE) confirmed the findings in TTE and found a silky lesion on the non-coronary cusp (NCC).

The infective endocarditis was highly suspected, so the investigations of risk factors were done and reported a positive HIV combo test, positive TPPA/TPHA and VDRL tests, absolute CD4 count: 369 cells/uL, HIV viral load: 143000 copies/mL. We initiated empirical antibiotic with Ceftriaxone 2g once daily and Vancomycin (adjusted by Trough level), oral antiretroviral therapy with Dolutegravir/Lamivudine 50/300 mg once daily, and intramuscular injection of benzathine penicillin G 2.4 million units once a week for 3 weeks.

The patient met the indication for early cardiac-valve surgery, including aortic-valve dysfunction, and cardiogenic pulmonary edema. The aortic valve replacement and modified Manouguian technique were performed smoothly 2 days upon admission. The extubation was performed a day after the surgery, and the clinical condition improved dramatically within 3 days. The culture of the aortic valve yielded *Roseomonas mucosa*, and the pathology reported chronic endocarditis with degeneration.

Discussion

The Roseomonas spp. were usually considered as an opportunistic pathogen, which mostly infected patients with immunocompromised host, including immunosuppressive steroid therapy, chronic renal disease, liver cirrhosis, diabetes, rheumatoid arthritis, malignancy,

organ transplantation and AIDS[1]. The most common Roseomonas infections were those of the bloodstream in 74.7% (74 patients), musculoskeletal infections in 8.1% (8 patients), skin and soft tissue infections (SSTIs) and peritoneal dialysis-associated peritonitis in 6.1% (6 patients) each[3]. We found a case reported in BMC infectious disease, who is a 44-year-old woman with systemic lupus erythematosus and *Roseomonas mucosa* bacteremia. By meeting the modified Duke criteria, the patient was diagnosed with infective endocarditis[4]. Whereas, the blood culture was negative in our case, and we confirmed the diagnosis by pathological evidence - the tissue culture of the aortic valve. We also found HIV infection in this case, which increased the risk of opportunistic infection with Roseomonas spp. By surgical intervention, combined with antibiotic and anti-HIV treatment, the patient recovered rapidly and resumed activities of daily living within 2 weeks.

Conclusion

The *Roseomonas mucosa* had been increasingly isolated in recent years, but the study of this pathogen remained inadequate. The opportunistic infection should be concerned in certain groups, including patients living with HIV, receiving immunosuppressant or chemotherapy, elderly individuals…etc. The investigations of Roseomonas spp. in the future were required.

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病例報告　112_C 86

境外移入之痲瘋分枝桿菌 – 個案報告

Multibacillary *leprosy* infection: An imported case in a nearly eradicated era in Taiwan

林羅威[1] 李鑒峰[1,2,3] 王唯堯[1,2,3] 曹世明[1,2,3] 李育霖[1,2,3] 李原地[1,2,3]
[1]中山醫學大學附設醫院內科部 [2]中山醫學大學附設醫院感染科 [3]中山醫學大學醫學院醫學系

Introduction

Mycobacterium leprae (*M. leprae*), known as Hansen's disease, an acid-fast, gram-positive obligate intracellular bacillus[1]. is ubiquitous in tropical countries, particularly underdeveloped and developing countries. In Taiwan, only 9 cases were reported in 2022, most of which were imported from Indonesia and Philippines[2]. Despite the low incidence rate in Taiwan, the complications caused by leprosy were non negligible, especially in children under 15 years of age, including neuropathy, ophthalmic injury, and immunologic reactions[3].

Case presentation

A 37-year-old woman, an Indonesian, working as a caregiver, presented with low-grade fever intermittently for a month, with multiple progressively scattering, reddish to violaceous, infiltrative papules and nodules on bilateral knees and calves. The initial laboratory data revealed elevation of high-sensitive C-reactive protein level (5.157 mg/dl), E.S.R level (124 mm/hr), leukocytosis (13550/ul) with segment predominance (77.2%), negative Anti-neutrophil cytoplasmic antibodies and Antinuclear antibodies, and C3 (119 mg/dl), C4 (24.8 mg/dl) within the normal limit. The cultures including blood culture, tissue culture and pus culture via skin biopsy yielded negative results. The oral doxycycline and topical fusidic acid prescribed at first were ineffective. 5 days later, the pathology reported mycobacterial infection, and microscopic examination revealed macrophages with vacuolated cytoplasm, innumerable acid-fast bacilli forming globi. The M. leprae-specific repetitive element (RLEP) PCR reported positive. With the diagnosis of Hansen's disease, the patient was transferred to designated hospitals for further treatment.

Discussion

In the beginning of this case, owing to low-grade fever, cutaneous manifestations, the physicians tended to investigate infections, connective tissue disease, and vasculitis. The differential diagnosis included rickettsioses, cellulitis, leptospirosis, infectious mononucleosis, adult onset Still's disease, Henoch-schönlein purpura, microscopic polyangiitis…etc[4]. In addition, because of the rarity of Hansen's disease, the practitioner might neglect the possibility of Leprosy infection and result in delayed or missed diagnosis[2]. If the acid fast stain of this case yielded negative, we might not perform PCR test for leprosy. In clinical practice, we might consider consultation of multiple divisions, including rheumatology, infectious disease, and dermatology, to improve the diagnostic rate.

Besides the *M. leprae*, other mycobacterium also cause cutaneous manifestations, including *M. tuberculosis*, *M. bovis*, *M. ulcerans*, M.*abscessus*. Although the cutaneous presentations were quite different, the diagnosis of cutaneous mycobacterial infections requires tissue biopsy[5]. If leprosy infection was confirmed by pathology or PCR test, the case will be transferred to designated hospitals for further treatment, including National Taiwan

University Hospital, MacKay Memorial Hospital, Taichung Veterans General Hospital, National Cheng Kung University Hospital, and Lo-Sheng Sanatorium hospital.

Conclusion

The case reports of infection with *M. leprose* were rare in Taiwan, whereas they were not eradicated. We shall take similar symptoms in populations with high risks into account, in order to make diagnosis early and prevent further complications.

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病例報告　112_C 87

冠狀動脈左迴旋枝阻塞引起之心肌梗塞合併左心室動脈瘤與腱索斷裂

A Rare Case Report of Left Circumflex Artery Myocardial Infarction Resulting in Co-occurrenceof Left Ventricular Aneurysm Formation and Chordae

黃立安[1] 蕭文智[1,2] 翁國昌[1,2,3]

[1]中山醫學大學附設醫院內科部 [2]中山醫學大學附設醫院心臟內科 [3]中山醫學大學

Introduction

With the introduction of early reperfusion therapies, substantial reduction in the frequency of mechanical complications of acute myocardial infarction (AMI) had been recorded. However, mortality rates have not decreased in parallel, and mechanical complications remain an important determinant of outcomes after myocardial infarction.

Case presentation

A 56-year-old male with hyperlipidemia and heavy smoking history presented to emergency departmentwith one-day history of sudden dyspnea, orthopneaand blood-tinged sputum.Jugular vein distention, bilateral basilar rales and tachycardia was noted onphysical examination. Laboratory testing was notable for elevation of NT-proBNP and troponin I. No evidence of ST-T change was seen on 12-lead electrocardiogram. Chest radiographshowed unilateralpulmonary congestion.Dual antiplatelet loading was prescribedfor suspected acute coronary syndrome, and the patient was intubatedfor respiratory failure.

Coronary angiography was done with indication of non-ST elevation myocardial infarction, which revealed coronary artery disease, single vessel disease, left circumflex artery total occlusion. Percutaneous coronary intervention and balloon angioplasty was done for left circumflex artery total occlusion lesion, and bare-metal stent was deployed. Owing to continuous dyspnea and unstable saturation, transthoracicechocardiogram was arranged, which demonstrated posterior mitral leaflet prolapse, accompanied with chordae tendineae rupture, severe mitral regurgitation, and left ventricular inferolateral wall trueaneurysm formation. Mitral valve replacement with xenograft mitral valve and left ventricular aneurysm repair was done smoothly. Follow-up echocardiogram revealed improvement of left ventricular contractility. Better respiration was observed, and the patient was discharged uneventfullyon 23rd day of admission.

Discussion

Mechanical complications of acute myocardial infarction (AMI) include papillary muscle rupture (PMS) and acute mitral regurgitation (MR), ventricular septal defect (VSD), ventricular free wall rupture (FWR), left ventricular aneurysm and pseudoaneurysm. These complications present with acute dramatic hemodynamic deterioration and result in high mortality rate. Prompt diagnosis and urgent management are crucial to improving outcomes. We presented a case of non-ST elevation myocardial infarction due to left circumflex artery total occlusion. There are several features worth mentioning in our case. First, co-occurrence of left ventricular aneurysm and chordae tendineae rupture wasa rare condition. Second, true LV aneurysms are most frequently seen after acute transmural myocardial infarction, and the location is typically at anterior wall or apex, the territory of left anterior descending

artery. However, our case presented with NSTEMI, and the culprit lesion was left circumflex artery.Third, based on critical condition of subsequent heart failure and respiratory failure, we suspected the patient to have left-dominant coronary circulation, accounting for less than 10% of all population. In this group of patients, nearly 60% of the left ventricular myocardium is supplied by the posterolateral branches and posterior descending artery (PDA)originating from the left circumflex artery (LCx). This less well-balanced coronary circulation might have a negative influence on prognosis of patients with coronary artery disease.
Cardiogenic shock or acute pulmonary edema are frequent presentationsin mechanical complications of AMI. Asymptomatic or isolated heart murmur are also possible. Echocardiography is usually the first-line practical tool to identify the type, location, and hemodynamic consequences of the mechanical complication. Initial management requires medical therapy,such as inotropes and diuretics, combined with mechanical circulatory support, eithernoninvasive ventilation or intubation. An intra-aortic balloon pump (IABP)or extracorporeal membrane oxygenation (ECMO)may also be required for unstable patients. Early surgery is the definitive treatment,but the optimal timing is unclear. Recently, percutaneous therapies are emerging as analternative treatment option for patients at prohibitive surgical risk.

病例報告　112_C 88

合併退伍軍人症肺炎以及堪薩斯結核分枝桿菌肺炎以及堪薩斯結核分枝桿菌肋膜炎：已持續發燒以及肺結節為表現的一位修格蘭氏症候群患者

Combined Legionella pneumophila pneumonia and Mycobacterium kansasii pneumonia and pleuritis infection: presenting with persistent fever and pulmonary nodules in a patient with Sjögren's syndrome

洪傳勝[1] 吳珈潤[1] 曲承鑲[1] 陳世彬[1,2] 王耀東[1,2]
[1]中山醫學大學附設醫院內科部 [2]中山醫學大學醫學系

Introduction

Fever and pulmonary nodules deserve aggressive studies, especially in a patient with immunocompromised status. Herein, we reported a serious infection with multiple pathogens in a patient with Sjögren's syndrome.

Case presentation

A 60-year-old woman with Sjögren's syndrome suffered from fever off and on for about 2 weeks prior to hospitalization. The chest radiography initially showed no obvious lung lesions. However, leukocytosis, left shift, and elevated CRP were found. Whole body inflammatory scan was obtained, and it showed increased uptake at the mediastinum and bilateral lung parenchyma. Chest CT with contrast disclosed right upper mediastinal abscess and several lung nodules at RUL, LUL, and LLL. Due to suspected malignancy and inflammation, she received VATS with decortication, and wedge resection of RUL and RLL. Mediastinal abscess, right yellowish pleural effusion about 30 ml, and right upper lobe consolidation were noted. No malignant cells were found by pathology. However, progressive RUL consolidation and shortness of breath happened to her after VATS surgery. Acute respiratory failure s/p endotracheal intubation and mechanical ventilation was found, and the follow-up chest CT showed RUL, RML, RLL, and LLL consolidation and moderate amount of pericardial effusion. Pericardiocentesis was done, and 180 ml turbid fluid was drained. Bilateral pneumothorax and subcutaneous emphysema happened to her during mechanical ventilation. Due to persistent RUL consolidation without any resolution even on broad spectrum antibiotics treatment, she was transferred to our hospital. The sputum film array showed presence of Legionella pneumophila and Acinetobacter baumanii complex; the urine Legionella antigen also showed positive; the bronchoalveolar lavage film array also showed presence of Legionella pneumophila. In addition, sputum acid-fast bacilli showed (++) for 2 sets, and MTB-PCR showed negative. The right pleural effusion TB culture yielded Mycobacterium kansasii in previous hospital. The blood culture yielded Stenotrophomonas maltophilia. She received levofloxacin, EMB, rifampin, meropenem, colistin, and tygacil for multiple pathogens infection.

Discussion

Multiple pathogens co-infection are not rare in patients with immunocompromised status, especially in ICU settings. However, limited diagnostic tools and inadequate pathogens work-up at the beginning put patients in the danger of deterioration. We took film array as early as possible, so that identifing Legionella pneumophila pneumonia and started anti-NTM

regimens as the NTM lung disease diagnostic criteria met. Finally, the VATS surgery also took an important role to deal with the mediastinitis, because delayed mediastinitis diagnosis and treatment caused high motality as 40 %.

Conclusion

Co-infection with Legionella pneumophila pneumonia and Mycobacterium kansasii pneumonia and pleuritis could be the cause of persistent fever and lung nodules in patient with Sjögren's syndrome. It can't be over-emphasized that Intensive work-up by sputum/BAL film array and early treatment of NTM lung diseases.

病例報告　112_C 89

罕見腸道沙門氏菌菌血症合併敗血性肺栓塞與多重器官衰竭 – 個案報告

Rare septic pulmonary emboli and multiple organ failure caused by Salmonella enteritidis

蔡安騏[1]　王唯堯[1,2]
[1]中山醫學大學附設醫院內科部　[2]中山醫學大學醫學系

Introduction

Nontyphoid *Salmonella spp.*, the second food-borne pathogen next to *Stahylococcus aureus* in United States, is a zoonosis which contributes to infectious diarrhea worldwide. Infections by nontyphoid *Salmonella spp.* result from consuming the contaminated products and therefore lead to bacteremia and sepsis. We present a clinical case of nontyphoid salmonellosis complicated with septic shock, septic pulmonary emboli, and respiratory failure.

Case presentation

A 75-year-old male with diabetic history for 10 years had a relative good health with independence before. He suffered from fever with dry cough for 3 days, and under diagnosis of severe acute respiratory syndrome coronavirus 2 infection on August 1st, 2023. He received symptomatic treatment only. However, watery diarrhea 5 times per day with general weakness attacked on August 15th, 2023. He then admitted to one community hospital because of unstable condition. Initial laboratory examination showed acute kidney injury, leukocytosis u pto 13500, and elevation of C-Reactive Protein. Severe acute respiratory syndrome coronavirus 2 antigen test still showed positive. The Chest X-ray showed bilateral lower lobe infiltration. Molnupiravir was prescribed for antiviral treatment of COVID-19 since August 15th, 2023, and the medication was shifted to remdesivir 2 days later due to progression of pneumonia. Because of progressive dyspnea and impending respiratory failure, he was transferred to the medical center on August 17th, 2023, where emergent intubation and ventilator support were instituted. The laboratory examination revealed acute kidney injury, hepatocellular dysfunction, leukocytosis, and elevation of C-reactive protein. Empiric antibiotic regimens with piperacillin-tazobactam and levofloxacin were prescribed for empiric antibiotics treatment of severe COVID-19 co-infections. The CT scan of chest showed multiple nodular lesions and some with cavitation and feeding vessels over periphery of both lungs. Microbiologic cultures including blood, stool, sputum, and bronchial alveolar lavage (BAL) all yielded *Salmonella enteritidis group B* on the 3rd day of admission. The targeted antibitoic therapy was then shift to meropenem and ciprofloxcin. His vital signs resumed to relative stable condition and the chest X-ray revealed resolution of pulmonary infiltrates. Successful weaning from the ventilator support and extubation were achieved and he was discharged at the 56th day of hospitalization.

Discussion

Complications of salmonellosis include endocarditis, mycotic aneurysm, or septic emboli to vital organs. Septic pulmonary emboli by nontyphoid *Salmonella spp* has rarely been reported in immunocompetent and immunocompromised patients.

病例報告　112_C 90

罕見致死性新型隱球菌腹膜炎於非人類免疫不全病毒之肝硬化病人

Rare fatal *Cryptococcus neoformans* peritonitis in a HIV-negative cirrhotic patient

蔡安騏[1]　王唯堯[1,2]
[1]中山醫學大學附設醫院內科部　[2]中山醫學大學醫學系

Background

Spontaneous peritonitis (SP), most were caused by *Enterobactericeae*. had been diagnosed of severe infectious complications in patients with liver cirrhosis and nephrosis. However, fungal peritonitis, most were caused by *Candida* spp., had seldom been reported. In contrast, *Cryptococcus* spp. had rarely been the microorganism responsible for spontaneous peritonitis.

Clinical Scenario

A 64-year-old male had been diagnosed of tongue cancer post operation and HCV-related liver cirrhosis complicated with hepatocellular carcinoma few years ago with radiotherapy and target therapy. He visited one community hospital because of refractory ascites in February, 2020 and abdominal tapping was done almost monthly to relieve abdominal fullness symptom. Conscious change and cold sensation of four limbs were noted by family member and he was sent to Emergency Department on July 25th, 2020. Just two days before ER visit, routine abdominal tapping was done at OPD and the subsequent culture yielded *Cryptococcus neoformans*. He was admitted to medical ward and unstable vital signs and decompensated liver function (SGOT/SGPT: 97/59 IU/l, total bilirubin: 3.3 mg/dl) and renal failure (BUN/Cr: 106/2.3 mg/dl) with severe hyponatremia (Na: 109 mmol/L) and hyperkalemia (K: 6.2 mmol/L) were observed during hospitalization. Subsequent blood cultures performed 3 days after admission also yielded *Cryptococcus neoformans*. HIV-ELISA test showed negative result. Because of unstable vital signs and multiple organ failures, antifungal therapy was not instituted and the patient died at 5th day of hospitalization.

Conclusion

By literature searching in PubMed database, *Cryptococcus* peritonitis has rarely reported in cirrhotic patients, which mostly is concomitant with HIV infection. Here we report a rare fatal *Cryptococcus* peritonitis in a HIV-negative cirrhosis patient that may raise concern in SP cirrhotic patients.

病例報告　112_C 91

痰液細胞學檢查於疑似肺腫瘤病案之功能

Roles of sputum cytology in case of suspecting lung cancer

李瑞源
衛福部台中醫院內科

Introduction

The role of sputum cytology in the diagnostic work-up of patients with suspected lung cancer. Spontaneously produced fresh sputum was analyzed Sensitivity of sputum cytology increased with an increase in the number of samples examined. Sputum cytology in suspected cases of carcinoma of lung is a useful and cheap diagnostic tool.

Materials and Methods

case introduction

This 72 y/o woman with past history of 1.Hypertension under regular medication treatment. 2. GERD. COUGH with whitish sputum FOR yrs, especially at night, PND, BW loss(-), well appetite, no night sweating, no fever, no headache, SOB-, no hemoptysis, GERD(+)DRUG ALLERGY-, DM-, H/T UNDER AMLODIPINE, asthma-, BP:143/90 mmHg, HR:96/min, PNEUMONIA EPISODE THIS APRIL TB CONTACT HX with her GRANDMOTHERT HROAT-MUCUS COATING(+)Family History: no lung cancer, no pul TB Personal history : alcohol (-), betel nut (-), smoking (-) Occupation :retired nurse BS: clear Allergic Hx: - Travel Hx: -, Contact HX: - CXR 10809- INFILTRATION AT RT HILAR(RB3); SAME AS 108-04 10810- ONLY IMPROVED LITTLE CXR 10810- SAME CXR 112.2. progression with RB3 consolidation with RUL satellite infiltrated CXR 112.3. nodule progression with RB3 consolidation with RUL satellite infiltrated after doxycycline Abdomen CT(2023.1.): some scattered GGO-consolidation over RLL, Right upper-third ureteral calculus with obstructive uropathy 10809 AFS(+), PCR(-), C(+), ID- M. ABSCESSUS 10810AFS(+)X3, C(+), PCR(-), ID- PENDING 112.2. sputum AFS(-) x 3, C:NTM x 3, ID: pending 112.3.3 sputum cytology: Suspicious for malignancy According the patient, She was cough with whitish sputum from cough with whitish sputum for 3 years(especially at night). She was sent to our hospital and arrange exam (112.2. sputum AFS(-) x 3, C:NTM x 3). Due to the cough with whitihs sputum symptoms persist, PND was also noted. So she was sent to chest OPD for help. There was no fever, chills, night sweating, headache, short of breathing, hemoptysis, poor appetite or BW loss. In chest OPD, the patient con's clear, R't decrease breathing sound, no neck lymphadenopathy, no abdomen distension or tenderness.

Results

Due to the 112.3. CXR showed: nodule progression with RB3 consolidation with RUL satellite infifltrating. 112.3. sputum cytology: suspicious for malignancy. Under the impression of RB3 lung mass with obstructive pneumonitis. Then arrange admitted for arrange chest CT and bronchoscopy for survey .lung cancer, adenocarcinoma, RB3, cT4N0M1a, stage IVA, with RML/RLL/LLL lung to lung mets, ECOG:1.

Discussion

It is a simple, cost-effective and noninvasive procedure for the assessment of respiratory diseases, including preinvasive and invasive pulmonary malignancies. In present study, the efficacy of sputum cytology with *Papanicolaou stain* in the detection of clinically suspected lung carcinoma is evaluated the existence of tumor cells, classifying the tumor as possible. Sputum cytology examination followed by bronchoscopy is a practical way of detecting early-stage lung cancer in these lesions Use of both sputum and BAL cytology increases the detection rate of lung cancer. Sputum examination alone is not effective for the detection of early stage lung cancer. In high risk individuals, the combination of LDSCT scans and sputum cytology is probably more effective in detecting early lung cancer than LDSCT alone even with Molecular sputum cytology analysis DNA mutation analysis. In lower economic underdeveloped countries sputum cytology is an affordable diagnostic instrument and still clinically implemented. LDCT is 4-10 times more sensitive than conventional chest radiography in detecting early peripheral lung cancer. Other auxiliary diagnosis Lung cancer-related tumor markers can be detected according to the needs of clinical diagnosis, to be used as auxiliary diagnosis and D.D. and to predict the possible subtypes of lung cancer.

病例報告　112_C 92

肺塌陷與意外後胸痛

Lung atelectasis by chest pain after chest blunt injury from bicycle traffic accident

李瑞源
衛福部台中醫院內科

Introduction

Focal hazy opacity of lung occurred in infectious, neoplastic non- infectious or nonneoplastic from acute or chronic condition. All should be made into differential diagnosis.

Materials and Methods

Case introduction

A 52 gentle man Self-reported: Riding a bicycle, he was hit by a car accelerating from behind and was thrown away. He had a helmet. denied head injury right chest pain with local ecchymosis bilateral elbow contusion and local abrasion bilateral knee contusion and local abrasion no initial loss of consciousness; no headache; no vomiting; no neck pain; no abdominal pain; no limb numbness can walk in ED PH: denied BT: 37 , HR: 95 , RR: 20 , BP: 164/102 mmHg, SPO2 96 Conscious : clear, E4V5M6 pupil: 3mm/3mm Light reflex:+/+Neck: no tenderness, no deformity no jugular vein engorgement no tracheal deviation Head; no tenderness Chest: breathing sound : clear Heart beat : regular ; Heart sound: no murmur right anterior and chest wall tenderness Abdomen : soft and flat no tenderness, no rebound pain bowel sound : normoactive Extremities : free movable, no edema no tenderness Impression: right chest contusion, suspect ribs fracture, r/o pnuemo-hemothorax, r/o lung .bilateral elbow contusion and local abrasion .bilateral knees contusion and local abrasion CT: right chest wall soft tissue swelling, suspect right rib9 linear fracture, no pneumothorax , no hemothorax right chest wall contusion with right rib 9 linear fracture. bilateral elbow contusion and local abrasion. bilateral knee contusion and local abrasion. Discharge with with tramadol and wound care OPD f/u tomorrow with finding of RML lung opacity, few pleural effusion.

Results

His RML opacity lung lesion cleared 3 day later, favored adhesive atelectasis.

Discussion

Symptoms of collapsed lung vary, may include falling in O2 saturation arrhythmias fever sharp chest pain. Causes for nonobstructive atelectasis include :Smoking COPD SCI or muscular dystrophy An illness or injury to breathe Medications: opioids or sedatives Obesity ,bed rest .elderly mucus plug, a tumor or fighter jet pilot Injuries, car accident Immobilization Scarring and shrinking of the membranes that cover the lungs and line the inside of the chest, exposure to asbestos smoking, surgery involved chest or abdomen .CXR is generally visible include lung opacification and loss of lung volume. atelectasis is reversible collapse of lung tissue with loss of volume; A large atelectasis may cause hypoxemia, but any other symptoms are due to superimposed pneumonia. Diagnosis is by CXR the cause is not clinically apparent, bronchoscopy or chest CT may be needed. Treatment involves maximizing coughing, deep breathing, and walking.

病例報告　112_C 93

案例報告與文獻回顧-刀傷致後天性橫膈膜脫疝

Return of the Pain: Delayed traumatic diaphragmatic hernia after penetrating trauma, a case report and review of article

趙泓翔[1] 蕭亦均[2] 黃偉彰[2]
[1]臺中榮民總醫院內科部 [2]臺中榮民總醫院內科部胸腔科

Introduction

Acquired diaphragmatic hernia is a rare complication after major traumas. The insidious nature and symptom of the disease render it difficult to be diagnosed. Moreover, the delayed or chronic type of traumatic diaphragmatic hernia could be unmasked months or even years after the index event. These make it difficult for physicians to detect this possible life threatening disease. We present a case of left diaphragmatic intestinal hernia 16 months after a knife-stab. We also review English-language literature of traumatic diaphragmatic hernia.

Case presentation

A 26-year-old male suffered from left lower chest tingling pain for 3 days and progressive shortness of breath. The patient was diagnosed with hemopneumothorax and received thoracostomy with chest tube after being stabbed in the left chest with a knife during a brawl 16 months ago. A mass lesion over left costophrenic angle was found on chest X-ray, which was confirmed as lateral diaphragmatic hernia with herniation of omental fat in chest computer tomography scan. Video-assisted thoracoscopic surgery was arranged and no disease recurrence during follow up period.

Discussion

Acquired diaphragmatic hernia (ADH) is a rare complication induced mostly from trauma, with an incidence ranging from 0.8% to 5% of thoracoabdominal trauma patient. About 80 to 85% of cases are caused by blunt traumas, while the rest are by penetrating trauma. Male patients are more likely to encounter traumatic diaphragmatic hernia than female patients. The left side is also a lot easier to develop such condition than the right, probably due to lacking the protection the liver provides, or the higher prevalence of right-handed assassins. In our literature review, the predominant clinical presentation among patients was characterized by either shortness of breath, chest pain, abdominal pain, or a combination of these symptoms. Given the potential for traumatic hernias to remain dormant for extended periods, it is important for physicians to maintain a high degree of vigilance when evaluating patients with a history of trauma, even if the inciting event occurred years ago. Furthermore, our review revealed that the majority of patients underwent exploratory laparotomy or laparoscopic surgery as the primary mode of treatment. Interestingly, our analysis did not uncover any case reports within our reviewed literature that documented the management of delayed diaphragmatic hernia using exclusively thoracoscopic techniques. Our case may highlight the possibility to manage delayed diaphragmatic hernia via minimal-invasive thoracoscopic surgery in selective patient.

Conclusion

Acquired diaphragmatic hernia, despite its rarity, may still cause fatal casualties if left untreated. Considering it can be fully reversed with surgical approach, the prompt diagnosis from the patient's history and image assistance is hence highlighted. We present a case with penetration trauma induced left diaphragmatic injury complicated with omentum hernia 16 months after the index injury, treated with VATS repair without residual symptoms.

病例報告　112_C 94

早期發生的抗甲狀腺藥物 Propylthiouracil 合併顆粒球低下與肝炎

Early-onset of agranulocytosis and hepatitis related with propylthiouracil

江偉廷[1]　曾耀賢[2]
童綜合醫療社團法人童綜合醫院 [1]內科部 [2]內科部新陳代謝科

Introduction

Propylthiouracil (PTU) is a commonly used antithyroid drug, but it also has plenty adverse effects. Although skin rashes, pruritus, and arthritis are common side effects, there are potentially more significant ones as well. Hepatotoxicity and agranulocytosis are two uncommon but potentially fatal adverse effects that must be monitored closely during treatment.

According to a study, agranulocytosis has a mortality rate of approximately 4%.[1] It most commonly occurs in the second and third months after starting treatment. We report a rare case of a 21-year-old woman who developed agranulocytosis and hepatotoxicity on the fifth day after initiation of the treatment. The early detection of agranulocytosis and liver damage is attributed to close monitoring during admission. White cell count and liver enzymes returned to normal range after we stopped PTU.

Case presentation

A 21-year-old woman with a history of type 1 DM and hyperthyroidism came to our emergency department due to dizziness and palpitation for a day.

She was diagnosed with type 1 DM at the age of 17 and was under Levemir 16U QD and NovoRapid 10U TIDAC currently. Hyperthyroidism was also diagnosed at the age of 17. A local hospital discontinued her treatment of antithyroid drugs one year later due to normal thyroid function. Follow-up of thyroid function was within normal range in February 2023.

She had been experiencing dizziness and general weakness since two days prior to the evaluation. She started to present with palpitations and nausea the night before she came to our emergency department.

On examination, her temperature was 38.9°C, the heart rate was 132 beats per minute, the blood pressure was 140/86 mm-Hg, the respiratory rate was 18 breaths per minute, and the oxygen saturation was 100% while the patient was breathing ambient air. The body-mass index was 19.1. She was alert, well-oriented and breathing smoothly.

A fingerstick blood glucose level was 492 mg per deciliter. The white-cell count was 16700/μL, the hemoglobin level was 13.5 g/dL, and the platelet count was 292000/μL. The creatinine level was 0.70 mg/dL, and the CRP was 0.14 mg/dL. The sodium level was 133 mEq/L and the potassium level was 5.3 mEq/L. Blood ketone was 4.0 mmol/L. Arterial blood gas revealed pH 7.3, PaCO2 35.2 mmHg, and HCO3 17.9 mEq/L. Urinalysis revealed 4+ sugar and 4+ ketones. An ECG showed sinus tachycardia.

The patient was admitted to the intensive care unit with a diagnosis of diabetic ketoacidosis and hyperthyroidism complicated with thyroid storm. Intravenous fluids and insulin were administered. Propylthiouracil 100 mg TID, propranolol 10 mg TID, hydrocortisone 100mg IV Q8h, and Lugol's solution 2 mL Q8H were prescribed for thyroid storm since admission.

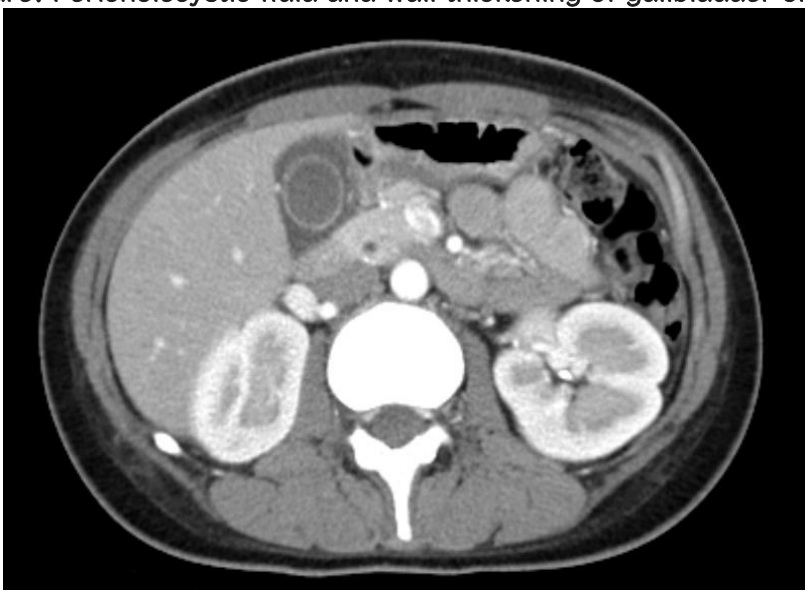
She presented with a sore throat on the fifth day of admission, and the fever continued.

Blood tests revealed a decrease in white cell count (3600/μL). Physical examination showed right upper quadrant abdominal tenderness so a computed tomography (CT) of the abdomen was ordered. CT showed pericholecystic fluid and non-specified gallbladder wall thickening without stone formation or gallbladder lumen distension. On the eighth day after admission, laboratory data showed an abnormal white blood cell count of 3200 per microliter and an abnormal ALT level of 280 U/L. Thus, PTU had been stopped since that day. Prednisolone 5 mg BID, lithium carbonate 300 mg BID, and propranolol 10 mg TID was prescribed instead. Her abdomen tenderness and sore throat abated the next day. The following laboratory data on the tenth day after admission showed a white cell count 5300/μL; AST 51 U/L, ALT 105 U/L.

Table. Timeline of symptoms, treatment and laboratory data of the patient(*: abnormal laboratory data)

	Day 1	Day 3	Day 5	Day 8	Day 10
symptoms	Fever	Fever and new sore throat	RUQ tenderness		Symptoms resolved
hydrocortisone	←	—	→		
Lugol's solution	←	—	—	→	
PTU	←	—	—	—	→
Lithium				←	→
WBC (/μL)	**16700***		**3600***	**3200***	5300
ASL (U/L)			10	**221***	**51***
ALT (U/L)	15		18	**280***	**105***

Figure. Pericholecystic fluid and wall thickening of gallbladder on CT



Hepatitis B antigen, antibodies, and ANA were check and were all negative.On the tenth day after admission, the patient had returned to her normal health status so was discharged. Liver enzymes were AST 14 U/L and ALT 7 U/L at out-patient follow-up.

Discussion

Carbimazole, methimazole, and PTU are commonly prescribed for hyperthyroidism. PTU is preferred in the treatment of thyroid storms because of its rapid onset of action. All antithyroid drugs, however, have a high incidence of side effects, including skin itching, rash, hives, arthritis, fever, and hepatitis.[1]

Although rare, agranulocytosis can be fatal. There are no specific risk factors for agranulocytosis, including age, dose, or gender. According to previous studies, agranulocytosis most commonly occurs in the second and third months of use.[2] Still, it may be presented one year after use.[3] In this report, a 21-year-old woman developed agranulocytosis after five days of PTU treatment for a thyroid storm, which is earlier than

expected. Another side effect in this case is hepatotoxicity. Hepatotoxicity may require a liver transplant in serious cases.[1] We found pericholecystic fluid on CT, which may indicate an inflammation process.

This patient experienced two side effects concurrently. Fortunately, agranulocytosis and hepatotoxicity were both detected in their early stages and had no sequelae after discontinuing PTU. The early diagnosis was attributed to the intensive care during the hospitalization. Patients who are being treated in an outpatient setting also need to be carefully monitored. Fever and sore throat are most common presentations.[3] Guidelines do not recommend routine follow-up of cell counts due to insufficient evidence but agranulocytosis must be promptly suspected if symptoms occur.[4] Research showed the median duration from the diagnosis to the recovery of agranulocytosis is 13 days.[3] The efficacy of granulocyte-colony-stimulating factor is uncertain.[5]

There is a significant risk of cross-reactivity between antithyroid drugs, so patients who develop agranulocytosis while taking any of them cannot be switched to another drug in the same category.

Conclusion

This case is noteworthy because it is a rare example of agranulocytosis occurring early in the course of PTU treatment. It also highlights the importance of monitoring patients closely for adverse effects when taking PTU. Patients should be educated to report any symptoms during antithyroid treatment.

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病例報告　112_C 95

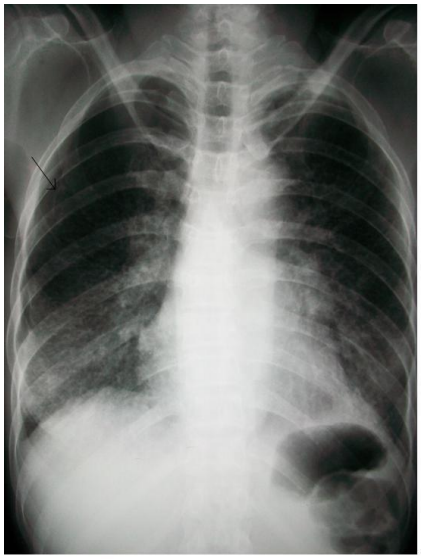
Uncommon cause of pneumothorax

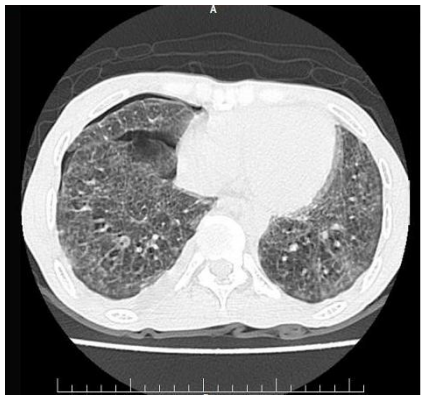
鄧世綸 吳整昌 陳德坤 蔡錦焜
澄清綜合醫院重症醫學部

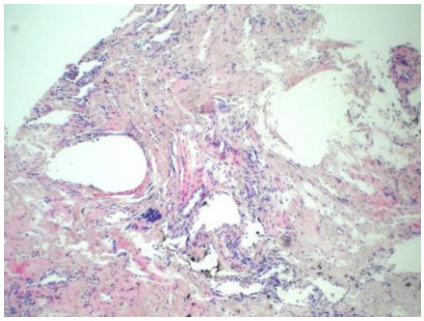
Introduction

Lymphangioleiomyomatosis (LAM) is an uncommon disease which affect the productive age women. It can involve the bronchioles, vessel and lymph system of lung and cause obstructive lung disease, pneumothorax and pleural effusion. In this report, we present a 40 year-old female who visited to our chest out patient department due to dyspnea and chest pain.

Case presentation







This 40 year old female is relatively well before and she denied any systemic disease including diabetes and hypertension. Besides, she does not have habit of cigarette smoking. However, she sufferred from dry cough, chest pan and intermittent SOB since two years ago and these symptoms progressed in recent two months. Then she visited to our OPD of Chest Medicine. At there, CXR showed diffuse interstitial pattern, right pleural effusion and pneumothroax and she was admitted. After admission, chest CT was arranged and disclosed diffuse centrilobular nodules, small cystics paces and right pneumothorax. Under the suspicion of lymphangioleiomyomatosis, bronchoscope was done for biopsy but no significant lesion was found. Thus thoracoscopy was performed and showed many blebs over RUL. Wedge resection and pleurodesis were done. Pathological report revealed diffuse infiltration of the pulmonary parenchyma with smooth muscle cells. Diagnosis of lymphangioleiomyomatosism was made and she was transferred to medical center for Sirolimus treatment.

Discussion

Lymphangioleiomyomatosis (LAM) is a rare, progressive, cystic lung disease which affect almost exclusively in productive age women. The most common symptoms of LAM include progressive dyspnea, wheezing, dry cough, hemoptysis, and pneumothorax. CXR of the patients could be diffuse reticulonodular interstitial infiltration and the typical chest CT of LAM shows bilateral diffuse round, thin-walled cysts. Obstructive physiology is the most common abnormality of pulmonary function testing. Diagnosis can be established by pathological report and typical microscopic examination revealed foci of smooth mucle-like spindle-shaped cells which invade to bronchioles, alveolar, vessels and lymph system of lung and cause thin-walled cystic change of involved area. Sirolimus, the mTOR inhibitor, is the drug proved by FDA to treat LAM and to prevent decline of lung function.

病例報告　112_C 96

病歷報告：原發性心臟腺癌

Primary cardiac adenocarcinoma—a case report

王譽達[1] 吳慧中[2] 吳靜怡[3] 惠群[1]
[1]澄清醫院中港分院內科部 [2]澄清醫院中港分院外科部 [3]澄清醫院中港分院病理部

Introduction

Cardiac myxoma represents the most prevalent benign primary cardiac tumor; however, this case presents a unique scenario in which the initial clinical diagnosis was cardiac myxoma, but it was ultimately identified as adenocarcinoma upon pathological evaluation.

Case presentation

We present the case of a 53-year-old female with a medical history of chronic obstructive pulmonary disease (COPD), type 2 diabetes mellitus (DM), and hypertensive heart disease without heart failure. She had been regularly monitored and managed as an outpatient. Her first hospitalization occurred on April 4, 2022, when she suddenly experienced right-sided weakness and slurred speech while working in the afternoon. A chest X-ray revealed cardiomegaly, an EKG demonstrated normal sinus rhythm, and the laboratory tests were unremarkable. Brain CT didn't show obvious intracerebral hemorrhage (ICH), and a brain MRI perfusion scan showed diffusion restriction in bilateral F-P lobes, indicating acute stroke. Considering that the onset of an acute cerebral infarction was within 3 hours, a neurologist was promptly consulted, and intravenous thrombolysis was administered. Cardiac echocardiography didn't identify any abnormalities or intra-cardiac mass. The patient was discharged uneventfully after a 20-day hospital stay with a diagnosis of acute cerebral infarctions in bilateral frontal-parietal lobes.

The second hospitalization occurred 10 months after the initial admission, on January 22, 2023, when the patient experienced vertigo while conversing with her family in the evening. She also reported right-sided limb weakness, headache, and difficulty swallowing while drinking water. She was promptly referred to the emergency room, where her limb muscle power had returned to normal. Laboratory results were unremarkable, except for mild liver function impairment with a GPT level of 64. Chest X ray did not reveal any pulmonary lesions or cardiomegaly. Brain CT showed no intracerebral hemorrhage nor large infarctions. However, Brain MRI, revealed a focal acute infarction in the right occipital lobe. Furthermore, an EKG indicated atrial fibrillation, raising suspicion of cardioembolic stroke. Transesophageal cardiac echocardiography performed three days after admission identified a mobile hyperechoic mass (1.5x4.4cm) within the left atrium with a pedicle attached to atrial septum. Five days after admission, she underwent the complete excision of the tumor mass without complications. The tumor mass measured 4.3x3x1.7cm and was found to have a pedicle attached to the atrial septum. The pathological exam revealed a tumor with myxoid stroma, abundant mucopolysaccharide ground substance, and a portion with glandular structures with mucin forming glands. The glandular cells appeared bland looking with atypia, hyperchromasia, nuclear pleomorphism and abnormal mitosis. The immunohistochemistry staining of the glandular cells showed the following results: CK7 (+, diffuse and strong), CK20 (+, focal), TTF-1 (-), CDX2 (+, focal), PAX-8 (+, focal), and GATA3 (+, focal). Additional

studies, including abdominal and chest CT scans, colonoscopy, and cervical smear, did not detect any neoplastic lesions elsewhere. Based on the pathologic findings and clinical studies, a primary cardiac adenocarcinoma originating from a glandular myxoma was considered.

Discussion

We present a unique case where the initial diagnosis of cardiac myxoma was later revised to adenocarcinoma based on pathological findings.

Primary cardiac tumors are exceedingly rare, with an estimated incidence of approximately 0.002-0.3%. The vast majority of these tumors are benign, with myxomas being the most prevalent among them. Other benign cardiac tumors include fibromas, lipomas, hemangiomas, rhabdomyomas, and papillary fibroelastomas. Malignant primary cardiac tumors account for about 15-25 percent of all primary cardiac tumors and can be broadly classified into two categories: sarcomas and lymphomas. Sarcomas, which make up approximately 95% of all malignant cardiac tumors, include angiosarcomas, undifferentiated pleomorphic sarcomas, and leiomyosarcomas. It's noteworthy that adenocarcinoma is not typically classified among primary cardiac tumors as per the 2021 WHO classification of heart tumors.

However, in our case, cardiac echocardiography detected a mobile hyperechoic mass within the left atrium, attached to the low interatrial septum—a characteristic location for cardiac myxomas. Consequently, the initial suspicion leaned towards either myxoma or thrombus formation, with myxoma being the primary consideration given the echocardiographic findings. Due to the potential life-threatening complications associated with intracardiac masses, including obstruction of blood flow, valvular dysfunction, and thromboembolic events, surgical resection of the mass was deemed necessary.

The microscopic examination of the pathological sample revealed features suggestive of adenocarcinoma, including hyperchromasia and nuclear pleomorphism. Immunohistochemistry further supported the diagnosis by indicating that metastatic disease was less likely. Additional investigations, including abdominal and chest CT scans, colonoscopy, and cervical smear, failed to identify neoplastic lesions elsewhere. Consequently, we arrived at the diagnosis of primary cardiac adenocarcinoma.

An intriguing case report by Boris P Eckhardt et al described a right-sided giant cardiac myxoma with malignant transformation, particularly within glandular structures. Histologically, the tumor exhibited characteristics of adenocarcinoma alongside areas with a typical myxomatous appearance. The tumor also featured dystrophic calcifications and calcified ossifications. The patient succumbed to acute heart failure shortly after admission. Post-mortem examination failed to uncover any evidence of extracardiac primary adenocarcinoma or metastasis. These findings led the authors to propose a hypothesis that the benign tissue within the myxoma had undergone malignant transformation into a mucinous adenocarcinoma.

Conclusions

Cardiac myxoma is a rare and almost always benign tumor. Surgical resection is usually curative and safe. Cardiac myxoma with glandular differentiation is rare and constitutes 1% to 5% of all cardiac myxoma. The origin of the glandular tissue has been attributed to epithelial differentiation of a totipotent cardiomyogenic precursor cells or the entrapped foregut rests in the tumor. Malignant transformation is an extremely rare condition and has only been reported in a few case reports. We present our case with typical clinical

presentation of a cardiac myxoma, but the final pathological report surprisingly revealed a malignant adenocarcinoma. Due to the rarity of the condition, there is no established guidance for further adjuvant chemo-radiotherapy. Fortunately, the pathologic report revealed a negative surgical margin. The patient is being monitored by a multidisciplinary team.

病例報告　112_C 97

原發性乳癌合併胃轉移：兩篇案例報告

Gastric metastasis from breast cancer: two case reports

余松霖[1]　李政祺[2]　吳佩儒[3]　陳美中[3]　惠群[2]
[1]澄清醫院中港分院一般科　[2]澄清醫院中港分院內科部　[3]澄清醫院中港分院病理部

Introduction

Breast cancer metastasis to the stomach is relatively rare, with an estimated incidence rate of approximately 0.3%. Gastric metastases are usually derived from a lobular rather than from a ductal breast cancer. Linitis plastica is the most frequent type observed on endoscopy, so it is difficult to diagnosis by EGD. The diagnosis is further established using histological and immunohistochemical analysis for gross cystic disease fluid protein-15(GCDFP-15), GATA Binding Protein 3(GATA-3), cytokeratin-7(CK-7) and cytokeratin-20 (CK-20). Here, we will present two cases of breast cancer metastasis to the stomach.

Case presentation

Case1

A 66-year-old woman had history of right ductal breast cancer with brain and bone metastasis s/p breast conserving therapy and augmentation mammoplasty of right breast in 2013/08 and completed adjuvant chemotherapy, radiotherapy was admitted to ward via ER due to nausea and epigastralgia for 2 days.

At ER, physical examination revealed epigastric dull pain. Lab revealed leukocytosis with elevated CRP level and anemia was also noted. Biochemistry study showed elevated lipase, GOT and GPT levels. Under impression of acute pancreatitis, she was admitted for further management.

After admission, the abdominal ultrasound showed hepatic tumors which were consistent with metastatic lesions. She also received EGD examination which showed 1. esophagitis and esophageal ulcers. 2.nodular lesion of treatment. 3.acute gastritis and erosions. Biopsy of the gastric body mucosa was done, and pathology report showed immunohistochemistry positivity for CK7, GATA-3, GCDFP-15, ER and PR, but negative for HER-2, consistent with metastatic breast carcinoma. Unfortunately, she had desaturation and severe dyspnea during admission. The family signed DNR and decided hospice care. So we kept supportive care and she expired in Oct 2019.

Case2

A 60-year-old woman with a history of invasive lobular carcinoma of the right breast, initial stage as cT2N0M0 in June 2015, underwent neoadjuvant chemotherapy until May 2016, when she received a right mastectomy. In January 2021, she was found to have multiple bone metastases. On October 14, 2022, she was admitted to the hospital via ER due to symptoms including coffee ground vomitus and tarry stool passage, suspicious of gastrointestinal bleeding.

At ER, physical examination revealed soft abdomen, no tenderness, hypoactive bowel sound. Lab data showed leukopenia and anemia. Chest x-ray showed 1. pneumonia in both lower lung. 2.extensive bony metastasis in bony thorax and spines noted. We also arranged the

EGD examination for evaluation of GI bleeding. And the report showed 1. reflux esophagitis LA Gr A. 2.diffue mucosal swelling of stomach, suspect linitis plastica. 3.esophagitis and esophageal lesion. 4.partial pyloric obstruction. During EGD examination, we performed biopsy of tissue from the fundus to the lower body of stomach for further survey.
After admission, PPI and transamin treatment were employed. But nausea and vomiting were still noted. So, we arranged UGI series which showed near total occlusion near the pylorus. And the pathology result showed the immunohistochemistry studies positivity for estrogen receptor, cytokeratin, GATA-3 and negative for progesterone receptor, HER-2/neu, E-cadherin, CDX-2, then Ki-67 demonstrates 20% labeling index in invasive tumor cells, consistent with metastatic breast carcinoma. Due to the above results and discussion with the patient and her family, they decided to transfer to medical center for further management.

Discussion

It is well known the most common metastatic sites of breast cancer are the bone, brain, liver and lung. Breast cancer metastases to the gastrointestinal(GI) tract are infrequent, and GI metastases are often not considered in daily practice. But the most common primary malignancies metastasize to the stomach include breast cancer, following by lung cancer, esophageal carcinoma, renal cell carcinoma, and malignant melanoma. The symptoms of metastatic tumors, include pain, nausea, vomiting, and bleeding. The mechanism underly gastric metastasis have not been clearly elucidated and are most likely different for each primary tumor. There are some pathways involved in the metastatic spread of original primary cancer to the stomach: hematogenous dissemination, lymphatic spread and direct tumor invasion. Following the diagnosis of gastric metastasis, the median survival rate is estimated to be between 10-28 months. Survival is further decreased in those with multiorgan metastasis.
The endoscopic findings can be presented with diffuse infiltration, nodules and/or ulcerations. The most common pattern of breast cancer metastasis to the stomach is a linitis plastica with diffuse infiltration of the submucosa and muscularis propria, which are usually present in the fundus and gastric body.
Immunohistochemical analysis are recommended for the accurate diagnosis. Tests for ER and PR biomarkers alone are not suitable because not all breast cancer cells express these hormone receptors. Other breast specific marker includes GCDFP-15 and GATA-3. GCDFP-15 is a pathological secretin released by the breast particularly in the setting of apocrine metaplasia of the breast. GATA-3 is a multifunctional transcription factor and part of the GATA family of zinc fingers DNA binding protein and it is only present in breast and urothelial carcinomas. When breast cancer metastasis to the GI tract is suspected, positive immunohistochemistry for CK7, GCDFP-15, and GATA-3 can effectively confirm the diagnosis, especially in those with CK-20 negative. These were consistent with our two cases.

Conclusion

Although gastric metastasis is rare with a negative impact on survival and it should be investigated in the patient with breast cancer who presents with dyspepsia or other upper gastrointestinal symptoms. Nonetheless, these symptoms lack any specificity considering that patients usually are receiving chemotherapy, radiotherapy or even suffering of electrolytic disorders. Because of that, there could be a delay in diagnoses. So, if the patients with a history of breast cancer, a high index of suspicion for potential metastasis to the stomach

should be considered when new gastrointestinal symptoms develop or an apparent primary gastric tumor is diagnosed. And the imaging and endoscopic findings are not enough to differentiate primary from secondary gastrointestinal lesions. Biopsy and pathology are essential for the diagnosis. Finally, diagnostic confirmation involves comparison of the histology of the primary tumor and the metastasis, with immunohistochemistry as an essential tool.

病例報告　112_C 98

妊娠糖尿孕婦合併高三酸甘油酯血症，酮酸中毒，及急性胰臟炎之個案報告

Acute pancreatitis and ketoacidosis in a pregnant woman with gestational diabetes and hypertriglyceridemia: case report.

胡菁芸[1] 蘇修緯[2] 蔡易婷[3]

[1]烏日林新醫院新陳代謝科 [2]臺中榮民總醫院婦女醫學部產科暨高危險妊娠科 [3]臺中榮民總醫院內科部新陳代謝科

Introduction

Acute pancreatitis (AP) in pregnancy is rare, with incidence about 1 in 6,790 pregnancies in Taiwan[1]. The fetal outcome included preterm deliveries (50%) and fetal losses (18%)[1]. Here we share an extremely rare case of AP-triggered DKA in a pregnant woman with gestational diabetes.

Case presentation

A 22-year-old nulliparous woman presented to the emergency department at 27+5/7 weeks' gestation with epigastric pain, fever and tachycardia. Serum exams found leukocytosis, elevated C-reactive protein, amylase, lipase, lactate, and ketone body; pH 7.27, base excess -16.2. Significant hypertriglyceridemia(3,660 mg/dL), was noted. Abdominal ultrasound demonstrated swelled pancreatic gland and normal biliary system. The patient received hydration, continuous IV insulin infusion, antibiotic, and Omega-3-Acid. After 7 days of treatment she was discharged. She kept using insulin and had an uncomplicated vaginal birth with a healthy 3,130g baby. At 6th week postpartum, she had stopped injecting insulin and had normal glucose level.

Discussion

Both AP and DKA in pregnancy are obstetric emergency, associated with maternal morbidity and fetal death[2,3]. Pregnant women with type 2 diabetes or gestational diabetes could also develop DKA[3]. Treatment of AP and DKA in pregnant and nonpregnant individuals is similar.

Conclusion

With immediate insulin therapy and proper supportive management, AP during pregnancy may not always related to dismal outcome.

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病例報告　112_C 99

移植後糖尿病之病例報告

A case of post-transplant diabetic mellitus

沈孜穎[1] 鄭畬方[2]
[1]彰化基督教醫院內科部 [2]彰化基督教醫院內分泌暨新陳代謝科

Introduction

Post-transplant diabetes mellitus (PTDM), resembling type 2 diabetes mellitus (T2DM), is influenced by transplant-related causes, such as steroids, immunosuppressive drugs, viral infections, and low magnesium levels, potentially leading to PTDM[1].It increases mortality, possibly linked to cardiovascular events, and raises the risk of opportunistic infections, with milder microvascular complications compared to type 1 and type 2 diabetes[2].

Case presentation

A 52-year-old male, post-deceased donor liver transplantation in July 2022, under Tacrolimus 2mg daily, presented with general weakness on March 12, 2023. His blood glucose and HbA1c were elevated (504 mg/dL and 11.8%, respectively), contrasting his pre-transplant HbA1c of 5.4% at January 19, 2022. New-diagnosed PTDM was suspected and managed with insulin therapy and oral hypoglycemic agents.

Discussion

PTDM's pathogenesis involves impaired insulin and glucagon release, reduced glucose uptake, and liver glucose release[1]. Deceased donor liver transplantation shows a higher PTDM incidence. Post-transplant risk factors involve medications, including steroids and calcineurin inhibitors, notably Tacrolimus, with associated electrolyte imbalances. CMV infection may contribute to PTDM development[2]. Incidence analysis reveals higher PTDM rates in liver, lung, and heart transplantation, with kidney transplantation showing lower incidence[3]. PTDM diagnosis requires confirming no pre-transplant DM history, with screening options like OGTT and HbA1c. HbA1c interpretation may be influenced within the first 3 postoperative months, thus recommending its use after this period or opting for OGTT for early diagnosis[4].Treatment goals differ from general DM, focusing on reducing mortality and CV events. Immunomodulatory medication adjustments are central, with ongoing debate on Tacrolimus replacement. Early prevention involves lifestyle modifications, including dietary changes, exercise, and weight management, with insulin considered the safest and most effective treatment for PTDM[5].

Conclusion

Post-Transplant Diabetes Mellitus (PTDM) shares features with Type 2 Diabetes Mellitus (T2DM), with distinct risk factors related to transplantation. PTDM is associated with increased mortality, particularly cardiovascular events, and heightened susceptibility to infections. Diagnosis and management require vigilance, with early intervention through lifestyle modifications and consideration of insulin therapy as a primary treatment approach.

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病例報告　112_C 100

泛視神經脊髓炎以昏迷及四肢無力表現的懷孕婦女

A Case of Pregnant Woman with a Neuromyelitis Optica Spectrum Disease of Unconsciousness and Quadriplegia

沈孜穎[1] 李培森[2] 楊小萱[3] 邱駿清[4] 陳昶華[5]
[1]彰化基督教醫院內科部 [2]漢銘基督教醫院神經內科 [3]彰化基督教醫院婦產科 [4]彰化基督教醫院內科重症醫學科 [5]彰化基督教醫院感染科

Introduction

Neuromyelitis optica spectrum disease (NMOSD) has been distinguished from multiple sclerosis based on the aquaporin-4 (AQP4)-IgG biomarker[1-5], clinical manifestations and magnetic resonance imaging (MRI) findings[6]. Common manifestations of NMOSD center on lesions of the corresponding CNS region, including optical neuritis[6], myelitis, and post-rema syndrome[7,8].

Case Presentation

A 26-year-old pregnant woman, 18 weeks of gestation (G4P2A1), with a lack of notable medical and family history, exhibited no mental or physical deficits.

In November 2020, she began experiencing persistent nausea, vomiting, and intermittent fever, initially treated as urinary tract infection with limited improvement. At the end of November, somnolence started to set in, leading to her admission to a medical center in December. The initial laboratory tests did not show significant abnormalities, possibly due to prior treatment. Cultures including blood, urine, and sputum did not produce growth, and autoimmune disorders were ruled out according to the negative findings of the ANA and anti-dsDNA antibodies. Treatment with cefazolin alleviated her fever, leading to discharge in mid-December. However, somnolence persisted, accompanied by disorientation and recurrent fever. She developed progressive bilateral weakness of the lower extremities and experienced multiple episodes of loss of consciousness with limb convulsions. Readmitted at the end of December, her lab results revealed an elevated WBC count, mild elevations of liver enzymes, and abnormal brain magnetic resonance imaging (Figure 1).

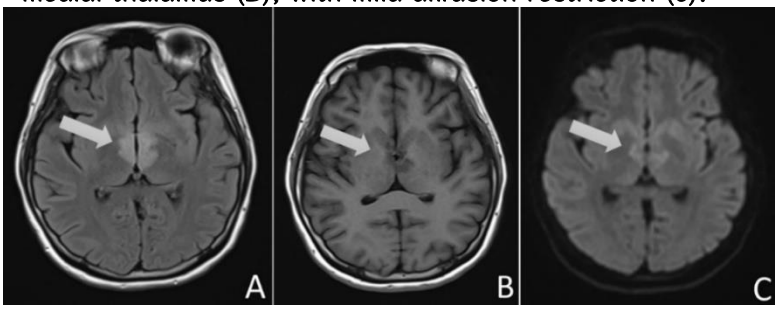

Figure 1. Brain magnetic resonance image
Presence of T2 / air hyperintensity (A) and hypointensity of T1 hypointensity in the bilateral hypothalamus and anterior medial thalamus (B), with mild diffusion restriction (c).

A lumbar puncture was performed, showing pleocytosis (WBC 25 /μL) in the CSF with lymphocyte predominance. She was treated for infectious meningoencephalitis, but febrile episodes persisted. The EEG showed abnormal brain waves.

Autoimmune and anti-aquaporin-4 (AQP4) antibody tests were performed, with positive AQP4 results.Despite IVIG and pulse therapy, her condition improved marginally. To address the optic neuromyelitis spectrum disorder (NMOSD), various therapies were considered, but due to pregnancy concerns, the family opted for termination at 23 weeks.

Post-abortion, her sensorium gradually improved over two weeks, but quadriplegia persisted. Plasma exchange was attempted, resulting in a slight improvement in muscle strength. She

was transferred from the intensive care unit to a general ward for continued care.

Discussion

Aquaporin, a vital membrane protein, regulates the balance of water in central nervous tissue[1] through osmotic and hydrostatic gradients[2]. In the optic nerve neuromyelitis spectrum disorder (NMOSD), AQP4-IgG serves as a biomarker, mainly in foot astrocyte processes within the brain, spinal cord, and optic nerve[3-5]. This triggers inflammation and localized edema, leading to neurological deficits.

NMOSD typically manifests as optic neuritis, myelitis, or post-rema area syndrome[6]. This case, marked by generalized motor impairment and the absence of typical signs of myelitis, suggests rarer presentations of NMOSD, such as narcolepsy[6], possibly due to hypothalamic damage that affects the hypocretin system that regulates wakefulness[9].

Studies explore the connection of AQP4 antibodies with placental expression during the second trimester of pregnancy[10], which can lead to placentitis, miscarriage, and pre-eclampsia[10,11]. Although intravenous immunoglobulin and corticosteroids treatment had no effect, concerns about teratogenicity and preterm birth led to termination of pregnancy.

Patients with NMOSD and tetraplegia/quadriplegia involving the peripheral nervous system (PNS) are rare. Other unidentified antibodies and humoral factors may contribute, with AQP4 expression in the transition zone of the CNS-PNS potentially targeted in radiculitis[12]. Plasma exchange showed some improvement in muscle strength after one cycle[12].

Conclusions

We presented a complex case of neuromyelitis ophia spectrum disorder (NMOSD) in a pregnant woman, highlighting the diagnostic challenges associated with this condition. In this case, the patient exhibited atypical symptoms, including features similar to narcolepsy, and faced difficulties in diagnosis due to factors related to pregnancy. Despite various treatments, including immune therapies and plasma exchange, the patient remained quadriplegic. The involvement of the peripheral nervous system in NMOSD is rare and poorly understood. More research is needed to elucidate the underlying mechanisms and treatment options for such cases.

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病例報告　112_C 101

毛髮糞石引起的急性腸阻塞-病例報告

A case of trichobezoar-related acute intestinal obstruction

陳建銘[1] 黃稚雯[1,2] 顏旭亨[1,2]
[1]彰化基督教醫院內科部 [2]彰化基督教醫院胃腸肝膽科

Introduction

Acute intestinal obstruction occurs when the normal flow of intraluminal contents is blocked. It can manifest as either functional or mechanical in nature. Functional obstruction, also known as ileus, is characterized by intestinal dysmotility with a radiologic appearance of obstruction in the absence of any mechanical blockage. Mechanical obstruction results from intraluminal, intramural, or extraluminal mechanical compression. An obstruction due to bezoars is relatively rare. Herein, we report a case of trichobezoar-related acute intestinal obstruction.

Case Presentation

A 13-year-old girl presented to the emergency department of another hospital with nonbilious emesis and abdominal pain for two days. Under the impression of acute intestinal obstruction, she was admitted to the hospital for conservative treatment. However, nonbilious emesis increased in frequency, and abdominal pain worsened. An abdominal computed tomography (CT) was performed and revealed small bowel dilatation with a transition point (Figure 1). Thus, she was transferred to our hospital for surgical intervention.

On examination, her vital signs were stable, and a physical examination showed abdominal distention with tenderness. Laboratory studies indicated leukocytosis(white blood cell count was 15600/uL, with 92.7 percent neutrophils),normal renal and liver function, Na:125 mmol/L, K:4.1 mmol/L, procalcitonin 0.04 ng/mL, and lactate level 1.0 mmol/L. A laparoscopic enterolysis with bowel resection (wedge) was performed, revealing small bowel obstruction caused by a trichobezoar located at the jejuno-ileum (Figure 2).

Figure 1 Abdominal CT showed small bowel obstruction with a transition point (arrow)

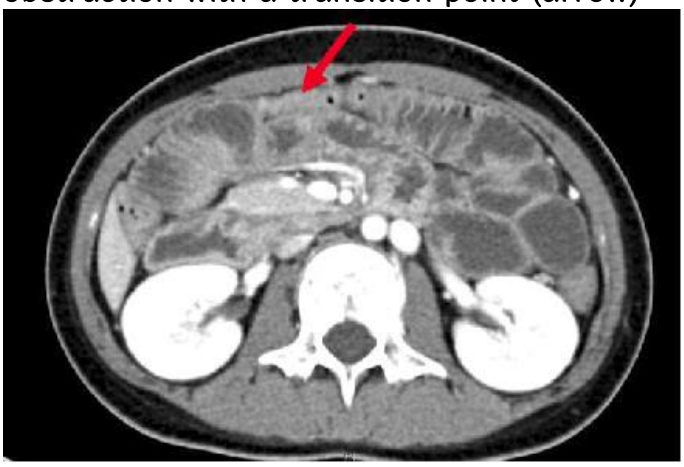
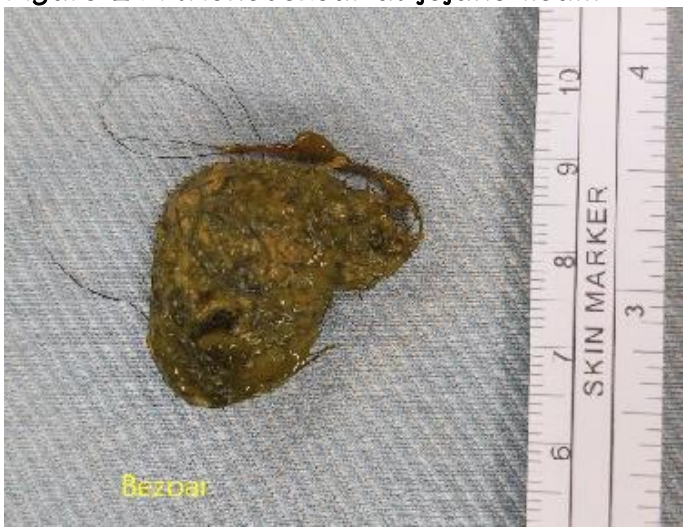


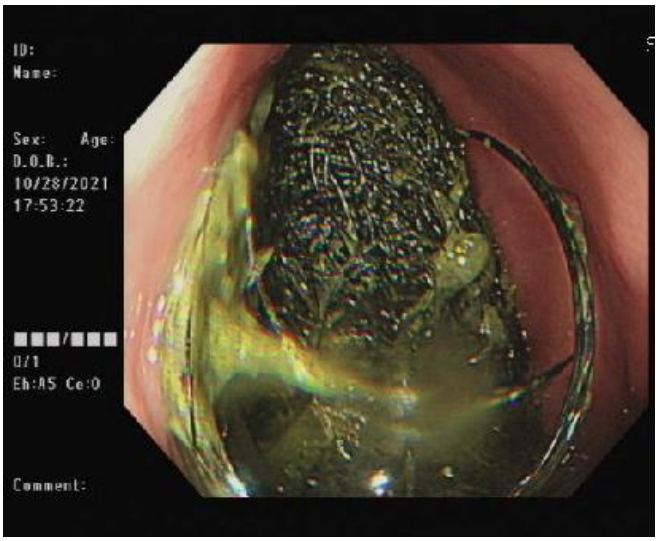
Figure 2 A trichobezoar at jejuno-ileum



Abdominal distention, vomiting, and obstipation persisted post surgery. Abdominal radiographs revealed gas distention of the small bowel.

A small bowel series indicated a filling defect at the stomach; suspect bezoar. An esophagogastroduodenoscopy (EGD) was performed and showed huge trichobezoars in stomach that could not be removed with forceps (Figure 3). Hence, a laparoscopic gastrotomy for the removal of the trichobezoars was performed. After the surgery, she had regular bowel movements, and her symptoms were alleviated. Eventually, she was discharged from our hospital.

Figure 3 Trichobezoars in stomach on EGD



Discussion

Functional obstruction (ileus) may result from abdominal surgery, metabolic or electrolyte abnormalities, the use of drugs such as opiates, or intestinal ischemia, intra-abdominal infections or inflammation, sepsis, and other possible causes. On the other hand, the most common etiology of mechanical obstruction is postoperative adhesion, followed by neoplasms and hernias[1]. Other contributing factors include inflammatory bowel disease, especially Crohn's disease, congenital abnormalities such as malrotation or atresia, traumatic hematoma formation, abscesses, and volvulus, bezoars, foreign bodies, gallstones, etc. Mechanical obstruction can be differentiated from functional obstruction through the patient's history and imaging studies. We should identify the risk factors mentioned above, as they may contribute to acute intestinal obstruction. Generally, abdominal imaging is necessary to confirm a diagnosis of acute intestinal obstruction and identify the patient who needs urgent surgical intervention. Abdominal plain films are an inexpensive diagnostic test to confirm the presence of intestinal obstruction. Abdominal CTs are valuable for determining the nature, precise location(transition point), and severity of the obstruction[2]. It is also helpful in detecting potential complications such as ischemia or perforation. In our case, bezoars are accumulations of indigestible materials that tend to gather in the gastrointestinal tract, most commonly within the stomach. Typically, trichobezoars are associated with psychiatric disorders, mental retardation, or pica. Abdominal CTs can be useful in detecting small bowel bezoars and assessing whether they might cause an obstruction based on their size, type, and location[3], although it may have limited sensitivity. The diagnosis of gastric bezoars is more definitive through EGD.

Conclusion

History-taking and abdominal imaging are essential for clinicians to confirm the diagnosis of acute intestinal obstruction and differentiate between mechanical bowel obstruction and functional bowel obstruction, allowing them to develop an appropriate treatment plan.

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病例報告　112_C 102

嚴重肺炎披衣菌感染造成的急性呼吸窘迫症候群-病例報告

A case of Chlamydial pneumonia with severe ARDS

陳建銘[1]　劉尊榮[1,2]
[1]彰化基督教醫院內科部　[2]彰化基督教醫院感染科

Introduction

Chlamydia pneumoniae (*C. pneumonia*) is a common cause of respiratory diseases in humans, including pneumonia and bronchitis. Typically, it is acquired within the community and tends to manifest as a mild infection. However, diagnosis of Chlamydial pneumonia is challenging due to the lack of standardized well-validated methods. Herein, we reported a case of Chlamydial pneumonia complicated with severe acute respiratory distress syndrome (ARDS), which was ultimately diagnosed through serological testing.

Case presentation

A 35-year-old man presented to the emergency department (ED) with fever and dyspnea for 3 days. On examination, a chest x-ray and a chest computed tomography (CT) revealed patchy consolidation over bilateral lungs, especially right lung (Figure 1). Initial tests, including a BioFire® FilmArray® Pneumonia (PN) Panel, Influenza A/B antigen, Covid-19 RNA test, blood and sputum cultures, all yielded negative results. His condition deteriorated rapidly to respiratory failure and was intubated at ED. Following admission, the pneumonia progressed to severe acute respiratory distress syndrome (ARDS) (Figure 2), necessitating the insertion of veno-venous extracorporeal membrane oxygenation (V-V ECMO).

On admission, his *C. pneumonia* IgM test was positive, while IgG was negative (measuring at 10.7 AU (analytical unit)/ml). We subsequently rechecked his *C. pneumonia* IgG levels 10 days later, which had become positive (58.6 AU/ml), indicating a 4-fold increase in IgG levels, confirming the diagnosis of *C. pneumonia*. Even 23 days after the initial test, the *C. pneumonia* IgG remained positive (49.6 AU/ml). He completed a 14-day course of intravenous clarithromycin therapy. ECMO was removed once his ARDS resolved, and he was successfully liberated from the ventilator (Figure 3). Ultimately, he was discharged from our hospital after a total of 43 days of hospitalization.

Discussion

Serology and PCR-based assays can be clinically used to diagnose *C. pneumonia* infection. Traditionally, the diagnosis of *C. pneumonia* relied on serology, with the gold standard serologic test being the microimmunofluorescence (MIF) test. To make this diagnosis, we typically obtain paired serum samples, separated by a 4-8 week interval. An acute *C. pneumonia* infection is indicated by IgM levels of >1:16 or a 4-fold increase in IgG levels. Serology is primarily employed for retrospective diagnosis, but it has some issues that can lead to reduced specificity. Firstly, *C. pneumonia* seroprevalence tends to increase with age. Secondly, the MIF method used to detect antibodies lacks standardization. Lastly, environmental Chlamydial species may interfere with serologic tests. In contrast, PCR amplification offers high sensitivity and specificity, along with rapid detection capabilities, although it is more expensive. PCR amplification has been approved by the US Food and Drug

Administration (FDA) for diagnosing *C. pneumonia* and is the preferred diagnostic method for *C. pneumonia* according to the Centers for Disease Control and Prevention (CDC).

Conclusion

PCR-based assays are the most recommended diagnostic tests for *C. pneumonia* infection. While serology tests can also be useful for retrospective diagnosis, they should be interpreted with caution.

病例報告　112_C 103

感染性主動脈瘤造成 Ortner 症候群之罕見病例

A rare case of Ortner syndrome caused by mycotic aneurysm

楊子祺[1] 劉尊榮[2]
[1]彰化基督教醫院內科部 [2]彰化基督教醫院感染科

Introduction

Ortner syndrome, also known as cardio-vocal syndrome, is a rare syndrome, presented with hoarseness due to external compression of the left recurrent laryngeal nerve by an enlarged cardiovascular structure. However, because of its unspecific clinical features, this disease is difficult to be diagnosed. We presented a case of Ortner syndrome caused by a mycotic aneurysm, an even rare etiology.

Case presentation

A 55-year-old male who was a smoker, with a history of hypertension and heart failure with reduced ejection fraction presented to the emergency department for sudden onset chest pain, hoarseness, and fever up to 39.1 degrees Celsius. The chest pain was sharp in nature and radiation to the back. The physical examination was unremarkable. Laboratory study revealed leukocytosis (WBC count: 10100/μl) with neutrophil predominance (80.2%), and elevated C-Reactive protein (13.24 mg/dl). A chest X-ray was arranged and showed a protruding mass over the aortic arch, which caused the trachea to deviate to the right. (figure. A) Computed tomography of the chest revealed an aortic rupture with aneurysm formation(size 47x31 mm) at the aortic isthmus portion and mediastinal node enlargement.(figure. B) After admission, blood culture yielded Salmonella enteritidis. Laryngoscopy was performed for dysphonia and found left vocal cord palsy(figure. C). The finding was compatible with the compression of the left recurrent pharyngeal nerve by a thoracic aortic aneurysm, which was known as Ortner's syndrome. Antibiotic treatment with Ceftriaxone was prescribed for Salmonella enteritidis bacteremia. The cardiovascular surgeons performed thoracic endovascular aortic repair with a bypass technique. The patient was discharged after a complete antibiotic treatment duration of three weeks. When the patient came back to the Infectious disease clinic for follow-up one week later, the symptom of hoarseness dramatically improved.

Discussion

Ortner syndrome is a rare disorder, also known as cardio-vocal syndrome, which results from any cardiac or vascular process that affects the recurrent laryngeal nerve and leads to vocal cord palsy. This syndrome was initially reported by Norbert Ortner in 1897 for left vocal cord palsy caused by mitral stenosis and expanded to other structural causes afterward[1]. Structural causes have been reported including aortic dissection[2], thoracic aortic aneurysm[3], left atrium enlargement[4], enlarged pulmonary artery due to pulmonary hypertension[5], or even congenital heart disease[6] and autoimmune vasculitis[7]. Left recurrent laryngeal nerve is particularly vulnerable to compression compared to the right due to its anatomical feature, the left vagus nerve gives off the left recurrent laryngeal nerve at the level of the transverse aortic arch, making it easy to be affected by cardiovascular lesion[8,9].

A meta-analysis of 256 patients with Ortner's syndrome showed that aortic pathology accounted for over half of such cases[10].In aortic causes, mycotic aneurysm accounted for around 40% of cases[11], but PubMed literature review showed only one case report documented mycotic aneurysm.

Treatment of Ortner syndrome mainly focuses on managing the structural disorder that caused recurrent laryngeal nerve compression. In aortic aneurysm, the most common cause of Ortner syndrome, the management mainly includes stent-graft repair of thoracic aneurysms and open surgery with aorta replacement. A case series published in 2022 once reported 4 cases with Ortner's syndrome due to thoracic aortic aneurysm underwent thoracic endovascular aortic repair from July 2014 to May 2020. The initial symptom in most patients was all hoarseness. The time from the onset of the symptoms to treatment ranges from 1 month to 2 years, and after a mean follow-up of 26.8 (8–77) months, the patient of 1 month experienced a full recovery of the voice, and the patient of 2 years had no improvement. The rest of 2 patients had partial improvement in hoarseness. These results indicate that for patients with Ortner's syndrome secondary to thoracic aortic aneurysm, early treatment may be beneficial in restoring vocal cord function[12].

Conclusion

We presented a rare case of Ortner syndrome caused by mycotic aneurysm. Ortner syndrome is a relatively rare disease, and it's also difficult to diagnose and recognize the underlying cause. If a patient had sudden onset hoarseness and without other associated symptoms, and the laryngoscopy examination indicated unilateral vocal cord palsy, Ortner syndrome may be listed as a differential diagnosis. According to the retrospective case series[13], early diagnosis leads to early treatment and that is, early and better recovery of the voice.

Figure A Chest X ray at ER, aortic arch protruding mass

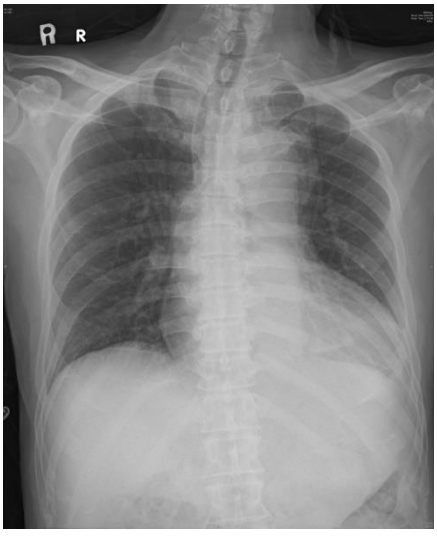


Figure B An aortic rupture with aneurysm formation(size 47x31 mm)

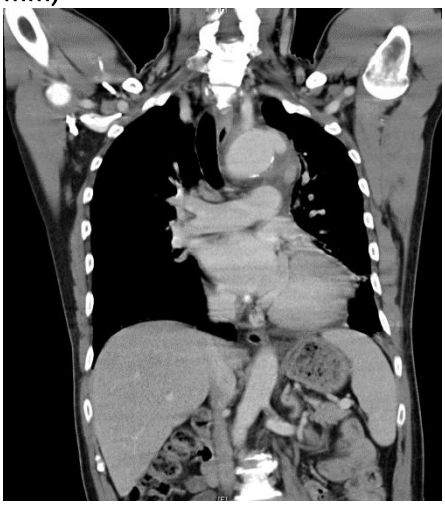
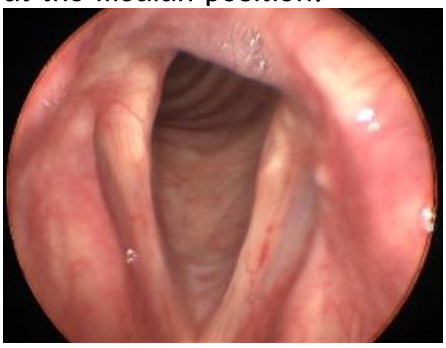


Figure C Laryngoscopy, revealed left vocal cord remain at the median position.



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病例報告　112_C 104

個案報告 — 因 tigecycline 引起的急性胰臟炎

A case report of tigecycline-induced acute pancreatitis

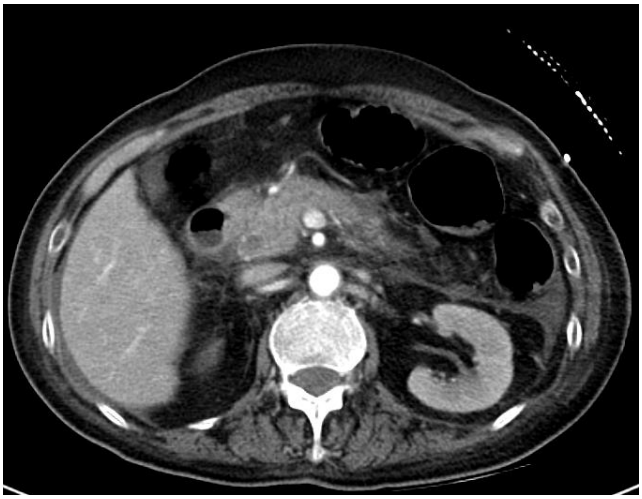
紀冠丞[1] 洪珮珊[2]
[1]彰化基督教醫院內科部 [2]彰化基督教醫院重症醫學科

Introduction

Tigecycline is a broad-spectrum antibiotic that is regarded as the last-line treatment option against multidrug-resistant (MDR) bacterial pathogens, including MRSA, VRE, ESBL, and CRAB. Due to these features, tigecycline is typically prescribed to critically ill patients. However, acute pancreatitis, a rare side effect caused by tigecycline, can worsen clinical conditions. We present a case of acute pancreatitis caused by tigecycline, which improved after discontinuing the antibiotic.

Case presentation

A 68-year-old female patient with a history of chronic hypercapnia and hypoxia respiratory failure, likely due to damage to her left lung caused by NTM infection, presented to the hospital. The patient had maintained clear consciousness but had been bedridden for an extended period and required ventilator support. She developed a new episode of fever accompanied by an increased amount of yellowish sputum. A diagnosis of nosocomial pneumonia was made, with sputum culture indicating the growth of carbapenem-resistant Acinetobacter baumannii. She was prescribed tigecycline 100mg every twelve hours as treatment. However, on the seventh day of the treatment course, the patient developed epigastric pain, along with nausea and vomiting containing food debris. The epigastric pain was characterized as dull and non-shifting, and there were no reports of chest tightness or cold sweating at that time. The physical examination revealed epigastric tenderness. Laboratory data showed a lipase level of 1948 U/L and an amylase level of 1253 U/L, while triglyceride and calcium levels were within the normal range. An abdominal CT scan with contrast revealed edematous changes in the pancreas with surrounding fat strands and peripancreatic fluid collection (Figure A). No biliary tract stones were found. We discontinued the use of tigecycline, and the patient's epigastric pain and nausea improved significantly. Follow-up lipase levels decreased to 370 U/L within two days.



Discussion

Tigecycline is a broad-spectrum antibiotic often considered the last line of defense against multi-drug-resistant bacterial pathogens. Common side effects include nausea, vomiting, and less common side effects such as elevated liver enzymes, acute pancreatitis, and

coagulopathy. Previously, a Phase 3 randomized double-blind trial was conducted in subjects with diabetic foot infections to compare the safety of tigecycline and ertapenem. In the randomized controlled trial, nausea, vomiting, and insomnia occurred significantly more often in the tigecycline group. Furthermore, a retrospective analysis of case reports of tigecycline-induced acute pancreatitis revealed that almost all patients experienced symptoms such as epigastric pain within two weeks, with a median onset time of 7 days. Tigecycline-induced pancreatitis can be resolved by promptly discontinuing the drug.

Conclusion

We should keep in mind that rare but severe adverse events can be related to the medication we are prescribed. Recognizing a drug-induced adverse event and discontinuing the medication immediately could improve the patient's outcome.

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病例報告　112_C 105

下腔靜脈感染性血栓性靜脈炎伴隨持續性菌血症之病例報告

Septic thrombophlebitis of the inferior vena cava with persistent bacteremia, case report

林芸[1] 葉菀婷[2] 施凱倫[2] 蘇培元[2] 陳昶華[3]
[1]彰化基督教醫院內科部 [2]彰化基督教醫院肝膽腸胃科 [3]彰化基督教醫院感染科

Introduction

Septic thrombophlebitis of the inferior vena cava(IVC) is a rare but serious disease. We present a case of IVC septic thrombophlebitis with persistent *Pseudomonas aeruginosa* and *Enterococcus gallinarum* bacteremia successfully treated by antibiotics combination therapy.

Case Presentation

A 78-year-old man with a medical history of hypertension, hyperlipidemia, hepatitis C virus infection with cirrhosis (Child-Turcotte-Pugh, classification B, Baseline Model for End-Stage Liver Disease (MELD) score 6), gall bladder stone with acute cholecystitis, status post laparoscopic cholecystectomy. Hepatocellular carcinoma was diagnosed in 2018, post ultrasound-guided Radiofrequency ablation (RFA). A recurrent tumor in S8 was detected 4 years later, in December 2022. Treatment with transarterial chemoembolization on January 9, 2023, and computerized tomography (CT)-guided RFA on February 8, 2023. Acute cholangitis developed and he underwent endoscopic retrograde cholangiopancreatography on February 13, 2023. However, there was recurrent chills and pain in the right upper abdomen. Patient came to our emergency department. Findings with fever and elevated biliary tract markers at our emergency department and he was admitted to the gastrointestinal ward for suspected hepatobiliary tract infection. Empirical treatment with piperacillin antibiotics. The results of the blood culture identified *Enterococcus avium*, *Enterococcus gallinarum*, and *Pseudomonas aeruginosa* (*PsA*). Antibiotics was changed to cefepime, combined with ampicillin, and subsequently to piperacillin-tazobactam. Blood cultures repeated at intervals of 3-5 days showed persistent bacteremia. A transthoracic echocardiogram did not show obvious vegetations. The subsequent abdominal ultrasound and abdominal contrast CT indicated the formation of a focal abscess at the previous RFA site in S8, extending to the inferior vena cava (IVC), resulting in the formation of thrombus (Fig. A, Fig. B). Anticoagulation therapy with low molecular weight heparin was initiated, followed by oral anticoagulant therapy. Over 3 weeks of medical treatment, refractory *Enterococcus gallinarum* and *PsA* bacteremia persisted. Antibiotics were modified to a combination therapy of ampicillin and gentamicin. The gallium scan did not find definitive gallium-avid lesions. Fosfomycin was added as a third antibiotic. Under this three-drug combination therapy, blood cultures eventually turned negative. An abdominal follow-up CT scan was performed to assess therapeutic effectiveness, revealing a resolving abscess and thrombus in the IVC (Fig. C). On day 64 of hospitalization, blood cultures were free from microbials four consecutive times. Antibiotics were discontinued or switched to oral antibiotics one after another, eventually with ciprofloxacin plus amoxicillin. The patient was closely monitored under oral antibiotics and discharged in a relatively stable condition.

Figure A

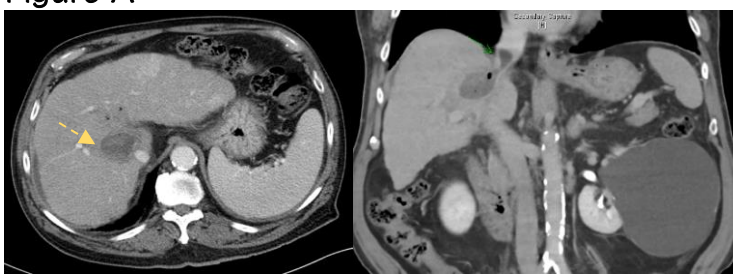


Figure B

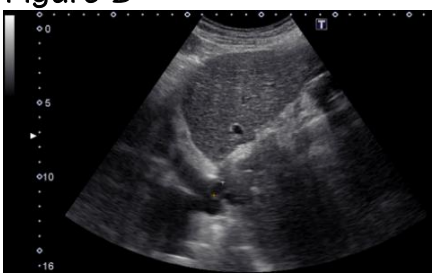
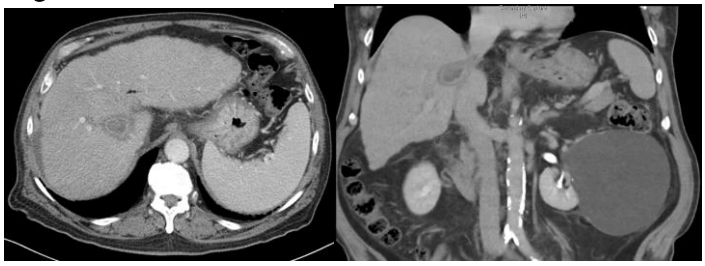


Figure C



Discussion

Infection and associated inflammation are potent inducers of thrombosis and thrombus formation. Platelets are activated by inflammation.[2-5] Vascular infections, including infective endocarditis (IE), infectious arteritis, and venous septic thrombophlebitis(STP), should be considered when pathogens persist in the bloodstream despite adequate antimicrobial therapy.[1] STP in deep vein systems, such as STP of the portal vein (pylephlebitis), pelvic veins, and the vena cava, is rare and difficult to detect due to its nonspecific presentations[6,7]. However, it is a serious condition that causes significant morbidity and mortality, especially when IVC is involved. Possible complications of septic thrombus include septic emboli originating from the infected thrombus.[11] STP of the IVC mostly occurs primarily as a complication of prolonged central venous catheterization(CVC)[8]. In the case of our patient, the IVC thrombus was not related to CVC, but rather due to the infection and inflammation processes that breached the wall of the IVC. STP treatment requires prolonged antibiotic use for at least 4-6 weeks[9]. Anticoagulants may be used in pylephlebitis to prevent thrombus extension, ischemia, and to increase the rates of recanalization[7]. However, the role of systemic anticoagulants in STP of the IVC has not been firmly established. In refractory cases with persistent fever, repeated bacteremia, and readmission, more invasive procedures may be considered[8,10]. In our patient, surgery was not considered a viable option for the site of infection. On admission day 25, a third antibiotic was added, ultimately terminating the bacteremia. The patient continues to follow up in our outpatient department and has remained free from bacteremia for four months.

Conclusions

STP of the IVC is a rare but serious and life-threatening condition. Infection is most commonly introduced through breaks in the skin, but in rarer cases, it can be related to invasion from adjacent primary non-vascular infections. Standard treatment involves prolonged antibiotic use, and many physicians also include systemic anticoagulants. Invasive interventions should be considered if there is no response to the above-mentioned management, but the location of the infection can increase the complexity of the approach.

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病例報告　112_C 106

瀰漫性大型 B 細胞淋巴瘤患者的多病灶侵襲性麴菌感染涉及眼、肺和中樞神經系統：病例報告

Multifocal Invasive Aspergillosis with Ocular, Pulmonary, and Central Nervous System Involvement in a Patient with Diffuse Large B-Cell Lymphoma: A Case Report

王祥瑋[1]　劉尊榮[2]
[1]彰化基督教醫院內科部　[2]彰化基督教醫院感染科

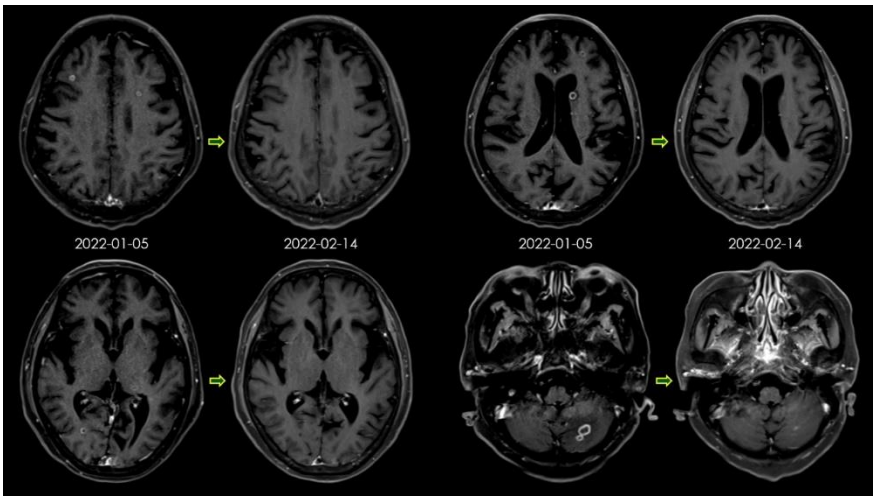
Introduction

Invasive aspergillosis is a life-threatening fungal infection, predominantly affecting immunocompromised individuals. It typically presents as pulmonary involvement; however, dissemination to other organs, including the eye and central nervous system, is uncommon but carries a high mortality rate. We report a case of multifocal invasive aspergillosis in a patient with a history of diffuse large B cell lymphoma, involving the eye, lung, and brain. We discuss the diagnostic challenges and successful management of this complex presentation.

Case presentation

A 71-year-old female with a history of diffuse large B cell lymphoma presented with sudden-onset blurred vision in her left eye after completing two cycles of R-CHOP chemotherapy. Due to her immunocompromised status, fungal endophthalmitis was suspected based on B-scan findings. Immediate anterior chamber irrigation with microincision vitrectomy was performed, but vitreous culture yielded no growth. Therefore, we contacted with the ophthalmologist to obtain cytological analysis of left eye, but procuring the required cytological samples proved to be challenging. Nevertheless, serum testing for Aspergillus galactomannan antigen was positive (1.9), suggesting a potential systemic fungal infection. Additionally, the patient experienced hemoptysis, and chest imaging revealed progressive airspace opacities in the left lower lung field, raising concern for angioinvasive pulmonary aspergillosis with hemorrhage. A subsequent chest CT scan confirmed consolidation in the left lingular lobe of the lung. Consultation with an otolaryngologist ruled out mucormycosis or fungal infection via fiberscope examination.

Figure A Nearly total complete remission of previously multiple thin-wall, ring-enhancing subcortical lesions, although a tiny enhancing spot in the left cerebellum persists.



Further evaluation with orbital MRI demonstrated multiple thin-walled, ring-enhancing nodular lesions in the bilateral cerebrum, left cerebellar white matter, right basal ganglion, and left thalamus, accompanied by mild peritumoral white matter edema. These findings raised concerns about brain abscess or B-cell lymphoma metastasis. Tissue biopsy was

recommended for definitive diagnosis, but due to the small and deep-seated nature of the lesions, it was considered high risk. Subsequently, cerebrospinal fluid (CSF) analysis was performed, revealing elevated Aspergillus galactomannan antigen levels (>6.7), thus confirming CNS involvement.
To manage invasive aspergillosis, the patient was initiated on voriconazole therapy for a duration of six months. Subsequent follow-up assessments demonstrated a gradual decline in serum aspergillus galactomannan Ag levels to within the normal range. One month later, a follow-up brain MRI (Figure A) revealed nearly complete remission of the previously observed multiple cerebral lesions.

Discussion

The presented case illustrates the rare occurrence of multifocal invasive aspergillosis involving the eye, lung, and CNS in an immunocompromised patient. The differential diagnosis for such a presentation includes other opportunistic fungal infections, malignancies, and non-infectious causes.
Ocular involvement in invasive aspergillosis is infrequent but may result from hematogenous dissemination or direct extension from adjacent structures. In our case, fungal endophthalmitis was suspected due to the patient's immunocompromised status and was confirmed by positive serum and CSF aspergillus galactomannan antigen.
Pulmonary aspergillosis often precedes dissemination to other organs. The angioinvasive nature of the infection in the lung can lead to hemorrhage and patchy airspace opacities, as seen in our patient. Prompt recognition and treatment of pulmonary involvement are crucial to prevent dissemination.
CNS involvement in invasive aspergillosis is associated with a high mortality rate. In our case, the diagnosis was established through CSF analysis and characteristic MRI findings. Although tissue biopsy is the gold standard for diagnosis, it may be challenging in cases with deep-seated lesions, as in our patient.
Treatment of invasive aspergillosis involves prompt initiation of antifungal therapy, primarily with voriconazole, which has demonstrated efficacy in CNS aspergillosis. Our patient responded well to voriconazole therapy, as evidenced by the gradual decline in serum aspergillus galactomannan antigen levels and near-complete remission of cerebral lesions on follow-up MRI.

Conclusion

This case highlights the importance of considering invasive fungal infections, particularly aspergillosis, in immunocompromised patients with hematological malignancies. Prompt diagnosis and initiation of appropriate antifungal therapy, such as voriconazole, can lead to favorable outcomes, even in cases with disseminated CNS involvement. Clinicians should maintain a high index of suspicion for invasive fungal infections in immunocompromised individuals to facilitate early intervention and optimize patient outcomes.

病例報告　112_C 107

以脊髓痨表現的神經性梅毒罕見案例

A rare case of neurosyphilis presenting with tabes dorsalis

楊午騰[1] 劉尊榮[2]
[1] 彰化基督教醫院內科部 [2]彰化基督教醫院內科部感染科

Introduction

Tabes dorsalis is a rare presentation of late-stage neurosyphilis in which Treponema pallidum involves the CNS system which causes the nerves degeneration in the dorsal columns of the spinal cord. Regarding that there would be routine to screen syphilis while the diagnosis of HIV and it would present early symptoms of syphilis of such as oral and genital painless ulcers called chancre or .Even not frequently, the patient could experience asymptomatic early neurosyphilis symptoms, almost syphilis infection can be recognized by history of coinfection with HIV and symptoms of syphilis and then the infection could be treated by penicillin G treatment. However, this patient is never occurred syphilis related symptoms like.

Case presentation

This 42-year-old man with no past history was admitted due to progressive unsteadily gait for 2 years.

The patient had been in his usual state of health until approximately 2 years ago in 2020. Initially, he experienced standing unsteadily when he held up his scooter, and then walked unsteadily when took about 20 Kg project during work, but he didn't not search for medical help due to consideration of fatigue. But the symptoms were not relieved and proceeding like felt difficulty when went up and more severely went down the stairs, unable to stand when closing his eyes which allowed him only to take a shower and wash his face with sit position or hold the wall and handrail. Sometimes lightning sensation went through his arms and legs was also noted. Thus, he visited a neurologist for help in July of 2021, where a neurological examination showed limbs' muscle power was full, the finger-nose-finger test showed no dysmetria, Romberg test was positive and DTR decreased at lower limbs. Then nerve conduction velocity examination was arranged and showed L-spine myelopathy and suspected posterior column lesion, but the subsequent L-MRI revealed no obvious lesion over L-spine.

However, after following up for a half of a year, symptoms were not improved, so he visited our hospital's rheumatologist with the same complaint. For suspect autoimmune myositis

autoimmune titer was examined but almost all results reported negative finding except ANA with equivocal level as 1:80, cryoglobulin and Anti-dsDNA positive. So further titer including HIV test was arranged and reported positive. Thus, he was transferred to our infectious department. Combination with HIV infection and unsteady gait, under impression of neurosyphilis presentation, neurological examinations were performed and showed both pupil without constriction when exposed to light but constrict when finger being close to his eyes, which is compatible with presentations of Argyll-Robertson pupil. Therefore, he was admitted for advance investigation.

During the hospitalization, besides the above finding, a detailed neurological examination presented a wide base gait and positive Romberg test. Formal lumbar puncture performed and proved VRDL titer with reactive as 1:2, so he was treated with penicillin G 3MIU Q4H, and following lumbar puncture after 10 days later reported negative VRDL. However, the Argyll-Robertson pupil still existed. Then he was discharged. Surprisingly, in the subsequent following, the unsteady gait seems to be improved.

Discussion

We may consider that neurosyphilis may be the late presentation of syphilis involving CNS system. However, actually, they may be presented with neurosyphilis in any stage of syphilis stage, not limited to late syphilis. Detailed history taking especially sexual history and having doubts of atypical neurological presentation may help with recognition of this ancient and rare disease.

Conclusion

During this era of penicillin existing, syphilis is easily to be treated. Our patient has trivially gotten neurosyphilis without symptoms of any syphilis infection. And due to its presentation limited to pupil and gait, it may be confused and focus on other spinal neuropathy. Fortunately he was diagnosed and has significant improvement of gait, though Argyll Robertson pupil would remain lifelong.

病例報告　112_C 108

惡性肝臟血管肌肉脂肪瘤:一個病例報告

Malignant hepatic angiomyolipoma: A case report

葉菀婷[1] 施凱倫[1] 顏旭亨[1,2]
[1]彰化基督教醫院消化內科 [2]中興大學醫學系

Abstract

Angiomyolipoma (AML) is usually a benign mesenchymal neoplasm which commonly located in the kidney, second in liver. It occurs mostly in middle-aged woman and accompanied with tuberous sclerosis complex (TSC). First reported by Ishak et at. in 1976, today, this rare tumor belongs to the family of perivascular epithelioid cell tumors (PEComas) and typically composed with variable proportions of blood vessels, smooth muscle cells and adipose tissue. In pathology, it shows strong immunoreactivity for HMB-45 and actin. It may be misdiagnosed as other diseases easily (e.g. hepatic cell carcinoma, IgG-4 disease) if it presents aggressive behavior like large size(>5cm), rapidly growth rate, atypical liver biopsy result, and multiple organs involvement. We present a rare case of a 64-year-old man with chief complain of abdominal pain for months. He had a history of renal AML 2 years ago and performed with right radical nephrectomy due to tumor rupture. There were not any liver tumors seen at abdominal computed tomography (CT) then. However, two years later, the abdominal CT showed multiple liver mass and the largest one was 17.8 cm in the S4. The liver biopsy result revealed the diagnosis of hepatic AML (HAML). After multidisciplinary discussion, the patient refused the hepatectomy, and only accepted conservative treatment like transcatheter arterial chemoembolization (TACE). Unfortunately, the complication of active bleeding of gastroduodenal artery happened after TACE. The patient then expired due to hypovolemic shock and multiple organ failure. Since 2000, there are only 17 cases of malignant HAML have been reported. They display more aggressive behavior with high recurrence and metastasis rate. The overall mortality rate associated with typical HAML was 0.8%, but the mortality rate of malignant HAML seems much higher than average. The further researchs of histological or radiological characteristics to predict this type of tumor is necessary.

病例報告　112_C 109

手術切除後克羅恩病的治療 – 病例報告

Management of Crohn disease after surgical resection - case report

吳京衡[1] 吳東龍[2]
[1]彰化基督教醫院內科部 [2]彰化基督教醫院胃腸肝膽科

Introduction

Crohn's disease (CD) is a type of inflammatory bowel disease that can invade anywhere in the digestive tract. About 2–5% of Asian patients have a family history of Crohn's disease, and it usually occurs between the ages of 20 and 39. According to statistics, the prevalence rate of CD in Taiwan increased from approximately 0.6 per 100,000 people in 2001 to approximately 3.9 per 100,000 people in 2015.

Case presentation

The patient is a 29-year-old male manual laborer with no significant medical history and no history of tobacco, alcohol, or betel nut use. He was admitted to the hospital due to persistent symptoms of fever, abdominal pain, nausea, and vomiting that had been ongoing for several days. Upon evaluation, he was diagnosed with Crohn's disease, which necessitated surgical intervention. The surgical procedure involved enterolysis, a small bowel resection (removal of 50cm of the small intestine), and side-to-side ileo-colic anastomosis (to T-colon) due to the presence of intestinal stricture, adhesions, and perforation with interloop abscess. After the surgery, it was determined that the patient was at high risk for disease recurrence based on specific criteria, including being younger than 30 years old, having perforating or long segment inflammatory disease, and a shorter duration of disease prior to surgery. The combination therapy of mesalazine, azaththioprine (discontinued after 4 months due to anemia and decreased WBC count) and prednisolone were initially used, followed by the addition of biologic agent: vedolizumab. The symptoms of abdominal pain and diarrhea did improve in the early stage after treatment, but recurrence of intestinal stenosis began to occur about more than 7 months after the operation. To address the recurrent intestinal stenosis, the patient underwent deep enteroscopy with balloon dilatation on three separate occasions(at 7, 8, and 9 months after surgery). However, due to the persistent nature of the stenosis, a decision was made to switch to a different biologic agent, Ustekinumab. Since transitioning to Ustekinumab, the patient's condition has remained stable, and he continues to receive regular follow-up care in the outpatient clinic.

Discussion

While surgery often leads to clinical remission of CD, most patients ultimately relapse. The risk and severity of recurrence after surgical resection is variable and needs to be balanced with the potential risk of preventative medical therapy. In 2021, the International Organization for the Study of Inflammatory Bowel Disease (IOIBD) focuses on various examinations of Crohn's disease, such as clinical, endoscopic, biomarker, imaging and histopathology, etc. Recommendations for short-, medium-, and long-term treatment goals are based on evidence and expert consensus. Clinical symptom relief was selected by patients as the most important short-term treatment goal. In addition to clinical relief, the mid-term

goal also included biochemical indicators: CRP and fecal calprotectin. The ultimate treatment goal is complete deep healing (i.e., clinical remission combined with endoscopic healing, histological healing, and transmural healing). However, currently available treatments are not sufficient to achieve this goal for most patients, and research is still needed to confirm the risks and costs. balance between benefits.

Conclusion

For many years, the primary approach to treating patients with Crohn's disease in Taiwan has relied on steroids, immunomodulators, and anti-inflammatory medications like 5-ASA. However, managing moderate to severe cases sometimes proved challenging and led to an increased incidence of surgeries and hospitalizations for patients. In recent years, Taiwan has gradually introduced a range of biological agents, including anti-TNF, anti-integrin, and anti-IL12/IL23 therapies, for the treatment of patients with moderate and severe Crohn's disease. While this expanded array of treatment options has made the decision-making process more complex for healthcare providers, it has also significantly enhanced the overall quality of medical care available to patients, providing them with a more comprehensive and holistic approach to managing their condition.

病例報告　112_C 110

Infective Endocarditis Presenting as Heart Failure with Lactic Acidosis in a Patient with Bicuspid Valve and a History of Permanent Pacemaker Implantation

方懿君[1] 李禎元[2]
佛教慈濟醫療財團法人大林慈濟醫院[1]內科部 [2]心臟內科

Introduction

A 74-year-old male with bicuspid valve with severe aortic regurgitation (AR) and sick sinus syndrome (SSS) status post-pacemaker implantation. He presented with heart failure and lactic acidosis, later diagnosed with infective endocarditis.

Case presentation

The 74-year-old man with a history of Af, bicuspid valve with severe AR, SSS status post-pacemaker implantation, Parkinson's disease. He presented to the emergency department (ED) due to shortness of breath for 2 days.

The patient's clinical presentation began with upper respiratory symptoms and purulent sputum production, accompanied by a sore throat. He initially sought care from a local medical doctor with symptom-relief medications. However, his condition deteriorated rapidly, leading to progressive dyspnea, orthopnea, chest tightness, and reduced oral intake. There were absence of fever, chills, abdominal discomfort, or gastrointestinal symptoms.

Upon ED visit, vital signs revealed a pulse rate of 75 beats per minute, respiratory rate of 28 breaths per minute, blood pressure of 127/60 mmHg, and oxygen saturation (SpO2) of 85%.

Chest X-ray demonstrated presence of cardiomegaly and increased lung markings. Elevated NT-pro BNP > 35,000.0 pg/mL, renal function was compromised, can be correlated with suspected heart failure with acute decompensation. However, arterial blood gas (ABG) showed unexplained metabolic acidosis (pH of 7.275, pCO2 of 21.7 mmHg, pO2 of 161.9 mmHg , bicarbonate (HCO3) of 9.8 mmol/L , and oxygen saturation (O2 sat.) of 99%) with elevated lactate level (5.3 mmol/L). The complete blood count (CBC) revealed leukocytosis with bandemia. POCUS at ED reported bilateral moderate pleural effusion, and engorged IVC. Right thoracentesis was performed, yielding transudative pleural effusion. The patient then received BiPAP support with impending respiratory failure and admitted to ICU for further care.

Just on the night of admission, the patient's condition deteriorated with progressive tachypnea and an increasing working load of breathing. ABG at that time revealed mixed metabolic acidosis and respiratory alkalosis (pH of 7.61, pCO2 of 12.7 mmHg, pO2 of 113.6 mmHg, bicarbonate (HCO3) of 12.5 mmol/L, and oxygen saturation (O2 sat. of 99.1% under BiPAP support) still elevated lactate level (4.4 mmol/L). Bedside echocardiography revealed massive vegetations on both the mitral and aortic valves. Intubation was done for impending respiratory failure.

A review of the patient's medical history revealed a previous ER visit for diarrhea and weakness, which was initially suspected to be AGE. However, blood culture results during that visit later yielded resistance strain of Streptococcus salivarius (Penicillin MIC = 0.25 and

0.5), infective endocarditis was impressed. Consulting infectious disease, empiric ceftriaxone 2 gm Q12H was initiated.
A diagnosis of infective endocarditis with valvular vegetations was confirmed via transesophageal echocardiography (TEE). Bicuspid aortic valve and valve prolapse resulting severe AR, one fluttering vegetation, measured 0.5cm*2.3cm in size; suspect mital valve A3 prolapse or vegetation with valve perforation, complicated with severe eccentric MR, total two MR jets.
On the second day of admission, the patient encountered a shock episode accompanied by AfRVR. Bedside sonography revealed worsening mitral regurgitation (MR), prompting consultation with the cardiovascular surgery team for potential ECMO and IAPB support and consideration of emergent surgery. The patient's condition stabilized after conversion of AfRVR back to sinus rhythm.
Given the critical condition with poor hemodynamic tolerance, the patient underwent aortic valve replacement (AVR) and mitral valve replacement (MVR) on the fourth day of admission. The aortic valve exhibited severe pathology with bicuspid morphology and extensive leaflet damage; the aortic annulus exhibited perianular abscess formation. Extensive vegetations were found on the anterior leaflet (A3) of the mitral valve.
The patient was transferred to the SICU for postoperative care. However, multiple organ failure with persisted metabolic acidosis noted, a CT scan was performed, revealing poor perfusion of the liver, spleen, and bowel, suspicions of a focal occlusion in the SMA, possibly related to vegetations.
On postoperative day 3, a sudden episode of PEA occurred. Immediate cardiopulmonary resuscitation was initiated; given the critical condition and poor prognosis, after explanation and discussion with the family, the patient was discharged with critical status on the same evening.

Discussion

Infective endocarditis is diagnosed based on pathologic criteria and clinical findings. Our patient met the 2023 modified Duke ISCVID criteria for definite IE, with two major clinical criteria (imaging and surgical major criteria). In Taiwan, IE incidence varies by age, ranging from 3.8 per 100,000 in patients <30 years to 33 per 100,000 in those ≥80 years. Fever is a common early symptom (95% prevalence), but its absence due to factors like immunosuppression or antipyretic use can complicate diagnosis. IE risk factors include age >60, male sex, intravenous drug use, dental issues, structural heart disease, and cardiac implantable electronic devices (CIEDs). Our patient had a bicuspid aortic valve (BAV), which increased his IE risk. BAV patients are at 12-fold higher risk of IE than the general population, with an incidence of 48 per 10,000 patients per year. In Taiwan, IE's mean in-hospital mortality rate is 18%, with factors like age, male gender, diabetes, malignancy, and more associated with increased mortality. For penicillin-resistant oral streptococci and S. gallolyticus, current ESC guideline suggest ceftriaxone combined treatment with aminoglycosides at least for 2 weeks; however, the patient's altered renal function led to ceftriaxone monotherapy. New-onset heart failure is a common IE presentation, and worsening pre-existing HF can also occur. HF in IE is linked to poor in-hospital and 1-year survival, with surgery offering the best chance for improvement. Urgent or emergency surgery is necessary for certain cases, such as patients with NYHA class IV HF, pulmonary edema, or cardiogenic shock. Other surgical indications include uncontrolled infection and prevention

of septic embolization, particularly to the CNS. Urgent surgery is needed within 3–5 days in some cases, while others require emergency surgery within 24 hours. Our patient underwent urgent surgery due to new-onset HF, poor hemodynamics tolerance, vegetation >1cm, with a high risk of septic emboli.

Conclusion

The diagnosis and management of IE, a condition associated with high mortality, require careful attention. Patients with a bicuspid valve is considered at increased risk of IE. Additionally, determining the optimal timing for surgical intervention in IE is crucial.

病例報告　112_C 111

一個與胰膽管連接異常相關的膽囊癌個案

A case of gallbladder cancer association with pancreaticobiliary maljunction (PBM)

李哲瑋[1]　曾志偉[1,2]，柯秉宏[1,2]
佛教慈濟醫療財團法人大林慈濟醫院[1]內科部　[2]腸胃內科

Introduction

Pancreaticobiliary maljunction (PBM) is a congenital malformation characterized by the union of the pancreatic and bile ducts outside the duodenal wall. This anatomical anomaly predisposes individuals to higher rates of biliary tract cancer and pancreatitis. Early flow-diversion surgery) is recommended before the onset of malignant changes. Here, we presented a PBM case with a gallbladder cancer found on incidental laparoscopic cholecystectomy (LC).

Case presentation

This 65-year-old female patient with a history of hypertension and recurrent choledocholithiasis underwent repeated endoscopic retrograde cholangiopancreatography (ERCP) procedures for endoscopic retrograde biliary drainage. CT imaging revealed a dilated common bile duct and intrahepatic duct (Figure 1). PBM was diagnosed based on the identification of a long common channel, measuring approximately 17 mm, as observed on magnetic resonance cholangiopancreatography (MRCP, Figure 2). This diagnosis was further confirmed by ERCP (Figure 3). Due to chronic cholecystitis and recurrent cholangitis, a LC was performed. Pathological examination revealed adenocarcinoma that had invaded the perimuscular connective tissue on the peritoneal side, with a tumor staging of pT2a (AJCC 8). A subsequent surgical procedure involving partial hepatectomy and regional lymph node dissection was carried out. No significant pathological changes were found and the patient was staged as pT2N0M0, stage IIa. Given the elevated risk of biliary tract cancer associated with PBM, a prophylactic surgical procedure involving extrahepatic bile duct resection and bilioenteric anastomosis was strongly recommended. However, the patient declined the procedure and opted for regular follow-ups at our outpatient department.

Fig1 abdomen Liver CT:
biliary dilatation of CBD and IHD

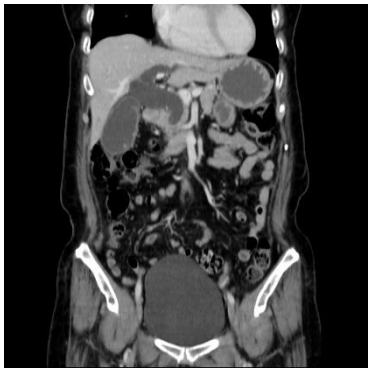


Fig2 ERCP:
a long common channel under fluoroscopy

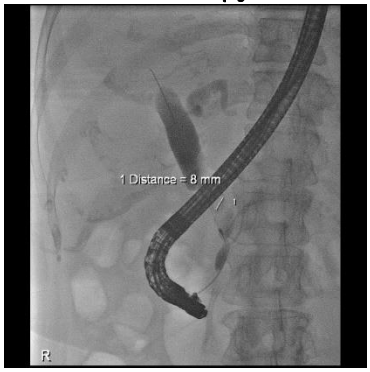
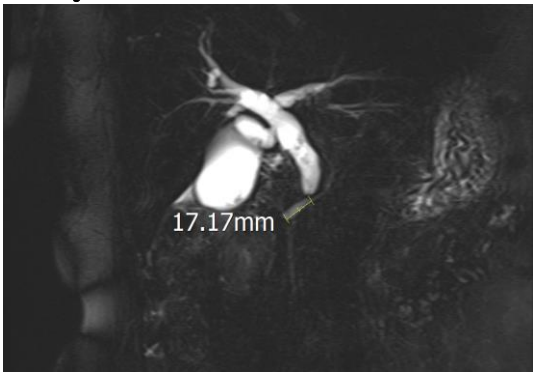


Fig3 MRCP:
long common channel about 17mm with biliary dilatation



Discussion

Pancreaticobiliary maljunction (PBM) is a congenital malformation characterized by the union of the pancreatic and bile ducts outside the duodenal wall. In PBM, a common channel longer than 6 mm results in the reciprocal reflux of pancreatic juices and bile. Elevated fluid pressure in the pancreatic duct often leads to reflux into the biliary tract, causing persistent damage to the biliary epithelium. This elevates the risk of biliary tract carcinogenesis. Activated proteolytic enzymes and phospholipase A2 from the pancreas contribute to the formation of cytotoxic substances such as lysolecithin, exacerbating mucosal damage and promoting cancer development. The leading mechanism in PBM-associated biliary cancer appears to be the hyperplasia-dysplasia-carcinoma sequence, distinct from the adenoma-carcinoma and de-novo carcinogenesis mechanisms found in non-PBM patients.

A Japanese survey found a high cancer rate (21.6%) among adult PBM patients with biliary dilation. Specifically, 6.9% had bile duct cancer, 13.4% had gallbladder cancer, and around 1% had dual cancers. Given the elevated risk, immediate prophylactic surgery, often cholecystectomy and extrahepatic bile duct resection ('flow-diversion surgery'), is advised upon PBM diagnosis. If surgery is declined, patients should be made aware of the increased cancer risk and closely monitored.

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病例報告　112_C 112

雙心室血栓：肺癌患者中罕見的發現

Biventricular thrombi: A rare finding in a lung cancer patient

張愷杰[1] 賴俊良[2] 李易達[3]
[1]大林慈濟醫院內科部 [2]大林慈濟醫院胸腔內科 [3]大林慈濟醫院心臟內科

Introduction

Thrombus is the most common intracardiac non-neoplastic mass, with isolated thrombi commonly affecting the right or left ventricle. Concurrent biventricular thrombi formation is a rare finding. We present a case of concurrent biventricular thrombi in a patient with stage IV lung cancer.

Case Presentation

A 47-year-old woman never smoker presented to our hospital with progressive shortness of breath for the past 3 days. A month ago, she was diagnosed with adenocarcinoma of the lung, right upper lobe, cT4N2M1c (bone and pleural metastases), stage IVb. Next generation sequencing of tumor tissue identified MET(13)-MET(15) exon 14 skipping. She received symptomatic therapy while waiting for the approval of NHI-reimbursed tyrosine kinase inhibitor Tepotinib. She started noticing worsening exertional dyspnea and decreased urine output 3 days prior to this hospital visit. Evaluation at the emergency department revealed "water bottle" sign and right pleural effusion. Transthoracic echocardiography (TTE) exam was significant for massive pericardial effusion with impending cardiac tamponade. Her dyspnea improved with prompt insertion of pigtail drain tube into the pericardial sac. During hospitalization, a chest CT scan incidentally identified biventricular thrombi and later confirmed with TTE. She initially received concurrent enoxaparin and warfarin therapy, and later switched to rivaroxaban at the time of discharge. A follow up TTE exam a month later revealed no residual thrombi in the ventricles.

Discussion

Biventricular thrombi are rare and there are only a handful of case reports available. It often occurs in patients with hypercoagulable states, such as those with antiphospholipid syndrome, protein C and S deficiency, hypereosinophilic syndrome, cardiomyopathies, and various infections (myocarditis, HIV, COVID-19). While lung cancer is associated with hypercoagulability, it is unknown if the MET(13)-MET(15) exon 14 skipping resulted in higher risk of thrombosis than other mutations. The sensitivity of thrombus detection by TTE is low but can be increased with contrast use. While cardiac MRI remained the gold standard for detecting intracardiac thrombus, CT angiography can yield more information besides intracardiac thrombus. These patients are at risk of pulmonary embolism and stroke, hence the need for timely management. Warfarin is the mainstay treatment for ventricular thrombi, while rivaroxaban or apixaban can be an alternative.

Conclusion

As biventricular thrombi are rare, treatment guidelines remained elusive. While oral vitamin K antagonist is the first-line medicine to treat the thrombi, our patient remained thrombi-free under rivaroxaban use.

病例報告　112_C 113

典型表現的 Mirizzi 症候群和意外發現的 Luschka 膽管

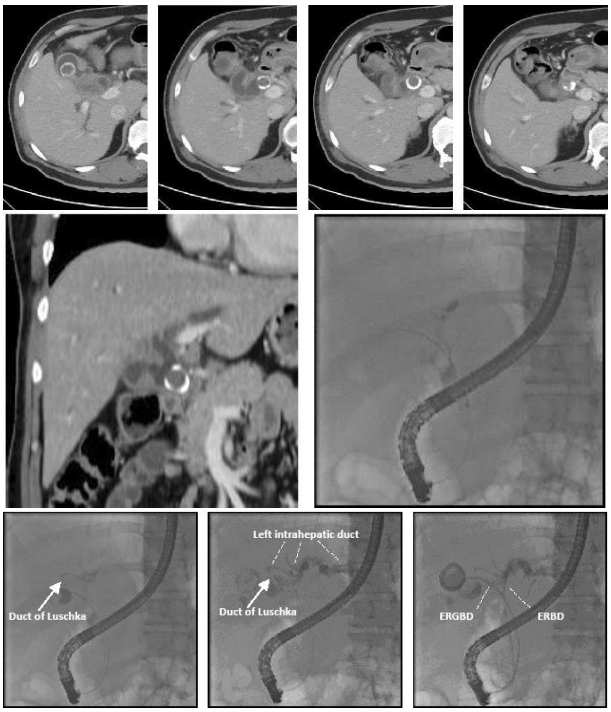
A Typical Presentation of Mirizzi Syndrome and an Incidental Finding of the Duct of Luschka

王耀新 [1]　柯秉宏 [1,2]
[1] 大林慈濟醫院內科部　[2] 大林慈濟醫院肝膽腸胃科

Introduction

Mirizzi Syndrome is a rare complication of cholelithiasis, which is defined as common hepatic duct obstruction caused by extrinsic compression from an impacted stone in the cystic duct or infundibulum of the gallbladder. Over time, the stones can erode and form cholecystobiliary fistula or cholecystoenteric fistulas. We here describe a case of Mirizzi Syndrome in a 48-year-old man presenting with obstructive jaundice.

Case presentation



.A 48-year-old man with type 2 diabetes and hypertension noticed a progressive yellowing of his skin over the past 10 days, which was associated with epigastric fullness, tea-colored urine, clay-colored stools, decreased appetite, nausea, and pruritus. The discomfort over stomach got worsen after having oily food or during sleep at night, and was relieved by sitting or after walking. He denied having any fever, chills, radiation pain to the back, weight loss, night sweats, recent alcohol consumption, new medications, abdominal surgery, or consumption of unboiled water or raw food. After a ten-day hospital stay in China, he returned to Taiwan for medical attention.

His vital signs were stable. He displayed jaundiced skin and icteric sclera. Respiratory and cardiovascular exams were unremarkable. Abdominal assessment revealed distension and yellowish skin, but no surgical scars or signs of tenderness. Laboratory results showed normal hematological and electrolyte parameters. Liver function test showed cholestatic liver injury and conjugated hyperbilirubinemia. Serological markers for hepatitis B and C were negative. CT showed a 19 mm stone impacted at junction of common duct and cystic duct, causing obstruction and dilatation of the upstream biliary tree. Besides, there were another 19 mm stone in gall bladder and non-distension of gall bladder.

Cholangiogram showed one large filling defect between CBD and cystic duct. Under the fuoroscope guide, Endoscopic sphincterotomy was done. One double pigtail (8fr. 9cm) was inserted into left side IHD. Another double pigtail (7fr. 12cm) was inserted into GB. Laparoscopic cholecystectomy was performed on the day 9. The inflamed gallbladder and the impacted stone were removed followed by closure of cholecysto-choledochal fistula. After postoperative recovery, he was discharged on the day 14.

Discussion

Mirizzi Syndrome is detected in 0.06% to 5.7% of patients during cholecystectomy, and in 1.07% of patients undergoing ERCP[1,2]. The clinical presentation includes obstructive jaundice, elevated liver enzymes, right upper quadrant abdominal pain, and constitutional symptoms such as fever, nausea, vomiting, diarrhea, and constipation.

Abdominal ultrasonography, CT, MRCP, and ERCP are commonly used for diagnosis. At present, MRCP is the preferred non-invasive diagnostic tool and ERCP is the invasive gold standard diagnostic tool[2]. A large number of patients are only diagnosed with Mirizzi Syndrome during surgery.

Mirizzi syndrome has been classified based on the presence and extent of a cholecystobiliary fistula. These types help doctors understand the condition's seriousness and plan treatment. Mirizzi syndrome increases the risk of intraoperative biliary injury during cholecystectomy. Preoperative biliary drainage facilitates the intraoperative identification of the main bile duct. Surgery remains the preferred approach for the treatment of Mirizzi Syndrome. For Type I, total cholecystectomy is feasible. For type II and selected type III, partial cholecystectomy leaves a remaining part of the infundibular wall that can be used for the closure of the cholecysto-choledochal fistula. For Type IV, there is consensus that the best surgical technique is cholecystectomy and Roux-en-Y hepaticojejunostomy[2].

Subvesical bile ducts (SVBD), also known as ducts of Luschka, represent anatomic variations of the biliary tree in which one or more bile ducts traverse in close contact with the gallbladder fossa. Inadvertent and undetected injury of these ducts are a frequent cause of cholecystectomy-associated bile leaks. Preoperative study of the biliary tree anatomic variations may be useful to detect thin ducts and avoid inadvertent injury.

Immediate repair is recommended to manage intraoperative SVBD leaks. Postoperative symptomatic minor bile leak is usually diagnosed during the first week after surgery[3]. Symptoms of subvesical bile ducts injury includes abdominal pain, fever, or peritonitis with sepsis, depending on the amount of bile leak and the presence of infected bile. A small amount bile leak often resolves spontaneously without any treatment. Endoscopic sphincterotomy and biliary stent placement is considered the gold standard treatment. Percutaneous transhepatic drainage is the alternative approach if ERCP is not possible or fails. Re-laparoscopy is also an effective procedure when previous approaches are not resolutive.

Conclusion

In conclusion, Mirizzi Syndrome is still a diagnostic challenge, despite the advancement of the available tools. A preoperative diagnosis is important to avoid intraoperative difficult conditions by choosing the right approach. The treatment may be variable for different anatomical situations. Besides, preoperative identification of ducts of Luschka allows to avoid injury during surgery. Therefore, it is crucial to recognizing preoperatively when planning laparoscopic treatment.

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病例報告　112_C 114

一位紅斑性狼瘡患者以來勢洶洶的廣泛橫貫性脊髓炎與心衰竭為表現

A case of SLE presents with raging extensive transverse myelitis and heart failure

陳乃慈 [1,2] 童建學 [1,2] 王思讚 [1,2]

[1] 佛教慈濟醫療財團法人大林慈濟醫院內科部 [2] 佛教慈濟醫療財團法人大林慈濟醫院風濕免疫科

Introduction

Acute transverse myelitis (TM) is an inflammatory disease that manifests with motor, sensory, and autonomic symptoms of rapid progression with catastrophic outcomes; the three main causes of acute TM are demyelinating diseases, infections, and autoimmune inflammatory diseases such as systemic lupus erythematosus (SLE). We present a case of SLE, who had rapid progression of quadriplegia, loss of limbs sensation and heart failure in few days. Spinal magnetic resonance imaging (MRI) revealed extensive transverse myelitis and cerebrospinal fluid (CSF) showed negative findings of infection. SLE related acute extensive transverse myelitis was diagnosed. Moreover, connective tissue disease related pulmonary hypertension and heart failure were also noted in the same event. Methylprednisolone pulse therapy and plasma exchange as treatment were done. Dolorously, she still expired due to worsening bilateral pneumonia and heart failure even aggressive management for SLE.

Case presentation

The patient is a 30-year-old woman who has a diagnosis of SLE and regularly takes prednisolone 5mg BID as control regimen. She didn't take Hydroxychloroquine due to allergic reaction before. She sometimes needed Methylprednisolone pulse therapy for high titers of C3, C4 and dsDNA at outpatient department during follow-up. In this event, she presented in emergent department as initial presentation of progressive quadriplegia and loss of limbs sensation for 4 days, acute urinary retention for 3 days and then fever and dyspnea for two days.

Chest radiography showed engorged pulmonary trunk and bilateral lungs congestion. Bedside echocardiography revealed dilated right atrium and ventricle with D-shape left ventricle, and revealed pulmonary hypertension. Computed tomography angiography (CTA) showed no pulmonary hypertension. Spinal MRI disclosed swelling of spinal cord with intramedullary hyperintensity of cervical and lumbar segment. She was admitted to intensive care unit (ICU) and emergent intubation was done for dyspnea and progressive paralysis. Lumbar puncture for CSF analysis revealed high total protein (272.1 mg/dL), relative low glucose level (41 mg/dL) compared to serum glucose (140 mg/dL) and WBC 0-2/HPF with monocytes dominant. Cryptococcal Ag in serum and CSF showed negative findings and CSF acid fast stain or culture also demonstrated negative results later.

Her autoimmune profile including low C3 (39.0 mg/dL), C4 (<8 mg/dL) level and high titer of Anti-dsDNA (135 IU/ml), Anti-Sm (15 U/ml), Anti-Ribosomal-P Ab (29.9 units), anti-coagulant antibody (30.2 GPL), anti-phospholipid antibody (43.22 units), and Anti-β2-Glycoprotein IgG (>150 units). Due to critical condition, we prescribed Methylprednisolone pulse therapy immediately after we excluded the possibility of infection. We also discussed to her mother about plasma exchange for the suspicious of SLE related disease and scheduled plasma exchange for 5 times after her mother agreed.

We also consulted Cardiologist, checked NT-proBNP. High level of NT-proBNP was noted and we prescribed Sildenafil for CTD-PAH. Furosemide and spironolactone were prescribed for fluid overload and low cardiac output. However, progressive bilateral pneumonia with evidence from sputum culture and worsening low cardiac output which had poor response to high dose of inotropic agents. Tachycardia and cardiogenic shock were noted and sudden pulseless electric activity happened. Emergent resuscitation and extracorporeal membrane oxygenation were done and got response initially, but her condition still went downhill rapidly later. Due to hypoxic-ischemic encephalopathy and poor neurologic outcomes, her family finally decided to sign DNR as a better choice for the patient.

Conclusion

SLE can present with multiple organ involvement and sometimes can be aggressive and life-threatening. Acute extensive transverse myelitis which is unusual can accompany with cardiac or pulmonary involvement present together and is a raging presentation. Therefore, immediate recognition and intervention are required to prevent catastrophic outcomes.

病例報告　112_C 115

腸道子宮內膜異位症案例報告

A case of bowel endometriosis with accidental findings

吳忠謙[1]　陳彥均[2]
[1]大林慈濟醫院內科部　[2]大林慈濟醫院腸胃內科

Introduction

Endometriosis is a chronic condition primarily affecting women of reproductive age. Although patients with rectovaginal or bowel endometriosis may present with the classic symptoms of endometriosis and/or with gastrointestinal symptoms, some patients with bowel endometriosis may be asymptomatic. In rare cases, bowel obstruction occurs.

Case presentation

This 50-year-old woman, G2P2 (NSD*2), denied any systemic diseases before.
She initially reported a history of irregular menstrual periods and vaginal spotting over the course of the past two years. She denied menorrhagia or dysmenorrhea. She initially attributed these symptoms to the onset of menopause. However, as the symptoms persisted, she sought medical attention and presented to our Gynecology Outpatient Department (GYN OPD) in June 2023. Gynecological sonography revealed an endometrial thickness of 9mm, a complex tumor measuring 84mm in the right ovary with a suspicion of malignancy, and a 29mm cyst in the left ovary. A pelvic CT scan performed on June 29, 2023, confirmed the presence of a cystic neoplasm in the right ovary, grouped cysts with thick walls in the left ovary, and incidental small gallstones.
In light of the ovarian cancer diagnosis, a colonoscopy was scheduled for July 31, 2023, which revealed a rectal tumor with suspected malignancy. Subsequent biopsy results of the rectum showed evidence of acute and chronic inflammation of the colonic mucosa with surface ulceration, without the presence of an identifiable tumor or granuloma. Repeat biopsies were recommended for further clarification, and the sigmoidoscopy was done on August 4, which revealed a rectosigmoid junction tumor. The biopsy results indicated the presence of both endometriosis and an ulcer.

Discussion

Ultrasound is the preferred imaging modality for women suspected of having rectovaginal endometriosis. Sigmoidoscopy or colonoscopy is rarely useful to diagnose bowel endometriosis as lesions that penetrate the mucosa are unusual. However, patients with symptoms or findings suggestive of bowel malignancy, obstruction, or an abnormal double-contrast enema study should undergo endoscopy as part of their evaluation.

Conclusion

The gastrointestinal symptoms associated with rectovaginal or bowel endometriosis are mostly nonspecific. Since intestinal endometriosis is a fairly uncommon condition, other etiologies should be considered first.

病例報告　112_C 116

An incidental finding of primary gastric malignant melanoma: a rare case report with 20 months of follow-up

施孟芸[1] 唐家沛[2,3]
[1]大林慈濟醫院內科部 [2]大林慈濟醫院腸胃內科 [3]花蓮慈濟大學醫學系

Background

Primary gastric malignant melanoma (PGMM) is an extremely-rare extracutaneous melanoma tumor with less than 45 case reports worldwide. PGMM has been reported to occur in older patients with an average age of 71 years with poor prognosis. Clinical manifestations resemble other gastric lesions, such as weight loss, abdominal pain, anemia, nausea, and melena. Histologic diagnosis of melanoma requires the exclusion of metastasis from a primary cutaneous or ocular lesion, with full skin and eye examination. The lack of awareness of the disease and extremely low incidence may lead to misdiagnosis for another gastric malignant tumor when there is no primary lesion present. PGMM is difficult to diagnose at an early stage because of the anatomical location of the disease and small amount of gastric biopsy samples. Early detection and surgical treatment are crucial for long-term survival. Survival rate and overall prognosis of PGMM are poor.

Case presentation

This 72 y/o woman with history of DM, HTN and heart disease. She was in normal independent activities of daily living. She visited OPD due to heartburn and acid reflux for years. She denied abdominal pain, appetite changes, vomitus or weight loss. The upper gastrointestinal endoscopy showed reflux esophagitis and a central pigmented ulcerative lesion of 0.4 cm in size with clean base at the post wall of mid-body (Figure 1). The biopsy of the tumor cells demonstrated hyperchromatic nuclei with irregular nuclear membrane, moderate pleomorphism, increased N/C ratio and scant mitotic figures. Few tumor cells contain brown pigments. In the immunohistochemistry study, all tumor cells are positive for SOX-10 and Melan-A, and some tumor cells are positive for HMB-45. The staining of cytokeratin is negative. The biopsy was consistent with a malignant melanoma. The CT scan showed no visible gastric mass. Whole body PET scan revealed a viable malignancy at the stomach (Figure 2). Clinical examination for possible sites of primary malignant melanoma (skin, other mucous membranes, scalp, palms, eyes, genitals) was negative. Based on these results, a diagnosis of PGMM with pT1N0M0, stage I was established. 3D laparoscopic subtotal gastrectomy with B-II surgical resection was performed. She had

figure 1 a central pigmented ulcerative lesion of 0.4 cm in size withclean base at the post wall of mid-body.

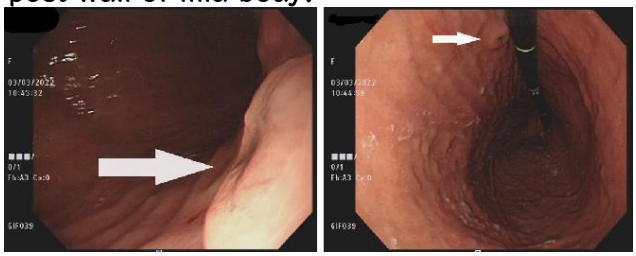
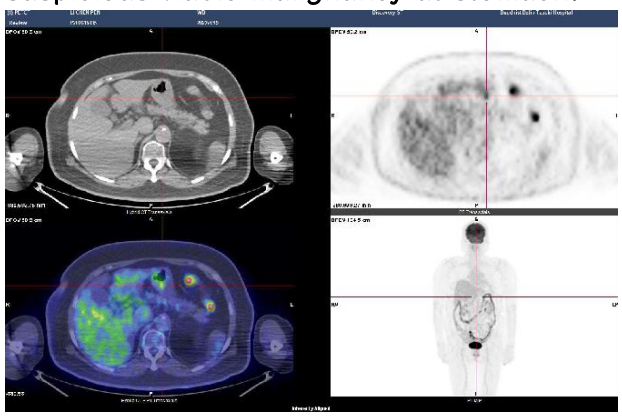
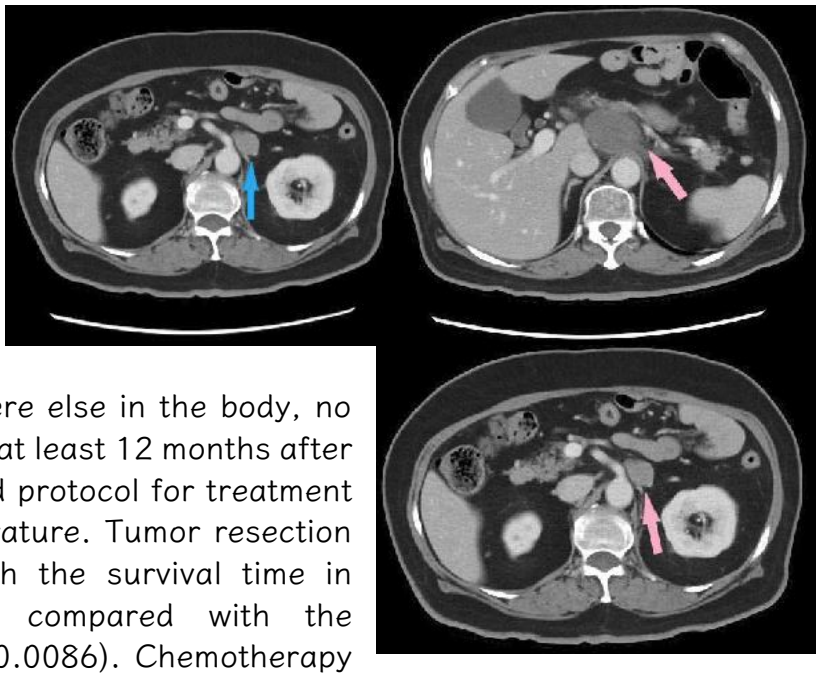


figure 2 Whole body PET scan revealed suspicious viable malignancy at stomach.



regular follow-up for 10 months until a CT scan showed multiple necrotic nodule/lymph nodes in the orifice of lesser sac, celiac root and left paraaortic region (Figure 3). Recurrence of PGMM with regional lymph nodes metastasis was diagnosed. The patient underwent concurrent chemoradiotherapy (CCRT)/ immunotherapy and is currently under aggressive salvage treatment and close follow-up.

Figure 3 followed up CT scan showed multiple necrotic nodule/lymph nodes (up to 5cm) in orifice of lesser sac, celiac root and left paraaortic region.



Discussion and Conclusion

The vast majority of gastrointestinal melanomas are metastases from skin-derived lesions. Non-cutaneous tumors such as ocular, oral, nasopharyngeal, esophageal, bronchial, leptomeningeal, vaginal, anorectal, and nail-bed melanomas occur rarely. The diagnostic criteria for PGMM include a histologically proven single gastric lesion of melanoma, no primary lesions anywhere else in the body, no history of melanoma, and a survival of at least 12 months after curative surgery. There is no standard protocol for treatment due to few cases reported in the literature. Tumor resection has the best long-term outcome with the survival time in surgical group of 21.05 months compared with the nonsurgical group of 4.5 months (p=0.0086). Chemotherapy and radiotherapy serve as an adjuvant for primary or metastatic PGMM is not fully elucidated, though most of the cases in the literature suggested systemic chemotherapy following surgery. Conventional dacarbazine chemotherapy has shown response rates of about 13.4% with no proven survival benefit. Other chemotherapy failed to demonstrate efficacy compared with dacarbazine alone. Targeted treatment for driver mutations of BRAF, KIT and NRAS needs more trials looking at the benefit in mucosal melanoma. Combining chemotherapy with immunotherapy has proven beneficial in cutaneous melanoma but needs more clinical trials to extend their use in mucosal melanoma. In patients with good performance, combination immunotherapy treatment in mucosal melanoma showed a 40% response rate. The prognosis of PGMM is extremely poor at 5 months of median survival time compared to other primary melanomas of the gastrointestinal tracts of 17 months. The 1-year and 5-year survival rate of PGMM are 56.5% and 3%, respectively. This shows that the PGMM has a good response to the initial surgical resection and chemotherapy, but a poor prognosis ensues as the metastatic lesion appears. In our case, PGMM was diagnosed asymptomatic in the early stage with no regional or distal metastasis. As far as we know, there is no literature report on PGMM discovered asymptomatic. Despite the complete surgical resection, recurrence occurs 10 months after the initial treatment. Salvage CCRT with dacarbazine and nivolumab are undergoing and need long-term follow-up for treatment effectiveness.

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病例報告　112_C 117

一位長期腹痛的病人患有克隆氏症：個案報告

A young male presenting with long-term abdominal pain and anal fistula: a case report

徐嘉甫[1] 陳彥均[2]
[1]大林慈濟醫院內科 [2]大林慈濟醫院肝膽腸胃內科

Introduction

The incidence and prevalence of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC) still remain low in Taiwan. Here we introduced a case of Crohn's disease in a young-aged male.

Case report

A 32-year-old man presented to our hospital with persistent abdominal pain for 3 to 4 months in 2020. He initially presented with intermittent abdominal pain and fullness over epigastric area and left abdomen, and multiple painful ulcers over hard palate, buccal mucosa, lips, throat since 2008. Previous colonoscopy revealed multiple colon ulcers and nodular lesions, and biopsy report showed mucosa with some acute and chronic inflammatory cells infiltrating within the stroma and focal ulcers with exudate and granulation tissue. Peri-anal fistula was also noted. He then regularly followed up at outpatient department. After he received 4 doses of self-pay adalimumab 40 mg Q2W, his oral ulcers and abdominal pain subsided. However, persistent low abdominal dull pain developed again in November 2018. He also complained of nausea after meal, bloody stool, left big toe cyanotic change with bulla formation, and multiple nails cracking. Esophagogastroduodenoscopy showed duodenal ulcers, and colonoscopy revealed multiple inflammation and serpiginous ulcerations, skipped lesions, size from 0.3-2.5cm, over whole colon but mainly located at rectum and sigmoid colon and anal fistula. Biopsy report also showed acute and chronic inflammation of the colonic mucosa with mucosal ulceration, and few epithelioid granulomas. Crohn's disease was diagnosed. After applying catastrophic illness card and adequate conservative conventional treatment, he was treated by 1-year of course of infliximab by national health insurance reimbursement. Later, his abdominal symptoms resolved. Follow-up colonoscopy 1 year later also revealed no more ulcers.

Discussion

Crohn's disease (CD) is one of the two major inflammatory bowel diseases (IBD). The disease typically presents in early adulthood, with frequent abdominal pain, diarrhea, hematochezia, and weight loss. However, symptoms vary from person to person and can range from mild to severe, depending on the severity and location of the inflammation. Inflammatory bowel disease has been increasing in both incidence and prevalence in many newly industrialized countries since the beginning of the 21st century. In addition, IBD are common chronic GI diseases in Western countries. However, analyzing data from the nationwide insurance registration system from 2001 to 2015, the incidence and prevalence of IBD are much lower in Taiwan.

The diagnosis of CD is made on the basis of symptoms and endoscopic and radiologic findings. Pathology can be confirmatory. In cases of colonic or ileal CD, endoscopic findings are classically characterized by skip lesions, with varying degrees of inflammation (including

erythema, friability, erosions, and ulcers) next to areas of normal-appearing mucosa. During endoscopy, luminal strictures, and less commonly fistulae, may be seen. On pathology, the classic finding of CD is a noncaseating granuloma. More common pathologic findings include varying degrees of infiltrates from lymphocytes, plasma cells and granulocytes.
The treatment of CD depends on disease severity, location of disease, and subtype of disease. Antibiotics are used in CD, but the evidence supporting their use is also limited. The main role of antibiotics is to treat the suppurative or perianal complications of CD. The immunosuppressants azathioprine/mecaptopurine and methotrexate have been used for many years to treat CD but because of slow onset of action they are typically used to maintain remission. More recently, these drugs are used in combination with anti-TNF drugs to decrease their immunogenicity and increase anti-TNF drug concentrations. The mainstay of therapy for CD has been anti-TNF agents More recently approved drugs are monoclonal antibodies directed against certain integrins (α4 or α4b7) or interleukins (IL-12/IL-23), including natalizumab and Vedolizumab. Ultimately, the goal of medical therapy is to induce and maintain a steroid-free clinical remission, prevent complications and surgery, and improve the patient's quality of life.

病例報告　112_C 118

病例報告: Gavreto(Pralsetinib)在 RET 融合陽性轉移性大腸直腸癌的治療

Case report: Gavreto(Pralsetinib) use in patients with RET fusion-positive metastatic colorectal cancer

林聖淳[1] 李思錦[2]
[1]大林慈濟醫院內科部 [2]大林慈濟醫院血液腫瘤科

Abstract

A 83 years old woman with past history of hypertension, was diagnosed with colorectal cancer, pT4aN2bM1a, stage IVA. She received radical right hemicolectomy, followed by salvage treatment with regimen of Panitumumab with FOLFOX. After 3 cycles, she experienced disease progression. NGS was done by ACT Onco and RET alterations were identified. She started receiving Pralsetinib and there was no disease progression through 1 months, then switched to Selpercatinib for the following one year, without recurrence.

RET (rearranged during transfection) is a transmembrane receptor tyrosine kinase and a receptor for the GDNF-family ligands. RET fusions have been described in a variety of solid tumors including thyroid, non-small-cell lung cancer and a small fraction (<1%) of CRCs. Pralsetinib is a selective RET inhibitor that potently targets RET kinases, including RET fusion proteins. We presented a experience sharing of Gavreto(Pralsetinib) use in patients with RET fusion-positive metastatic colorectal cancer.

病例報告　112_C 119

胸管引流術的一種罕見併發症: 迷走神經性房室傳導阻滯

Vagally mediated atrioventricular block: A rare complication of tube thoracostomy

許哲維[1] 賴俊良[2]
[1]大林慈濟醫院內科 [2]大林慈濟醫院胸腔內科

Introduction

New onset of arrhythmia is a rare complication after tube thoracostomy. Here we report a case of vagally mediated atrioventricular block after tube thoracostomy insertion.

Case presentation

A dyspneic man in his late 70s with bullous emphysema and metastatic left upper lung squamous cell carcinoma was admitted with secondary spontaneous pneumothorax. On admission, he was tachycardic with heart rate of 109 beats/min (bpm). Oxygen saturations was 93% on air, blood pressure was 102/73 mmHg, and body temperature was 35.9°C. Electrocardiogram revealed sinus tachycardia. Plain chest radiography disclosed small pneumothorax(<2cm) adjacent to left lower lung bullae. Conservative treatment with oxygenation therapy was initiated. On the next day, his pneumothorax converted to tension type, presenting with profound shock and increased size. Emergent tube thoracostomy with 10-french pigtail was performed. Negative pressure drainage was applied. His hypotension relieved briefly, but relapsed few ours later. Vasopressor with Norepinephrine pump was required to maintain mean arterial pressure>65 mmhg. Electrocardiogram monitor revealed new onset of 1st degreee AV block with variable PR interval around 208 ms to 344 ms, and a narrow QRS complex of 90ms. Besides, he also had relative bradycardia with sinus arrhythmia, with ventrucular rate around 50 bpm to 76 bpm. Emergent computed tomography over chest demonstrated right apical lung ground glass opacity patches with tube dislocation into left lower lung bullae. The dislocated thoracostomy tube was removed and reinserted. Profound shock and atrioventricular block resolved within 24hrs.

Figure 1. EKG on admission day (2023/06/26)

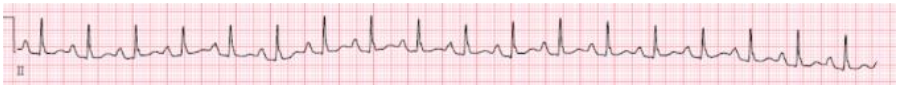


Figure 2. Serial EKGs during second shock episode after pigtail insertion (2023/06/27)

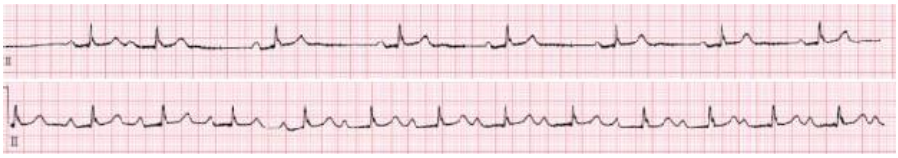
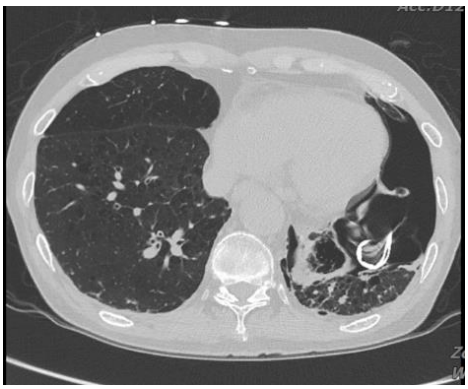


Figure 3. The dislocated pigtail



Discussion

Secondary spontaneuous pneumothorax harbors higher rate of complication compared to primary spontaneous pneumothorax. Pneumothorax, chronic obstructive lung disease, and community acquired pneumonia have been reported to have higher risks of arrhythmia. Most of them are reported to be supraventricular tachycardia(especially atrial fibrillations) and

ventricular arrhythmias.
To evaluate his sudden onset atrioventricular block, differential diagnosis must include medication effect, electrolyte imbalance, myocardial ischemia, recent cardiac surgery, and elevated vagal tone.
Our patient has no recent exposure to beta blockers, non-dihydropyridine calcium channel blockers, digitalis, adenosine, or amiodarone. He received inhalative beta agonist as part of conservative treatment instead. Lab data showed normokalemia with 4.0 mmol/L, relative low serum NT-proBNP level with 130.8 pg/mL and no significant change of high sensitivity troponin I (from 5.5 to 6.6pg/ml in 3 hours).
Considering the paroxysmal nature of atrioventricular block with spontaneuous resolution after tube removal, increased vagal tone is more likely to be the main culprit. Vagally mediated atrioventricular block is defined as a paroxysmal first-, second- or third-degree atriventricular(AV) block associated with slowing of the sinus rate. It is generally deemed to be benign due to its abscence of anatomical abnormality in AV conduction system. It is a common cause of syncope, and may be triggerred by a surge of parasympathetic tone with identifiable causes including vomiting, micturition, intense coughing, or phlebotomy.
Several pulmonary causes have also been reported to precipitate bradycardia via increased vagal tone including tube thoracostomy, chylothorax, and thoracic surgery. New onset of arrhythmia is a rare complication after tube thoracostomy. Patients complicating with atrial fibrillation, ventricular tachycardia, sinus bradycardia, or high degree AV block has been described in previous case reports. Most of them have poor response to medical treatment, but resolves after thoracostomy tube removal. In our case, the mechanism of dislocated thoracostomy tube into lung bullae may increase vagal tone by (1) direct irritation of left vagus nerve/anterior vagal trunk or (2) stimulation of pulmonary C-fiber receptors due to hyperinflation, especially under negative pressure suction.

病例報告　112_C 120

新冠疫情下一位多重共病患者醫療相關感染的治療經驗

The experience of one multimorbidity case co-infected with COVID-19 and healthcare associated infection

廖忠信[1]　周晏立[2]
[1]衛福部嘉義醫院內科　[2]嘉義長庚醫院胸腔科

Introduction

Chia-Yi Hospital is a community hospital at *Southern Taiwan*. It owns 411 hospital beds (acute- 244 beds and others- 167 beds, including respiratory care bed-40 and ICU bed- 20). The origin of most patients (80%) are coming from elderly and chronic care facility. There are two features of this cohort- fralility and multimorbidity. So, we present one typical case who is acquired healthcare associated infection and discuss the importance of liver-renal function evaluation before drug prescription.

Case presentation

This 75 years old male was a victim of old stroke with R't hemiplegia, CBD stone s/p, diabetes, hypertension, congestive heart failure, hepatitis B/C carrier, chronic kidney disease (CKD) and bed-ridden with pressure sore s/p. He was referred to our RCW for weaning ventilator and infection control on May 9, 2023. Nearly 2 months of supportive and wound care, he was kept in stable status. On Jul 31, 2023, he was noted to have shock with multiple organ dysfunction. Nosocomial infection of lung, urine and wound were noted simultaneously. Intensive care and broad spectrum antibiotics (including levofloxacin, amikacin, ertapenem/colimycin) were given during Jul 31 and Aug 21, 2023. Unfortunately, he was still critical discharged on Aug 21, 2023 at 11:4 a.m.

Discussion

There are two point of views from this case. The former is healthcare related infection in the last month. Multidrug resistant (MDR) bacteria are isolated from clinical specimens (S/C c *CRPA, CREC, MRSA*; U/C c *MRSA, CREC*; W/C c *MRSA, CREC,* anaerobic and BAL/C c *Prevotella, C. tropicalis*). The latter is antibiotic used (levofloxacin => amikacin => ertapenem/colimycin-INH) for the above nosocomial infection. BMI of this patient is 23.6 and renal function is CKD (stage 3A) on 7/31. So, levofloxacin (0.75g IVD QD 7/31~8/3) and amikacin (0.375g IVD q12h 8/3-8/14) might induce renal function impaired (GFR 52.5 => 14). The peak/trough level of amikacin are 53.2/46.9ug/mL on 8/12. Then antibiotics are shifted to ertapenem (1g IVD QD) / colimycin (1 pack q12h INH) regimen since 8/14. Though his renal function is improved (GFR 62.7) gradually, he is still died of GI bleeding and multiple organ failure.

Conclusion

During COVID-19 pandemic period, MDR pathogens are emerging and antibiotics prescription are often used with ant-viral agents for high risk groups of COIVID-19 infected patients. Appropriate dose of medication and real time of liver-renal function are both important tools for clinical practice.

病例報告　112_C 121

第十三因子缺乏症以自發性大腿血腫表現

Acquired Factor XIII Deficiency Presented with Spontaneous Thigh Hematoma

王澄[1] 張力常[2] 陳雅萍[2]
[1]戴德森嘉義基督教醫院急診部 [2]成大醫院血液科

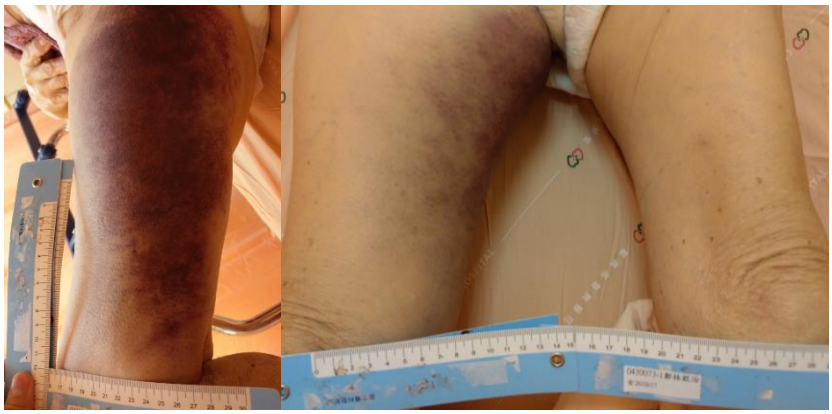
Introduction

Acquired factor XIII deficiency is a rare disorder characterized by abnormal bleeding presentations, which can manifest as spontaneous, delayed, life-threatening, or minor bleeding events. The underlying causes may be immune-mediated inhibition or non-immune factors, such as hyperconsumption or hyposynthesis. The diagnosis relies on quantitative FXIII testing and additional inhibitor studies in cases of immune-mediated etiology. The treatment approach is contingent upon managing the underlying disease if it is immune-mediated in its pathophysiology.

Case Presentation

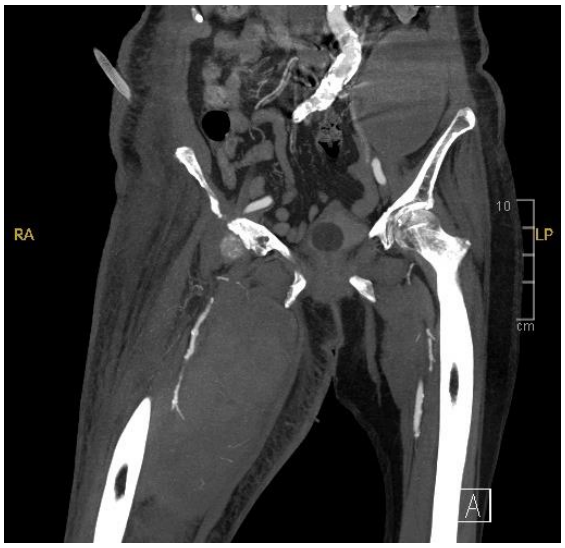
An 85-year-old woman, without any underlying medical conditions, presented with hematuria persisting for two weeks. Initially, she was treated for a urinary tract infection. Additionally, she experienced acute lower abdominal pain accompanied by left flank ecchymosis. A diagnosis of left retroperitoneal hematoma was established at that time. The patient received conservative treatment and blood transfusion. However, she returned to the CYCH emergency department a few months later due to the development of a right thigh hematoma and ecchymosis (Fig.1 and Fig.2). No evidence of thrombocytopenia or coagulopathy was observed, but mild chronic kidney disease with anemia was noted. Consequently, she was admitted to the hospital.

Fig.1 and Fig.2 showed left thigh swelling and ecchymosis.



Given the progressive swelling on her right side, a CT angiography was performed, revealing a right medial thigh hematoma measuring approximately 20 cm (Fig.3). No contrast extravasation was observed. Due to suspected bleeding diathesis, the patient was subsequently transferred to the NCKH hematology department. Further investigation revealed no deficiency in factor VIII or von Willebrand factor. The

Fig 3. showed left thigh hematoma without contrast extravasation.



urea solubility test yielded positive results, while factor XIII activity was determined to be 0%. Acquired factor XIII deficiency was diagnosed. Anti-HCV and anti-HBc antibodies were reactive, and Entecavir was prescribed for HBV prophylaxis. The patient received cryoprecipitate infusion, high-dose prednisolone, and cyclophosphamide. She was discharged without progression of the right thigh hematoma.

Discussion

Acquired factor XIII deficiency is an uncommon bleeding disorder that can manifest as spontaneous or delayed hemorrhages. The causes include immune-mediated inhibition as well as non-immune factors such as hyperconsumption or hyposynthesis. Most cases of acquired factor XIII deficiency are non-immune-related and asymptomatic, whereas immune-mediated cases are typically associated with spontaneous or delayed bleeding episodes. Spontaneous hemorrhages predominantly occur in subcutaneous or intramuscular compartments, with intracranial bleeding being a leading cause of mortality in these patients. Factor XIII deficiency should be considered in patients presenting with bleeding symptoms and normal coagulation or platelet function without thrombocytopenia. The median age at presentation is approximately 70 years old.

Factor XIII deficiencies are typically screened using qualitative assays like the clot solubility test, followed by confirmation through quantitative FXIII activity and antigen level testing. In Taiwan, concentrated urea is commonly used as the solubilizing agent in these tests. However, it is important to note that there are certain limitations and pitfalls associated with the clot solubility test. Its sensitivity can be influenced by fibrinogen levels and factor XIII activity, rendering a negative clot solubility test insufficient to rule out factor XIII deficiency. Therefore, quantitative FXIII activity assessment remains essential for the diagnosis of acquired factor XIII deficiency.

Conclusion

Acquired factor XIII deficiency is a rare bleeding disorder that should be considered in patients with normal coagulation or platelet functions who present with unexplained bleeding. Screening may involve the use of the urea solubility test, but confirmation requires quantitative FXIII activity assessment.

病例報告　112_C 122

短期使用 dexamethaxone 誘發慢性穩定 C 型肝炎帶原者之急性爆發：病例報告
Short-course dexamethaxone medication induce flare up of Chronic hepatitis C in a stable case

沈振榮 [1] 葉婕婷 [2] 莊千瑩 [1]
[1] 台南市立安南醫院內科部新陳代謝科 [2] 台南市立安南醫院護理部

Introduction

The corticosteroids are widely used in medicine largely for their potent anti-inflammatory and immunosuppressive activities. Corticosteroids are used in several liver diseases. The adverse effects of long-term corticosteroid therapy (which are rarely hepatic) are still major causes of morbidity and even mortality. Short course of dexamethaxone is rarely reported to be hepatic injury or cause acute flare up of chronic hepatitis C.

Case presentation

A 71-year-old male with Hypertension and hepatitis C carrier state in stable condition without treatment. He received antitussives, mucolytics, antihistamine and dexamethaxone (8 mg per day 14 days) then develop general discomfort and fever up to body temperature 38.1℃. Associated symptoms with fatigue, nausea, abdominal distension and persistently right-epigastric-dull pain.

Liver tests were markedly elevated with ALT 475 U/L and bilirubin 3.2 mg/dL. He was admitted. On examination, he had jaundice and clear mental state. At this point, he tested negative for HBsAg, HBeAg, and HBV DNA levels but h*epatitis C* RNA quantitative test 669975.20 IU/mL, HCV genotype:2. Abdominal image with echography, CT and MRI reveal normal liver and gallbladder appearance with mild dilatation of CBD and pancreatic duct. He was admitted for symptom treatment, intravenous fluid supple and prophylactic antibiotics. Clinical condition improved after one week treatment and liver test ALT 213 U/L and bilirubin 2.5 mg/dL. He was discharged. One month later, oral anti-hepatitis C medication with maviret 100mg/40mg was prescribed for 8 weeks. After treatment, no clinical discomfort and liver test reveal ALT 13 U/L and bilirubin 1.6 mg/dL.

Discussion

Dexamethasone have greater glucocorticoid potency and less aldosterone-like activity than prednisone, and is used widely for their potent anti-inflammatory and immunosuppressive activities. Corticosteroids have effects on the liver, particularly when given long term and in higher than physiologic doses. The adverse effects of corticosteroid therapy seem to relate with long-term use (which are rarely hepatic) and rarely reported in short course treatment less than 2 weeks. Corticosteroids can trigger or worsen nonalcoholic steatohepatitis. Long term use can also exacerbate chronic viral hepatitis B and C. Exacerbation of hepatitis becomes particularly evident when corticosteroids are withdrawn or lowered to physiological levels. Acute flare-up of chronic hepatitis C in stable state is rarely reported in short course treatment with physiology doses. Further investigation, if possible, should include a prospective, randomized study of the safety and efficacy of corticosteroids in patients with chronic hepatitis. In the interim, based on the data presented, the risks and benefits of

corticosteroid administration should be carefully weighed and early discontinuation considered in the absence of a clear salutary effect.

Conclusion

The current case indicates that corticosteroid medication is a potential risk factor for worsening the course of chronic viral hepatitis. Corticosteroids should be avoided, if possible, in patients with underlying chronic viral hepatitis.

病例報告　112_C 123

由金黃色葡萄球菌引起的全脊椎硬膜外膿瘍：導致呼吸器依賴的診斷挑戰

Pan-Spinal Epidural Abscesses Secondary to Staphylococcus aureus: A Challenging Diagnostic Dilemma Leading to Ventilator Dependency - A Case Report

邱魏嶙 陳寶珍 王旌祖 陳怡芝
台南市立醫院內科部

Abstract

Spinal epidural abscesses continue to be a diagnostic challenge, often remaining undetected until advanced neurological symptoms arise, even with MRI technology. In this report, we present a case of pan-spinal epidural abscesses caused by Staphylococcus aureus. The patient initially presented with flank pain and was diagnosed with a psoas muscle abscess. The deterioration of neurological function was masked by the use of sedative agents to manage ventilator dyssynchrony. Despite surgical intervention, the patient's neurological function did not improve and ultimately progressed to a ventilator-dependent state.

The incidence of spinal epidural abscesses is rising, noted in 2 to 8 cases per 10,000 hospital admissions, possibly due to advanced MRI technology or increased spinal surgeries. Infection can spread through contiguous expansion (one-third of cases) or hematogenous dissemination (half of cases). Predisposed individuals, like those with Diabetes Mellitus or HIV, often exhibit local or systemic infections. Staphylococcus aureus is implicated in two-thirds of cases, with MRSA incidence possibly linked to spinal surgery advancements.

The case of Spinal Epidural Abscess (SEA) outlined here emphasizes the diagnostic challenges and the critical importance of early intervention in managing this rare yet serious condition. Despite the advancements in MRI technology, timely detection and appropriate surgical intervention remain crucial to prevent severe neurological deterioration.

病例報告　112_C 124

海藻希瓦氏菌引起的壞死性筋膜炎：一例台灣罕見的病例報告

A case report of necrotizing fasciitis caused by Shewanella algae: an unusual pathogen in Taiwan

陸冠廷　陳柏齡
國立成功大學醫學院附設醫院內科部

Background

Shewanella algae is a rod-shaped Gram-negative bacterium, and mainly exists in marine environments in tropical areas. There is an increasing number of cases reported of *Shewanella algae* infection worldwide. It could cause severe skin and soft tissue, hepatobiliary, respiratory infections, and bacteremia.

Case Report

We reported a 54-year-old man with a history of morbid obesity and type 2 diabetes mellitus. The patient, who is employed at a power station adjacent to a harbor, had experienced recurrent cellulitis over his left lower limb for over a decade. He had been treated with antibiotics at local clinics for recurrent cellulitis of the left lower leg several times and even was admitted for medical treatment two times. He has suffered from chronic swelling and a non-healing wound over the left calf. The patient recently presented to our hospital due to the worsening condition of his left leg. Upon examination, his left calf displayed extensive hyperpigmentation, scaling, multiple bullae, and serous exudates. Erythematous changes were also noted, extending to the left ankle, with gangrene change over the left dorsal foot. Blood culture yielded two sets of *Shewanella algae*. Treatment was initiated with cefotaxime, but the patient's condition rapidly deteriorated. He developed acute renal failure, impaired liver function, and septic shock, requiring intensive care and fluid resuscitation. Computed tomography revealed evidence of necrotizing fasciitis of the left lower limb. The patient underwent fasciotomy and debridement. The intra- operative wound culture yielded *Shewanella algae* and extensively drug-resistant *Acinetobacter baumannii*. He received antibiotic therapy with tigecycline and colistin, followed by ampicillin/sulbactam and minocycline intravenously, in conjunction with several courses of debridement.

Discussion

Shewanella spp. are widely distributed throughout nature, particularly in marine environments. Previous reports have highlighted various risk factors, including diabetes mellitus, chronic leg wounds, and occupational or recreational exposure to marine environments. *Shewanella* algae has been isolated from the respiratory tract, blood, bile ducts, soft tissues, and skin. It frequently causes hepatobiliary or soft tissue infections. The effective drugs include third-generation cephalosporins, moxifloxacin, and carbapenems. The majority of infections follow a benign course. Herein, we reported a case that exhibited cellulitis that progressed to necrotizing fasciitis which needed emergency fasciotomy in addition to antibiotic therapy.

Conclusion

Shewanella algae is an emergent pathogen to humans, and can cause life-threatening necrotizing fasciitis in patients with risk factors. This species should be considered as one of the pathogens causing severe soft tissue infection in endemic areas.

病例報告　112_C 125

鈣離子感應接受器新型基因突變引起的家族性低尿鈣高血鈣症：家系案例報告

A case of familial hypocalciuric hypercalcemia type 1 due to novel CASR mutation

吳尚翰[1] 王建中[2] 蔡孟哲[3] 孫健耀[4]

[1]國立成功大學醫學院附設醫院內科部 [2]佑馨診所 [3]國立成功大學醫學院附設醫院小兒部小兒遺傳科

[4]國立成功大學醫學院附設醫院高齡醫學部

Introduction

Familial hypocalciuric hypercalcemia (FHH) is a rare genetic disorder, predominantly inherited in an autosomal dominant manner. It is crucial to differentiate FHH from primary hyperparathyroidism (PHPT) to avoid unnecessary surgical interventions in FHH families. The disorder is mainly attributed to mutations in the calcium-sensing receptor (CaSR), G-protein-subunit-α11 (GNA11), or adaptor-related-protein-complex-2-sigma-1-subunit (AP2S1) genes, resulting in subtypes FHH1, FHH2, and FHH3. FHH1 is caused by a mutation in the CaSR gene, impacting calcium-sensing in parathyroid glan ds and kidneys, leading to CaSR resistance to extracellular calcium and reduced renal calcium excretion. This case explores a novel pathogenic mutation in the CaSR gene in a patient with a significant family history of FHH.

Case presentation

A 58-year-old woman presented to our outpatient clinic with right calf pain and bilateral lower limb weakness for 2 months. She had a height of 154.5 cm, weight of 52.5 kg and Body Mass Index of 22. Her serum calcium, ionized calcium, phosphate and intact-PTH (iPTH) levels were 11.0 mg/dL (reference: 8.6-10.0 mg/dL), 1.39 mmol/L (reference: 1.15-1.33 mmol/dL), 3.1mg/dL (reference: 2.5-4.5 mg/dL) and 35.2 pg/mL (reference: 15-65 pg/mL). Her serum 25-Hydroxyvitamin D was 24.2 ng/mL (reference ≧30 ng/mL). Her urine calcium level (3.1mg/dL, reference: 6.8-21.3mg/dL), fractional excretion of calcium (FECa, 0.1%), 24 h urinary calcium excretion (79.2mg, reference: 100-300 mg) and calcium creatinine clearance ratio (CCCR, 0.004, reference range>0.01) were low. Parathyroid sonography revealed an elongated isthmus nodule, and 99mTc-MIBI scintigraphy showed no definite focus of radiotracer stasis in bilateral thyroid regions and mediastinum. Suspecting FHH, whole exome sanger sequencing revealed no variations in the AP2S1 gene, seven benign variants in the GNA11 gene, and a missense mutation (c.499T>G (p.Y167D)) in the CASR gene. This CASR variant was previously of uncertain significance due to insufficient evidence and its absence in major population databases (Exome Aggregation Consortium (ExAC), and Genome Aggregation Database (gnomAD)). Silico algorithms predicted the variant likely to be pathogenic with a PolyPhen-2 score of 1.000 and a MetaRNN score of 0.986. Genetic conservation analysis revealed a Consurf score of 7 and a phyloP100 score of 8.017, supporting its functional importance. The same CASR variant was identified in her mother and her two daughters. Her mother's blood test also showed hypercalcemia (11.8 mg/dL) and non-suppressed iPTH (31.9 pg/mL). Clodronate was given to the patient (400mg per day), and her serum calcium was around 10 -11mg/dL.

Discussion

The calcium-sensing receptor (CaSR) is a pivotal G protein-coupled receptor (GPCR) in calcium homeostasis. It functions as a homodimer, and its calcium-sensing function is altered when a mutant CASR heterodimerizes with a wildtype CaSR. A heterozygous missense variant c.499T>G was identified in our patient, leading to a tyrosine to aspartic acid substitution at codon 167 (p.Y167D). This amino acid is evolutionarily conserved, highlighting its functional importance. Considering the supporting evidence, this novel CaSR variant is likely pathogenic according to the American College of Medical Genetics and Genomics Standards and Guidelines (PM1+PM2+PP1+PP3). It locates in the extracellular ligand-binding domain of CaSR, adjacent to the L-tryptophan binding site, potentially affects L-Trp binding and leads to FHH1 phenotype. FHH1 is an autosomal dominant disease with high penetrance; however, it is often benign, with morbidity typically resulting from misdiagnosis and unnecessary surgery. Accurate genetic testing is crucial to differentiate FHH from PHPT, preventing unwarranted surgical interventions.

Conclusion

This study reports a novel pathogenic missense single nucleotide variant of the CaSR gene in a family, highlighting the importance of genetic testing and the potential need for further in vitro / vivo functional studies.

病例報告　112_C 126

消化道出血常被忽略之成因其一－梅克爾憩室出血

Bleeding from Meckel's Diverticulum - An Often-Overlooked Cause of Gastrointestinal Bleeding

江健銘　姜學謙　郭欣瑜
國立成功大學醫學院附設醫院　消化內科

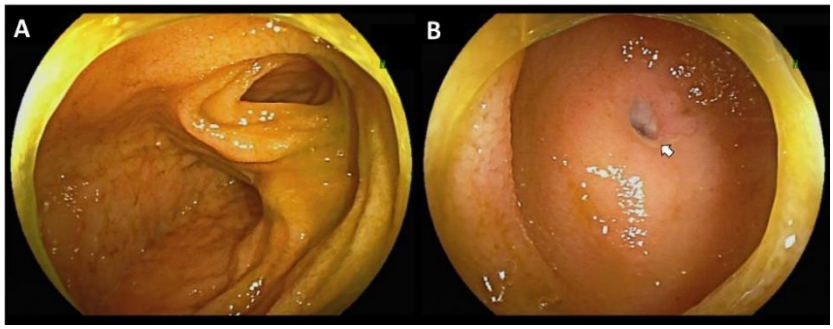
Introduction

Meckel's diverticulum is an uncommon, yet not rare, cause of gastrointestinal bleeding. We are presenting a case of 24-year-old man with small bowel bleeding. In our case, the patient underwent tests including esophagogastroduodenoscopy, colonoscopy, Tc-99m pertechnetate scan and balloon-assisted enteroscopy. Eventually the diagnosis of Meckel's diverticulum was made, and it was proven by histopathology after surgery.

Case presentation

A 24-year-old healthy gentleman visited the emergency department for one week of intermittent tarry-bloody stool and lightheadedness. There was no abdominal pain, coffee ground vomitus, or significant body weight loss. Physical examination was generally unremarkable except for pale conjunctivae. Hemogram showed anemia with a hemoglobin level of 5.4 g/dl. Esophagogastroduodenoscopy (EGD) revealed clear gastric content without coffee ground substance or blood till the visible portion of duodenum. Instead, bloody content could be seen during emergent sigmoidoscopy, but the procedure ended up incompletely due to poor preparation.

Figure 1 Endoscopic findings that were noted during double-balloon enteroscopy. (A) An out-pouching structure at 60cm cephalad from the ileocecal valve. (B) A clean-base ulcer (arrow) was observed within the out-pouching lesion.



After admission to the gastroenterology ward, the stool gradually became yellowish during bowel preparation. Following colonoscopy demonstrated clear colonic content; no colonic ulcer, diverticulum, polyp, tumor, or vascular lesion was noted. Contrast-enhanced computed tomography of the abdomen suggested there was no tumorous lesion or active bleeder along the gastrointestinal (GI) tract. Small bowel series with barium revealed no filling defect or abnormal contrast accumulation. Neither blood nor potential bleeder was identified by push enteroscopy via the oral route and small bowel capsule enteroscopy. Since the absence of active GI bleeding, the patient was discharged home.

However, one month later, the patient experienced recurrent tarry-bloody stool which led to his second hospitalization. Repeated EGD and colonoscopy showed clear content over the examined parts of GI tract. Tc-99m pertechnetate scan demonstrated a faint, radioactive spot over the right lower quadrant of the abdomen. Therefore, a double-balloon enteroscopy via the anal route was performed, which revealed an out-pouching structure (Fig. 1A), about

60 centimeters from the ileocecal valve, 2cm in depth and a clean-base ulcer within it (Fig. 1B, arrow). Hemoclips were deployed and mucosal tattoo marking was done to mark the lesion for further surgical intervention. The patient then underwent laparoscopic resection of the small bowel segment including the labeled lesion. Macroscopically, a diverticular structure (Fig. 2A) covering gastric mucosa and an ulcer were identified (Fig. 2B, white arrowhead). The pathology report confirmed the presence of ectopic gastric glands (Fig. 2C; Fig, 2D, black arrowheads) within the tissue, suggesting the final diagnosis of Meckel's diverticulum. After the operation, the patient tolerated well to stepwise diet advancement with fair bowel movement. No recurrence of tarry-bloody stool was ever noticed after the surgery. The patient was discharged 6 days after the operation.

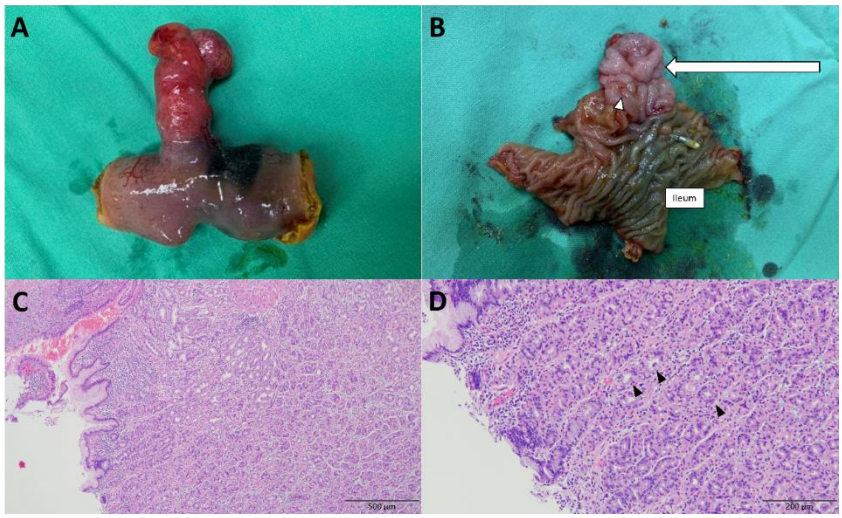


Figure 2 Macroscopic and histopathologic findings that were recorded after segmental small bowel resection. (A) A diverticular lesion was seen connecting to the ileum. (B) The covering gastric mucosa (white arrow) with an ulcer (white arrowhead) could be visualized. (C, D) The architecture of gastric glands (black arrowheads) was depicted using the optical microscopy with hematoxylin and eosin stain (scale bar 500 μm and 200 μm, respectively).

Discussion

Meckel's diverticulum is a true diverticulum containing all 3 layers of bowel wall, including mucosa, muscularis, and serosa[1]. As the remanent of incomplete-obliterated vitelline duct, Meckel's diverticulum is the most common congenital GI tract anomaly[1]. While most of Meckel's diverticula remain asymptomatic, some may be complicated with bleeding, obstruction, inflammation, and the development of malignancy[1]. Bleeding is caused by the peptic ulcer within the Meckel's diverticulum secondary to acid production of the ectopic gastric mucosa[1]. Literature reported that Meckel's diverticulum is the leading cause of obscure GI bleeding in patients younger than 50 years old with a low comorbidity index[2].

A Meckel's diverticulum is often found in the ileum, 2 feet away from the ileocecal valve – the location that is usually out-of-reach via colonoscopy in the routine examination[1]. Therefore, the diagnosis of Meckel's diverticulum is often challenging. Ultrasound and CT scan only have low detection rate. Tc-99m pertechnetate nuclear scans, the Meckel scan, should be the initial diagnostic study for patients suspect Meckel's diverticulum[1]. When the mucus secreting cells of the gastric mucosa uptakes Tc-99m pertechnetate, the Meckel scan allows imaging of the gastric mucosa[1]. However, even a Meckel scan has only approximately 85% sensitivity and specificity[1]. Therefore, a negative finding of Meckel scan doesn't rule out the diagnosis of Meckel's diverticulum. For small bowel bleeding patients with suspicion of Meckel's diverticulum, a capsule endoscopy may miss the intraluminal lesions when bleeding stopped during the exam[3]. Compared to the capsule endoscopy, balloon-assisted enteroscopy provides a higher diagnostic accuracy for bleeding Meckel's diverticulum[3].

Conclusion

Meckel's diverticular bleeding is an easily overlooked cause of GI bleeding in clinical practice. In our case, a healthy young man with small bowel bleeding gave rise to the suspicion of Meckel's diverticulum. Timely diagnosis by Meckel scan and balloon-assisted enteroscopy and subsequent surgery preclude further complications.

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病例報告　112_C 127

肋膜腔鏡診斷以肋膜積液表現的肺部矽肺誘發之 IgG4 疾病 -病例報告

Pulmonary Silicosis-Induced IgG4 Related Disease Presented with Pleural Effusion Diagnosed by Medical Pleuroscopy - A Case Report

林輔仁[1] 郭鈞瑋[2]
[1]國立成功大學附設醫院內科部 [2]國立成功大學附設醫院內科部胸腔內科

Introduction

Silicosis is a significant occupational lung disease with a long latency period, while pleural silicosis is characterized by pleural plaques and thickening. Pleural silicosis with effusion is rare. IgG4-related disease (IgG4-RD) is a chronic fibroinflammatory condition, often affecting the lungs and pleura. Medical pleuroscopy is a minimally invasive tool for diagnosing pleural diseases. We present an 89-year-old patient with recurrent lymphocytic pleural effusion related to silicosis.

Case presentation

An 89-year-old retired architect presented with a dry cough. He had a history of hypertension and dyslipidemia. A chest X-ray in January 2022 revealed left-sided pleural effusion. Further tests showed lymphocytic exudative pleural effusion with negative tuberculosis and cancer findings. Chest CT revealed pleural thickening with calcified plaques. Medical pleuroscopy revealed lymphoplasmacytic infiltration, IgG4-positive cells, and silicotic nodules in the pleura, confirming pleural silicosis-induced IgG4-RD.

Discussion

Silicosis is caused by silica dust exposure and is known to affect the pleura. IgG4-RD is a systemic disorder characterized by inflammation and fibrosis, often involving the lungs and pleura. Our case demonstrates the co-occurrence of these conditions in the pleura, confirmed by pathological findings. Diagnosis relied on occupational history, radiological features, and histopathology.

Conclusions

Pulmonary Silicosis-Induced IgG4 Related Disease is a rare condition with subtle presentations. Medical pleuroscopy proved valuable in diagnosing this disease.

病例報告　112_C 128

少動鞘氨醇單胞菌感染引發之皮膚軟組織感染以及菌血症

A rare case of *Sphingomonas paucimobilis* bacteremia complicated with skin soft tissue infection

余昇叡[1]　蔡進相[2]

[1]成大醫院教學中心(PGY2 內科組) [2]成大醫院內科部

Introduction

Sphingomonas species are commonly found in environments, such as in soil and in water, even water sources in the hospital environments. The only one species of *Sphingomonas* that can cause human infection is *Sphingomonas paucimobilis*. It is an occasional pathogen accounting for human infections.

Case presentation

We presented a case of 75-year-old man with history of abdominal aortic aneurysm status post endovascular aneurysm repair, persistent atrial fibrillation under dabigatran treatment and coronary artery disease. He lives in the urban area of Luzhu, Kaohsiung. He suffered from fever and right ankle swelling for 2 days. He ever went to the park during a rainy day. His shoes were totally wet without trauma or skin lesion over his right pedal foot. Right ankle and leg swelling accompanied with erythematous change and pain developed. He went to the local clinic but no improvement after initial treatment. Then he was brought to our emergent room. The computed tomography of right leg revealed extensive soft tissue swelling. A bulla over right pedal foot was found; the aspirate culture showed no growth. His blood culture revealed *Spingomonas paucimobilis*. Ceftriaxone was administered according to antibiotic sensitivity test. The condition of right leg significantly improved after antibiotic treatment and intensive wound care. The patient was discharged with cefixime on the 8th day of hospitalization.

Discussion

Sphingomonas paucimobilis is an opportunistic pathogen, typically in immunocompromised individuals. It can lead to soft tissue infection, urinary tract infection, central catheter-related bacteremia, ventriculoperitoneal shunt infection, peritoneal catheter-associated peritonitis, meningitis, brain abscess, and a variety of visceral abscesses. Previous study revealed community-acquired infection, diabetes mellitus and alcoholism are risk factors for *Sphingomonas paucimobilis* primary bacteremia. However, this is a case with immunocompetent status without catheter indwelling and without risk factors mentioned above. There are few reports about *Sphingomonas paucimobilis* bacteremia complicated with skin soft tissue infection.

Conclusion

Skin soft tissue infection complicated with *Sphingomonas paucimobilis* bacteremia can be found in the community setting. Primary care physicians should take it into consideration, especially when patients have exposure to dirty water or soils.

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病例報告　112_C 129

Nebivolol 和 prochlorperazine 之間的藥物交互作用誘發致命性的心搏過緩
Life-threatening bradycardia induced by drug-drug interaction between nebivolol and prochlorperazine

孫承怡　張維倫
國立成功大學附設醫院

Background

Nebivolol is a β1-selective beta blockers with vasodilatory properties used to treat hypertension and heart failure. It is reported to have less bradycardia adverse event (0.7%) than the other beta blockers. We reported the first case of life-threatening bradycardia induced by a combined use of nebivolol and prochlorperazine.

Case presentation

A 69-year-old man was admitted for increasing severity of chronic abdominal pain. He had past medical history of end-stage renal disease (ESRD), coronary artery disease (CAD) status post-stent placement, heart failure with a reduced ejection fraction (EF), hypertension, and type 2 diabetes complicated by gastrointestinal autonomic neuropathy. He used nebivolol 5mg once daily regularly for heart failure and hypertension.
During hospitalization, the patient experienced sudden episodes of junctional bradycardia (35 bpm), hypotension and consciousness disturbance after receiving prochlorperazine for nausea and vomiting. An alarming clinical observation emerged as the patient's heart rate progressively slowed down, particularly following the administration of Prochlorperazine, ultimately leading to a life-threatening bradycardic event. He received inotropic agent treatment to increase heart rate and blood pressure, and discontinued nebivolol. He regained normal sinus rhythm gradually after treatment. Nebivolol was switched to hydroxyzine for control of his hypertension and heart failure. An alarming system was set to avoid combined use of nebivolol and prochlorperazine.

Conclusion

This case underscores the intricate nature of managing patients with multiple comorbidities and highlights the importance of closely monitoring medication responses. Specifically, it draws attention to the potential risks associated with nebivolol, especially when combined with other medications, as seen in this case with prochlorperazine, which led to a life-threatening bradycardic event.

病例報告　112_C 130

縱隔腔腫瘤引起之肺動脈狹窄合併右心衰竭

A Mediastinal Tumor with Acquired Pulmonary Artery Stenosis Causing Right Heart Failure

葉建寬[1] 李純慧[2,3] 蘇柏嵐[4] 張獻元[1,3]

[1]國立成功大學醫學院附設醫院內科部心臟血管科 [2]國立成功大學醫學院附設醫院腫瘤醫學部

[3]國立成功大學醫學院臨床醫學研究所 [4]國立成功大學醫學院附設醫院內科部胸腔內科

Introduction

Acquired pulmonary artery (PA) stenosis is rare in adults. Etiologies include external compression by mediastinal tumors and inflammatory causes. This case reports 71-year-old woman with right heart failure, highlighting the diagnostic aspects of acquired PA stenosis.

Case presentation

This is the case of a 71-year-old woman who presented with dyspnea. She had insidious onset, progressive dyspnea and orthopnea six months prior to admission. The symptoms were accompanied generalized weakness and unintentional weight loss of 5 kilograms. She visited a primary care physician, and was referred to our hospital after a heart disease was suspected. Upon presentation, the patient appeared thin and chronically ill. Physical examination was remarkable for pedal edema. Basic hematologic and biochemical analyses were normal. Her electrocardiogram showed sinus rhythm with relative low voltage in the limb leads. Chest radiograph disclosed bilateral lung nodules and a suspicious mass over the left upper lung field. Heart failure was clinically suspected. Transthoracic echocardiography showed right-sided chamber enlargement, normal left ventricular systolic function, normal right ventricular function. Doppler interrogation indicated the maximum tricuspid regurgitation jet velocity was 4.46 m/sec, giving a right ventricular systolic pressure (RVSP) of 79 mmHg, indicating high probability of pulmonary hypertension (PH). The patient was treated with diuretics. A ventilation/perfusion (V/Q) lung scan was arranged, and showed perfusion deficits in both lungs, with the deficits more prominent over the left lung. Right heart catheterization one month later showed normalization of pulmonary hypertension, with measured mean pulmonary arterial pressure (PAP) being 22 mmHg. The pulmonary arterial wedge pressure was elevated (20 mmHg). Pulmonary angiography was performed to rule out partially-resolved pulmonary embolism and showed 70% stenosis of the left main PA with normal distal pulmonary arteries. External compression was highly suspected. Contrasted chest computed tomography (CT) showed a large tumor (6.8 × 3.2 × 4.3 cm) with calcification, located at the anterior mediastinum and left upper lung with encasement of the left main pulmonary artery. Bilateral lung metastases were also present. CT-guided needle biopsy of the mediastinal mass was performed. Histopathology findings revealed infiltrating thymic carcinoma with epithelial cells arranged in nests within a fibro-hyaline stroma. Immunohistochemically, the tumor cells are positive for p40, CD5 and CD117. Thus, the final diagnosis was thymic carcinoma, Masaoka stage IVB. The patient declined further treatment after thorough explanation, and is on best supportive care.

Discussion

Acquired PA stenosis may be caused by extrinsic compression by various mediastinal neoplasms,

while reported non-neoplastic etiologies include fibrosing mediastinitis, mediastinal cyst, thoracic aortic aneurysm (Batra et al., 2021). It is rare for mediastinal neoplasm to cause enough compression of the PA to produce hemodynamically significant obstruction. This may be due to the tendency of mediastinal tumors to grow laterally rather than anterior-posteriorly (Marshall & Trump, 1982). Chest pain and dyspnea are the most common symptoms, and the clinical manifestations may resemble pulmonary embolism (Shields et al., 1980). Compression of either the right or left main PA without involvement of the main PA is more common when the mediastinal neoplasm compresses the pulmonary vasculature (Batra et al., 2021). In such instances, right heart catheterization with pulmonary angiography can assess hemodynamics and to confirm and assess the degree of stenosis. The treatment of extrinsic compression of the PA is treating the underlying cause (Batra et al., 2021). Treating unilateral PA stenosis with stenting caused by external compression may lead to clinical improvement temporarily, and may be considered as a palliative management option in selected cases (Fierro-Renoy et al., 2002; Müller-Hülsbeck et al., 1998).

Among mediastinal tumors, around 20-50% are thymic epithelial tumors (Kelly, 2013; Venuta et al., 2010). Thymic carcinomas represent less than 1% of all thymic malignancies, and are commonly located in the anterosuperior mediastinum (Eng et al., 2004). Common presenting symptoms include cough, chest pain, phrenic nerve palsy, and invasion of the great vessels (Jung et al., 2001). On chest CT, thymic carcinoma may contain necrosis or calcification (Lee et al., 1991). Thymic epithelial tumors may directly invade or compress mediastinal structures, including the great vessels, cardiac chambers, even the coronary arteries (Arrossi et al., 2022; Ayuna et al., 2021). Thymic carcinomas are aggressive tumors, and survival depends on initial clinical staging and whether negative margins during resection could be achieved. The 5-year overall survival for stage IV thymic carcinoma is 17-24% (Litvak et al., 2014). For thymic carcinoma with distant metastases, systemic chemotherapy is utilized, and commonly includes cisplatin (Eng et al., 2004).

In our case, the presence of chronic symptoms, right-sided chamber enlargement, high probability of PH together with perfusion defects on lung perfusion scan indicates the possibility of chronic thrombo-embolic PH (CTEPH). However, the presence of significant unintentional weight loss implies that CTEPH-mimics should be considered (Narechania et al., 2020). The calcification of the tumor may harden its texture to cause significant compression. The discrepancy between the estimated RVSP on echocardiography and the measured mean PAP may be caused by treatment of diuretics, but also highlights the importance of correct measurement by right heart catheterization.

Conclusion

In patients with symptoms of pulmonary hypertension and features of CTEPH who also has significant weight loss, mimics CTEPH should be excluded. Thymic carcinoma is a rare cause of acquired PA compression, and endovascular stenting may be considered if conservative measures fail as a palliative treatment option to alleviate symptoms.

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病例報告　112_C 131

登革熱患者合併次發抗藥性豚鼠產氣單胞菌菌血症：菌株毒性分析

Secondary *Aeromonas caviae* bacteremia with antimicrobial resistance in a patient with Dengue fever: a study of virulence factor

周宣彣 陳柏齡 蔡進相
成大醫院內科部

Introduction

Dengue fever is a well-known mosquito-borne tropical viral disease in southern Taiwan. The symptoms of dengue fever range from asymptomatic to life-threatening condition. Secondary infections in dengue patients are common, especially among elderly patients. Timely appropriate antibiotic treatment is needed to decreased mortality of the patients. *Aeromonas caviae* can be isolated from a variety of aquatic environments including drinking water, and can lead to serious infections such as diarrhea and other extraintestinal disease including soft tissue infection, pelvic abscess, bacteremia, and meningitis. Here, we reported a case of dengue infection with *Aeromonas caviae* bacteremia with multiple drug resistance.

Case presentation

An 87-year-old man who has asthma under inhalation steroid, presented to emergency department with high fever for one day with dizziness, sputum production, fatigue and poor appetite. Routine lab showed impairment of renal function test and anemia. He was tested positive for dengue fever by serum NS1 antigen and dengue virus nucleic acid amplification tests. Initially he received supportive care; five days after admission, fever recurred with shortness of breath. Lab revealed no leukocytosis but thrombocytopenia. Empirical antibiotic ceftazidime was prescribed due to suspicion of secondary bacteremia infection, and then was switched to ertapenem since *Aeromonas caviae* was yielded from blood cultures, resistant to third-generation cephalosporins. He experienced intermittent asthma attack during hospitalization and short-acting bronchodilator is needed. His symptoms improved after medication and so did thrombocytopenia. The patient was discharged under the relatively stable condition with oral ciprofloxacin. Further identification by *rpoD* sequencing to re-confirmed the species by comparison with reference sequences available in the GenBank database using BLAST, which showed the isolate was 99% identical with *A. caviae.* Study of virulence factors was conducted to detect the genes encoding heat-stable enterotoxin (ast, 331bp), heat-labile enterotoxin (*alt*, 442 bp), cytotoxic enterotoxin (*act*, 232 bp), hemolytic gene (*hlyA*, 597 bp), lipase (*lip*, 382 bp), aerolysin (*aerA*, 252 bp), collagenase (*acg*, 792 bp), polar flagella (*fla*, 608bp), elastase (*ela*, 513 bp), and components of the type III secretion system (*ascF-ascG*, 789bp; *ascV*, 710 bp; *aexT*, 535 bp). The study of virulence factors included the reported isolate showed positive of lipase (*lip*, 382 bp), collagenase (*acg*, 792 bp), polar flagella (*fla*, 608bp) and elastase (*ela*, 513 bp).

Discussion

Concurrent bacteremia in adult patients with dengue fever is not common. Therefore, routine use of antibiotic is not recommended. However, according to previous research, 1/4 dengue patients with prolonged fever (>5 days) had a bacterial isolate. Appropriate antibiotic

treatment is needed to decreased mortality. *Aeromonas* can infect both immunocompromised and immunocompetent patients. While most of *Aeromonas* are susceptible to a wide range of antibiotics, include fluoroquinolones, co-trimoxazole, and cephalosporins (not including cefazolin), *Aeromonas caviae* isolated in our patient is resistant to co-trimoxazole and 3rd generation of cephalosporins.

Conclusion

Dengue fever is usually a self-limited disease. However, empirical antibiotic should be prescribed if the patients have signs of developing bacteremia or other secondary infection especially in immune compromised patient. *Aeromonas caviae* bloodstream infections and even with antimicrobial resistance can occur in such patients.

病例報告　112_C 132

Infective Endocarditis Masquerading as Pulmonary-Renal Syndrome: A Case Study

曾毓婷[1]　林威任[1,2]
國立成功大學醫學院附設醫院 [1]內科部 [2]內科部腎臟科

Introduction

Infective endocarditis (IE) refers to an infection of the endocardial surface of the heart, usually involves in heart valves or intra-cardiac devices. The most common manifestation is fever. The disease can cause systemic symptoms through multiple mechanisms, such as heart failure, septic emboli, metastatic infection or systemic immune reactions. Kidney involvement is one of the most common complications of IE, including renal infarction, abscesses, and glomerulonephritis (GN). Here, we shared a case presented with acute GN complicated by IE, mimicking with pulmonary renal syndrome.

Case presentation

The 56 years-old man had a past history of hypertension. He was an alcoholism and denied illicit drug use.

The patient had been experiencing an indolent onset of left chest pain for two weeks. He reported dyspnea on exertion and general edema. He denied fever, foamy urine, or decreased urine output. He visited NCKUH Douliu branch clinic for help. Laboratory data showed poor renal function (blood urea nitrogen (BUN): 61.2 mg/dL, Creatinine (Cr): 4.38 mg/dL), leukocytosis (WBC: 14,100/μL, Seg: 73.2%), anemia (Hemoglobin: 10.3 mg/dL) and thrombocytopenia (Platelet: 59,000/μL). Urine analysis revealed microscopic hematuria, pyuria and proteinuria (RBC ≥100/HPF, WBC 10-19/HPF, ACR 1909 mg/g, PCR 4153 mg/g). Chest plain film showed mass-like lesion over left upper and right lower lung, along with right pleural effusion (Fig.1). He was admitted on 15, March 2021.

During the stay, progressive kidney injury (BUN 83.8 mg/dL, Cr 5.8 mg/dL) and hemoptysis were noticed. Bronchoscopy showed fresh bloody sputum in bilateral bronchi, which indicated diffuse alveolar hemorrhage. Renal echogram showed bilateral enlarged kidney size (Rt 12.5cm, Lt 13.5cm) without hydronephrosis. Computed tomography revealed ground glass opacities with consolidation foci and nodular opacities in the right middle lobe (RML), right upper lobe (RUL) and left upper lobe (LUL) (Fig 2). Blood culture on March 17 yielded gram-positive cocci. Empirical Ampicillin/sulbactam was administered. Under suspicion of rapidly progressive GN with pulmonary hemorrhage, he was transferred to NCKU-Tainan.

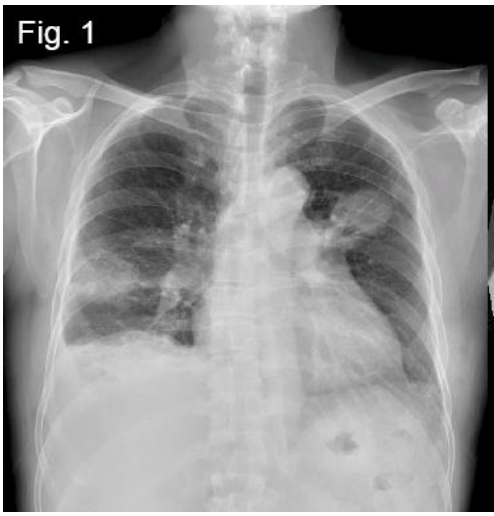
After transfer, he was intubated due to hypoxemic respiratory failure. Chest-X ray showed bilateral diffuse alveolar pattern with multiple focal consolidations (Fig 3). Bronchoscopy revealed bilateral bloody sputum, which was suspected to be indicative of diffuse alveolar hemorrhage. Plasmapheresis was performed on March 19 and 20. Hemodialysis was initiated since March 19 for progressively refractory metabolic acidosis and oliguria.

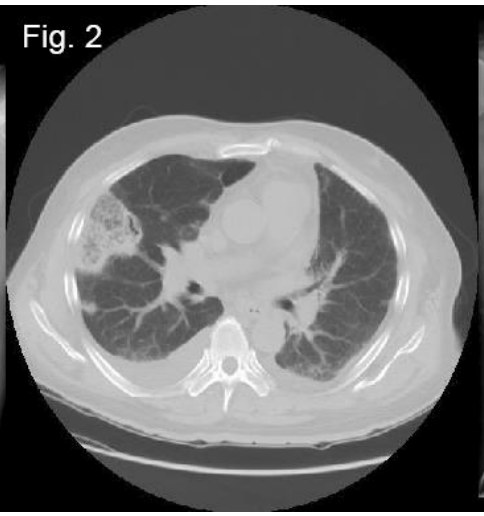
Serology study showed a mild decrease in C3 level (C3: 50.3 mg/dL) and normal C4 level (C4: 20.1 mg/dL). Serum antinuclear antibody (ANA), anti-double-stranded DNA antibody, anti-glomerular basement membrane (GBM) antibody, and anti-neutrophil cytoplasmic antibody (ANCA) were all negative.

Fig1 Left upper lobe, right lower lung mass-like lesion, right pleural effusion

Fig2 Ground glass opacities with consolidation in RML and RUL

Fig3 Diffuse alveolar pattern with multiple focal consolidations





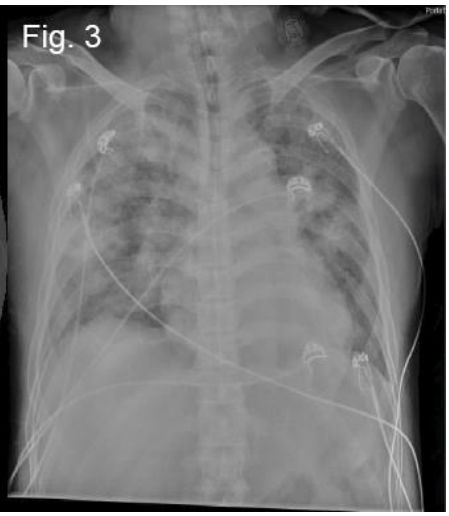
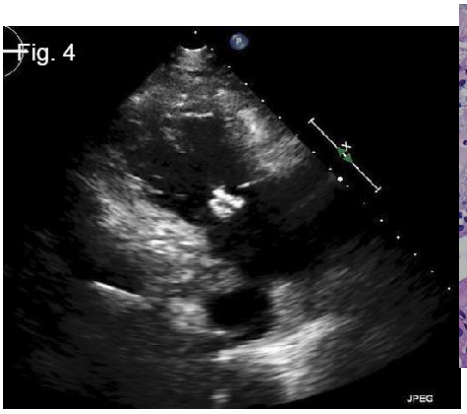
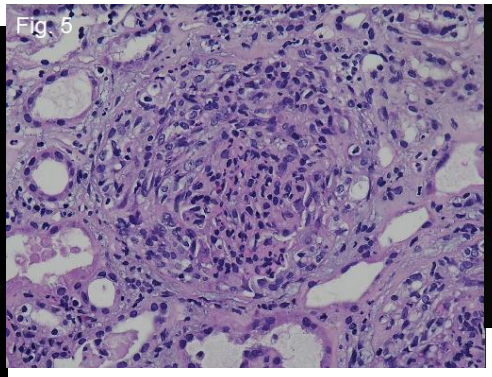


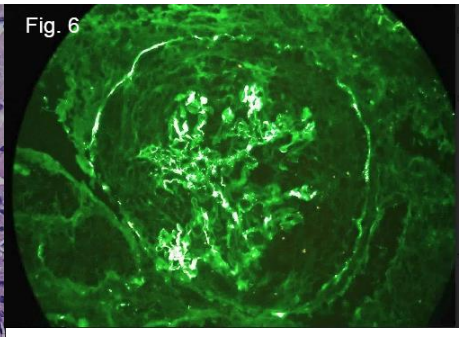
Fig4 A heterogeneous 1.3 cm mass- like lesion on tricuspid valve

Fig5 Cellular crescent under light microscopy

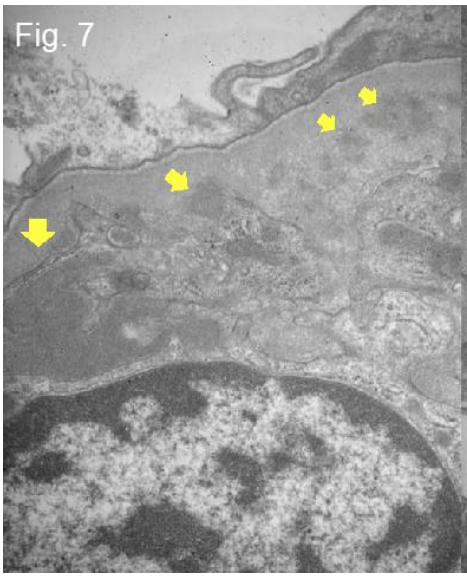
Fig6 Diffuse IgM/C3 deposits in the mesangium and capillary wall in immunofluorescence

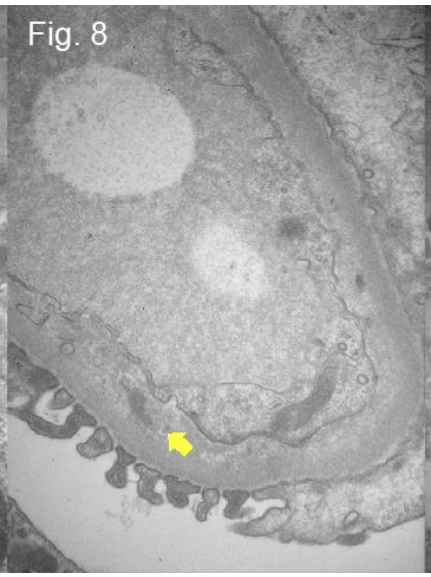


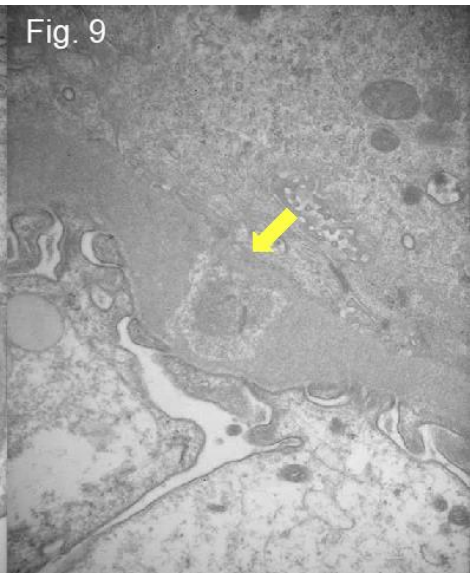




Electron microscopy showed multiple electron-dense deposition at mesangium (Fig.7); and scant deposition at subendothelial (Fig.8) and subepithelial area (with lucent area) (Fig. 9)







Persisted Enterococcus faecalis bacteremia was observed. The echocardiography revealed a

heterogeneous 1.3 cm mass-like lesion on the tricuspid valve (Fig 4). Renal biopsy showed cellular crescents under light microscopy (Fig 5), diffuse IgM/C3 deposition in the mesangium and capillary wall in immuno- fluorescence staining (Fig 6), and electron-dense deposits in the mesangium, subendothelial and subepithelial areas (Fig 7-9). Based on the presentation, laboratory results, imaging and histology, the final diagnosis was infective endocarditis-associated crescentic GN, complicated by pulmonary septic emboli with pulmonary hemorrhage. Definite antibiotics, ceftriaxone and ampicillin, were administered. His general condition gradually stabilized, and he was extubated on April 6. Renal function also improved gradually (BUN 27 mg/dL, Cr 2.34 mg/dL) with adequate urine output; hemodialysis was discontinued on April 16.

Discussion

The depression of complement, the diffuse deposition of immunoglobulins, and electron-dense deposits support an immune complex mechanism for IE-associated GN. The symptoms may present similarly to other autoimmune-associated rapid progressive glomerulonephritis (RPGN), such as anti-GBM disease or ANCA-associated vasculitis. Pulmonary-renal syndrome may be misdiagnosed when pulmonary involvement and hemoptysis are complicated by IE- related septic emboli. Inappropriate immuno-suppressive therapy could lead to a poor prognosis and even mortality. Therefore, we need to consider this differential diagnosis before initiating immunosuppressant therapy for RPGN.

病例報告　112_C 133

B 細胞急性淋巴性白血病/淋巴癌伴隨罕見髓外侵犯部位：胸腔積液和縱膈腫塊

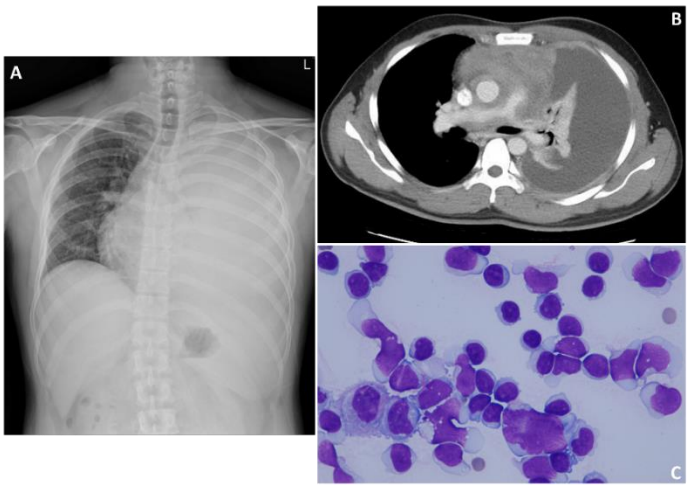
B-cell acute lymphoblastic leukemia/lymphoma with unusual sites of extramedullary involvement: pleural effusion and mediastinal mass

劉柏岑[1] 許雅婷[2]
[1]國立成功大學醫學院附設醫院內科部 [2]國立成功大學醫學院附設醫院內科部血液科

Introduction

B-cell acute lymphoblastic leukemia/lymphoma is a rare but highly aggressive hematologic malignancy and frequently affects extranodal sites, including bones and skin.

Case presentation



A 36-year-old male with no past medical illness developed dry cough and progressive dyspnea on exertion in 2 weeks. At the outpatient department at National Cheng Kung University Hospital, a chest radiograph revealed massive left pleural effusion with mediastinum shifting to the right side (panel A). He underwent thoracentesis, and the analysis revealed exudate characteristics (fluid protein 4.6 g/L protein; serum protein 4.8 g/L). The leukocyte count was 2871 cells/μL, with abnormal cells >50% present as lymphocytosis. The gram stain, acid-fast stain, and cultures were sterile. Therefore, he was admitted to the ward, and laboratory investigations showed a white blood cell count of 6200 cells/mm comprising 4.1% of blasts. Bone marrow biopsy demonstrated a focal excess of blasts, around 10%, which is positive for CD34, PAX-5, TdT, and negative for CD3. B-lymphoblastic leukemia with bone marrow involvement is favored. Whole-body computed tomography revealed a tumor in the anterior mediastinum that is approximately 9 cm in diameter with encasement of the great vessels (panel B). CT-guided biopsy for anterior mediastinal tumor was performed, which revealed monotonous small lymphoid cells with scant cytoplasm and indistinct nucleoli, positive for PAX-5 and TdT, while negative for CD3. Pleural effusion was sent for flow cytometric analysis and showed abnormal cells with positive for CD45, CD34, CD19, and TdT, and negative for CD3, which suggested acute B-cell lymphoblastic cells (panel C). Cytogenetic analysis of the sample from pleural effusion revealed complex karyotypes with 44~47, XY, add(3)(?q29)[18], t(5;12)(q13;q24.3)[14], ?add(7)(p15)[18], +19[17][cp18].

Discussion

B-cell acute lymphoblastic leukemia may present as pure leukemia, primary involvement of extramedullary lesions, or both. Extramedullary involvement is frequent with common sites of the central nervous system, spleen, liver, lymph nodes, and testis. B-ALL with mediastinum involvement is extremely rare.

病例報告　112_C 134

Acyclovir neurotoxicity in a peritoneal dialysis patient presented with herpes encephalitis

蘇億祥 [1]　吳安邦 [1,2]
國立成功大學醫學院附設醫院 [1] 內科部 [2] 內科部腎臟科

Introduction

Acyclovir is commonly used as an antiviral medication in herpes zoster viral infection. However, it has some adverse effects that need to be put in mind such as acute kidney injury, neurotoxicity, and thrombotic microangiopathy. Because the excretion of the acyclovir is from urine, those with kidney impaired should pay attention to the dosage of the acyclovir and its side effects. Especially the patients with end stage kidney disease.

Case description

This 69 year old man has underlying disease of hypertension, vertebral arterial aneurysm, gout and end stage kidney disease (ESKD) under peritoneal dialysis (PD). He has a past history of colonic carcinoma in situ after operation. His basic activity of daily life is independent with clear consciousness.

The patient was under his usual status 5 days before admission, then complained of painful zosteriform group vesicles over the left buttock and left scrotum. He received valaciclovir from the dermatologist outpatient department with daily dosage 500 mg. However, he had general weakness with decreased memory and auditory hallucinations. So he was brought to the emergency room one day before admission. At our emergency room, a non-remarkable finding showed on hemogram and biochemistry. No mass lesion nor intracranial hemorrhage was noticed by brain computed tomography (CT). He was admitted under the impression of herpes encephalitis and valacyclovir encephalopathy needed to be ruled out.

Cerebrospinal fluid (CSF) showed lymphocytic dominant pleocytosis and positive varicella-zoster virus nucleic acid. Awake electroencephalography (EEG) revealed mild diffuse cortical dysfunction and subcortical dysfunction without epileptiform discharges. Brain magnetic resonance imaging showed subcortical and periventricular white matter changes. Acyclovir was administered with daily dosage 300 mg (5 mg/kg/dose) for the impression of varicella zoster virus encephalitis after discussion with a neurologist. The PD therapy was kept.

Nevertheless, the patient began progressive deteriorating consciousness from the second day after admission with coma scale falling from E4V4M5-6 to E4V1M4. The awake EEG showed diffuse severe cortical dysfunction. No evidence of intracranial hemorrhage or large territory infarction was noticed by brain CT.

Nevertheless, CSF study showed improving pleocytosis. Therefore acyclovir neurotoxicity was suspected. Although acyclovir dose was adjusted based on the recommendation for peritoneal dialysis, we still tried to taper down the dosage from 300 mg to 150 mg per day.　Moreover, PD was shifted to hemodialysis for enhancing the clearance of acyclovir since the fourth day after admission based on the uncertainty medicine clearance of PD.

His consciousness gradually improved after acyclovir adjusted and HD. He returned to his basic consciousness – E4V5M6 on the eighth day after admission (ie. 4 days after acyclovir adjusted). His EEG reported the condition went better and his pleocytosis of CSF was

improved. The 21 days course of acyclovir was finished and he was finally discharged on the 30th day after admission with fair consciousness.

Discussion

Acyclovir neurotoxicity is a rare condition but it is a serious condition that might cause the patient confusion, altered level of consciousness, hallucinations, agitation and dysarthria. Especially in the patient with impaired kidney. A systematic review reported in 2021[1] that included 119 cases documented 83.3% cases had renal impairment and 57.1% (n = 68) with ESKD.

TABLE 1. The CSF study during the patient's admission

	2022/12/12	2022/12/16	2022/12/29
	0 day	4th day	27th day
WBC(/μL)	49	38	18
GLU(mg/dL)			63
TP(mg/dL)			59
Lactate(mmol/L)			1.3

The global mean of onset of symptoms was 3.1 days ± 4.3 (0.2-28) after the start of antivirals. 74.4% of the patients had a recovery of ≤7 days.

In this case, we changed the RRT strategy to HD because of the uncertainty clearance of PD. A case report published in 1992[2] presented that the neurotoxicity might be successible to be treated with hemodialysis for lowering the concentration of serum acyclovir.

In conclusion, we must adjust acyclovir dose in the CKD patient, especial those under dialysis. Due to uncertainty clearance of acyclovir during PD therapy, temporary hemodialysis may be a choice in those suspecting with acyclovir neurotoxicity.

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病例報告　112_C 135

肺炎鏈球菌感染導致的壞死性筋膜炎與腦膜炎作為多發性骨髓瘤的初始表現：個案報告

Pneumococcal necrotizing fasciitis and meningitis as the initial manifestation of multiple myeloma: A case report

方鏡齊[1] 謝宗達[2] 李仁傑[2]
[1]成大醫院內科部 [2]成大醫院重症加護科

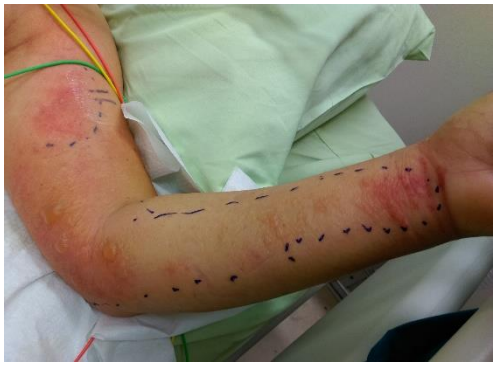
Introduction

Invasive pneumococcal disease (IPD) poses a consistent threat to elderly population, with an annual incidence ranging from 6.3 to 12.4 per 100,000 population and case fatality rate of 22.3-35.3% in Taiwanese elders between 2008 and 2017[1]. We report a diabetic patient who presented with necrotizing fasciitis and meningitis caused by *Streptococcus pneumoniae*, and how this severe infection unveiled the underlying multiple myeloma.

Case Presentation

A 73-year-old woman presented with an acute onset of consciousness disturbance. She experienced progressive painful erythema with weakness of left shoulder and bilateral thigh for two weeks. Her medical history included hypertension and diabetes mellitus with a hemoglobin A1c of 7.9%. She worked in an orchard and reported no fever, productive cough, or trauma. She had received 23-valent polysaccharide vaccine (PPV23) for *S. pneumoniae* five years before presentation.

Figure 1 Wound appearance



The physical examination showed erythematous patches with bullae formation on her left shoulder, upper arm and forearm (Figure 1). Her laboratory studies revealed leukocyte count of 5800/μL with 31.5% in band forms, hemoglobin of 10.9 g/dL, creatinine of 2.2 mg/dL, sodium of 120 mmol/L, C-reaction protein of 43.1 mg/L, glucose of 712 mg/dL, as well as hyperlactatemia and ketoacidosis. The computed tomography disclosed subcutaneous soft tissue swelling and fascial thickening of left shoulder, upper arm and forearm (Figure 2).

She underwent endotracheal intubation for respiratory failure and was admitted to the intensive care unit (ICU), where she received intravenous ceftriaxone 2 grams once daily, and clindamycin 600mg every 8 hours. The blood culture yielded *S. pneumoniae*, serotype

Figure 2 CT image

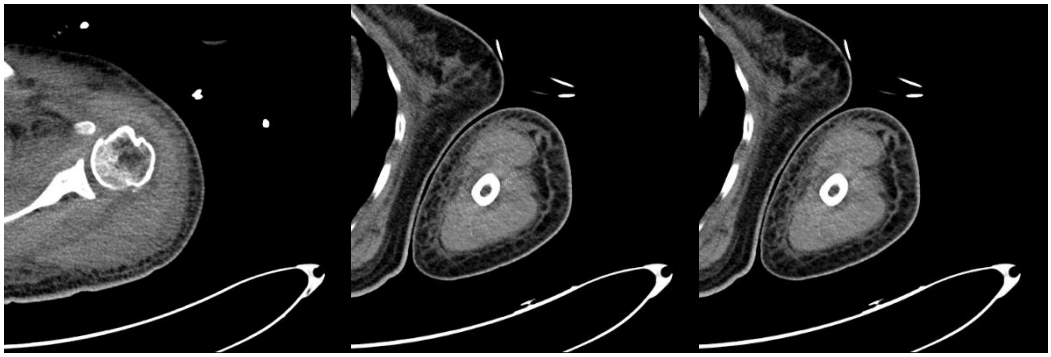
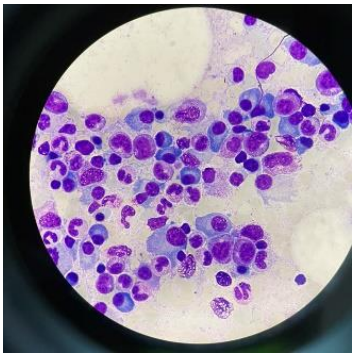


Figure 3 Bone marrow examination



15B, with penicillin MIC of 2 μg/mL and ceftriaxone MIC of 1 μg/mL. The urine pneumococcus antigen was positive. She underwent fasciotomy at the left upper arm and forearm on the second day, with *S. pneumoniae* yielded from the intra-operative specimen.
The cerebrospinal fluid (CSF) analysis on the fourth day showed an opening pressure of 32.9 cmH_2O, pleocytosis (leukocyte count of 235/μL, with 95% in segmented forms and 4% of lymphocytes), glucose of 59 mg/dL, total protein of 125 mg/dL, and lactate of 7.3 mmol/L. Although CSF bacterial culture showed no growth, *S. pneumoniae* nucleic acid was detected by the FilmArray® meningitis/encephalitis panel (BioFire, Salt Lake City, UT). The dose of ceftriaxone was increased to 2 grams every 12 hours accordingly, then shifted to cefotaxime on the fifth day due to cholestasis.
On the other hand, normocytic anemia and hypoalbuminemia of 1.8 g/dL were found upon admission. Further studies disclosed reversal of albumin/globulin ratio and monoclonal gammopathy. The bone marrow examination on the fifth day showed hypercellularity with plasmacytosis, confirming the diagnosis of multiple myeloma (Figure 3). She received induction therapy with VTd regimen (bortezomib, thalidomide, and dexamethasone) on the sixth day.
She regained full consciousness on the 13rd day, and was extubated on the 14th day. She was once transferred to the medical floor, but eventually died of hospital-acquired aspiration pneumonia on the 30th day.

Discussion

Necrotizing fasciitis (NF) caused by *Streptococcus pneumoniae* is extremely rare compared to other forms of IPD_2, as there were only 19 cases reported during 1970 and 2010, with ten of those patients died[3]. The patient represents the second reported case of pneumococcal NF and the first with concurrent meningitis in Taiwan[4]. The case highlights the importance of considering disseminated infection involving other organs in patients with pneumococcal NF[5]. Patients with multiple myeloma (MM) bear the highest risk of IPD amongst all chronic medical conditions, with a relative risk of 11.9 compared to that of general population[6]. The risk is followed by other conditions in which the production of antibodies to capsular polysaccharides is disrupted, including HIV infection, leukemia, asplenia, lymphoma, and end-stage renal disease. The fact that the patient remained susceptible to IPD despite proper vaccination against the same serotype implies an underlying immunocompromising condition to be aware of.

Conclusion

The case serves as a reminder that IPD could present in concurrent NF and meningitis, and the diagnostic workup should include searching for underlying compromised immunity.

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病例報告　112_C 136

免疫檢查點抑製劑導致腦下垂體炎合併第一型糖尿病 - 病例報告

Immune checkpoint inhibitors cause hypophysitis combined with type 1 diabetes - case report

黃冠喬[1] 鄭凱比[1,2] 歐弘毅[1,2]

[1]國立成功大學醫學院附設醫院內科部 [2]國立成功大學醫學院附設醫院內分泌暨新陳代謝科

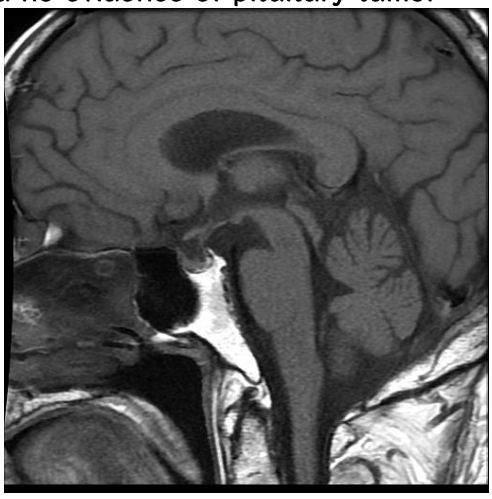
Introduction

Immune checkpoint inhibitors (ICIs) have been shown to improve the clinical outcomes of various advanced cancers. However, various kinds of endocrinopathies have been reported as the side effects of this novel therapy. Among them, thyroid dysfunction and hypophysitis are two of the most common endocrine side effects. Other less common endocrine disorders include type 1 diabetes mellitus (T1DM) and primary adrenal insufficiency, which occur in less than 1% of patients treated with ICIs. In recent years, several cases of multiple endocrinopathies related to ICIs have been discovered. However, cases of concurrent hypophysitis and T1DM are very rare. Here, we report a case of combined these two ICIs-related endocrine disorders with 2 years of follow-up.

Case presentation

A 64-year-old man with esophageal cancer who was receiving immunotherapy with ipilimumab (anti-CTLA4) and nivolumab (anti-PD-1) was admitted with nausea and vomiting. The patient has no history of diabetes. The fasting blood glucose 1 month before admission was 87 mg/dL. However, on admission the blood glucose was 1026 mg/dL, the A1C was 7.6%, and ketoacidosis was found (pH 7.13, HCO3- 5.3 mmol/L, blood ketones (β-HB) 6.6 mmol/L). Further testing showed low C-peptide level (<0.01 ng/mL) and negative for glutamic acid decarboxylase (GAD) antibody.

Figure 1. Sellar MRI with contrast (T1 sagittal) showed no evidence of pituitary tumor



Therefore, a diagnosis of T1DM associated with ICIs was made. In addition, despite euthyroid, panhypopituitarism with central adrenal insufficiency (ACTH < 1.0 pg/mL, cortisol AM 0.94 μg/dL), hypogonadotropic hypogonadism (LH 2.1 mIU/ mL, FSH 3.4 mIU/mL, testosterone 14.9 ng/dL), low prolactin (<0.1 ng/ml) and low IGF-1 (29.07 ng/ml) levels were found. An MRI of the sella was arranged, and no pituitary lesions were seen. Therefore, intensive insulin therapy with a basal bolus regimen and steroid supplementation were started during admission. Later outpatient follow-up showed that the patient's endogenous insulin secretion function was still poor (C-peptide was still <0.01 ng/mL 2 years after the onset of diabetic ketoacidosis), and the pituitary function was still low. In an ACTH stimulation test performed two years after hypophysitis diagnosis, baseline cortisol level was 0.36 μg/dL and one hour after ACTH injection was 2.77 μg/dL.

Discussion

Immune checkpoint inhibitors (ICIs) are monoclonal antibodies that bind to cytotoxic T-lymphocyte antigen 4 (CLTA-4), programmed cell death ligand-1 (PD-1) and its ligand PD-L1, thereby enhancing the antitumor response. Hypophysitis is an ICIs-induced endocrinopathy which the clinicians need to pay attention on. Once it happens, the most common manifestations are central adrenal insufficiency, hypogonadotropic hypogonadism, and central hypothyroidism. Of these, central adrenocortical insufficiency is an urgent and potentially fatal complication if not recognized. In this case, prompt treatment with corticosteroids is essential. Insulin-dependent diabetes, although uncommon, is also a noteworthy side effect of immunotherapy. Patients often suffer from a rapid loss of beta-cell function accompanied by an acute progression to hyperglycemia. What's more, about sixty percent of patients present with diabetic ketoacidosis, which is a life-threatening condition. Most ICIs-related endocrine disorders are irreversible and require long-term follow-up and management.

Conclusion

Hypophysitis and T1DM are two potentially fatal complications of ICIs if undiagnosed. Although the simultaneous occurrence of both complications is rare, clinicians must be aware of this possibility. In this case, timely diagnosis and prompt supplement of insulin and hormones are crucial.

病例報告　112_C 137

以漸進性嚴重蛋白尿及顯微性血尿為表現的增生性腎絲球體腎炎

Proliferative glomerulonephritis with monoclonal immunoglobulin deposits presenting as progressive heavy proteinuria and microscopic hematuria

林靚鈞[1] 陳盈妊[2] 李佳駿[1]

[1]國立成功大學附設醫院內科部腎臟科 [2]國立成功大學附設醫院病理部

Introduction

Monoclonal gammopathy of renal significance (MGRS) is a newly emerging disease entity that refers to kidney diseases caused by monoclonal gammopathy of undetermined significance (MGUS). In MGUS, production of monoclonal gammopathy is presented, yet the criteria of hematological malignancy are not met. The term "MGRS" fills the diagnostic gap between the premalignant stage with end-organ damage and hematological cancers. MGRS disorders have various forms and are classified based on distinct pathological patterns. One rare form that was just described recently is called proliferative glomerulonephritis with monoclonal gammopathy deposits (PGNMID). We present a case of 63-year-old female patient with MGUS and progressive heavy proteinuria, who was diagnosed with PGNMID through renal biopsy.

Case presentation

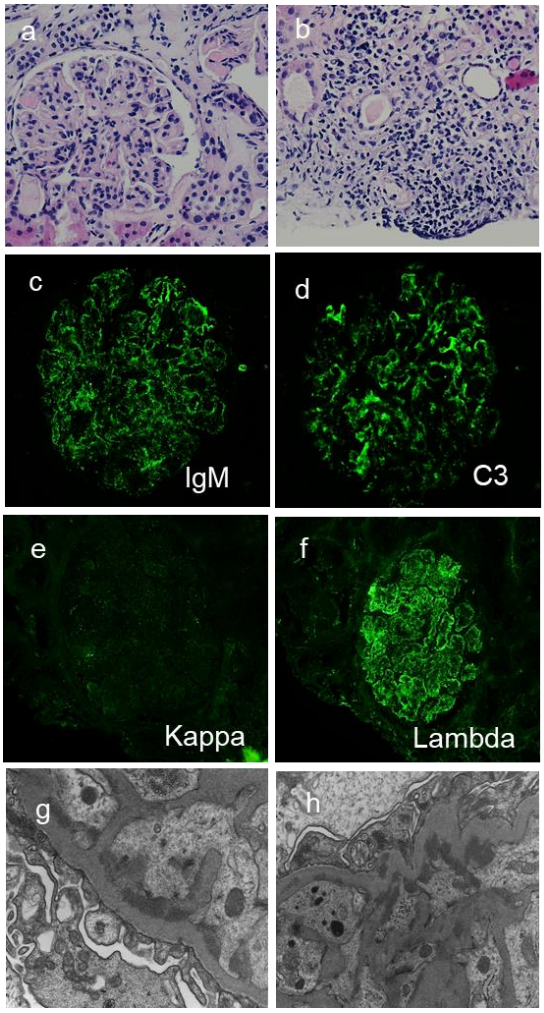
Variable	Result	Unit
Blood		
WBC	4.3	10^3/μL
Hb	9.1	g/dL
Plt	305	10^3/μL
Seg	67.3	%
Eos	0.4	%
Baso	0.9	%
Mono	13.2	%
Lymph	18.2	%
BUN	26	mg/dL
CREA	0.47	mg/dL
eGFR	≧90	
AST	39	U/L
ALT	30	U/L
Albumin	3.8	g/dL
Total protein	3.8	g/dL
Urine		
CREA	65	mg/dL
PCR	2338	mg/g
ACR	1723.1	mg/g
TP	152	mg/dL
MICROALB	112	mg/dL
Urinanalysis		
SG	1.014	
pH	6	
PRO	100	mg/dL
GLU	Negative(<50)	mg/dL
Blood	10	cells/μL
RBC	20-29	/HPF
WBC	0-5	/HPF
Bacteria	Negative	Negative
Hyaline	Negative	/LPF
Cast	Negative	/LPF

Variable	Result	Unit	Range
HBs Ag	Non-reactive		
HCV Ab	Non-reactive		
RPR/VDRL	Non-Reactive		
ASLO	<25.0	IU/mL	<116
C3	17.1	mg/dL	58-147
C4	<1.7	mg/dL	11-35
Anti-DNA Ab	Negative		
Glomerular basement	0.9	U/mL	
ANA*	1:1280		Speckled
ANA*	Positive		Cytoplasm
ANCA	Negative		
Cryoprotein	Negative		
IgG4	3.53	mg/dL	3.92-86.4
IgG	1190.0	mg/dL	751-1560
IgA	535.0	mg/dL	82-453
IgM	105.0	mg/dL	46-304
IgE	3.92	IU/mL	<=100
Free kappa	37.88	mg/L	3.30-19.40
Free lamda	31.94	mg/L	5.71-26.30

A 63-year-old woman has underlying diseases of coronary artery disease, hypertension and hyperlipidemia under medical control. She was diagnosed with Sjögren's syndrome in January, 2017 based on typical symptoms of dry eye and dry mouth, positive anti-SSA and SSB antibodies and salivary scintigraphy. Regular follow-up of serum and urine immunoglobulin level, electrophoresis (EP) and immunofixation electrophoresis (IFE) was performed because of higher risk of lymphoma in patients with Sjögren's syndrome. Monoclonal free lambda light chain was firstly detected in serum IFE in October, 2017. The bone marrow biopsy revealed hypocellular marrow with increased plasma cells (mature plasma cells accounted for 15% of total bone marrow cells), leading to a diagnosis of MGUS with free lambda. The serum IFE result switched to monoclonal IgM lambda gammopathy in October, 2019. Besides, persistent microscopic hematuria and increasing heavy proteinuria

were detected (urine protein-to-creatinine ratio (UPCR) trend: 930 mg/g in July, 2022; 1200 mg/g in December, 2022; 2800 mg/g in February, 2023), with stable renal function. No peripheral edema, gross hematuria, nor urinary tract infection symptoms was reported. The immune profile revealed a high titer of antinuclear antibody (1:1280), low C3 and C4 levels. No cryoprotein, HBV, nor HCV infection was detected. Renal biopsy in February, 2023 revealed membranoproliferative glomerulonephritis (MPGN) pattern, moderate tubular atrophy, interstitial fibrosis, and interstitial infiltrations with mononuclear cells (mainly lymphocytes, some plasma cells and scant eosinophils) in light microscopy. Mesangial and capillary wall granular deposition with IgM and lambda restriction and C3 positivity were noted on immunofluorescence (IF). The electron microscopy (EM) study revealed diffuse electron dense deposition, predominantly in subendothelial and mesangial regions, with scant deposition in subepithelial area. Combining the findings of MPGN, with monoclonal immunoglobulin deposition in glomeruli and previously noted MGUS status, PGMNID was diagnosed. Since PGNMID is usually associated with hematological disorders including MGRS, multiple myeloma, and lymphoma, a second bone marrow biopsy was performed in March, 2023. The result demonstrated nearly normal cellularity, with increased mature plasma cells (15-20%). Since the clonal plasma cells did not exceed 10%, the result was compatible with MGRS status. Although clone-directed therapy with self-paid rituximab was suggested for treatment of PGNMID with IgM lambda, the patient refused due to financial concerns. Instead, she only received losartan and pentoxifylline for controlling proteinuria. One episode of acute kidney injury due to non-steroidal anti-Inflammatory drug exposure was ever noted in June, 2023, but was then improving after cessation of the drug. Moreover, proteinuria was stabilized with UPCR decreasing to 1532 mg/g in September, 2023 under current management.

Figure 1. The pathology findings of renal biopsy
(a) MPGN pattern in H& E stain (b) mild tubular atrophy and interstitial fibrosis, accompanied with mononuclear cell infiltration in interstitium, (c)-(f) strong granular positivity of IgM, lambda light chain and C3 in mesangial and capillary regions in IF, (g) and (h) electron dense deposition in subendothelial and mesangial regions in EM.



Discussion

MGRS belongs to one of the spectrums of renal diseases caused by monoclonal immunoglobulins. MGRS disorders are typically classified by organized or non-organized depositions. The first major classification is the organized depositions, which includes fibril type (naming immunoglobulin-related amyloidosis and fibrillary glomerulonephritis), microtubule type (such as immunotactoid glomerulonephritis and type 1 cryoglobulinemic

glomerulonephritis) and light chain proximal tubulopathy. The second is non-organized depositions, composed of monoclonal immunoglobulin deposition disease (MIDD), PGNMID, and C3 glomerulopathy with monoclonal gammopathy. PGNMID has its distinct features of (1) mostly MPGN, followed by endocapillary proliferation and membranous glomerulopathy pattern, (2) non-organized monoclonal immunoglobulin deposition in mesangial, subendothelial and sometimes subepithelial regions, (3) no extraglomerular involvement, and (4) absence of cryoglobulinemia. The pathogenesis involves monoclonal immunoglobulin deposition in glomerulus, causing complement activation and subsequent inflammation and cell proliferation.

Workup for hematological disorders and pathogenic clone identification are important. However, detecting circulating paraproteins and pathogenic clones are challenging in patients with PGNMID, especially in case of IgG3 deposition. Clone-directed therapy can improve renal and patient survival. In patients with plasma cell clones that usually secret IgG, IgA or light chain alone, a Bortezomib-based regimen, resembling treatment for multiple myeloma, should be given. In those with lymphocytic or lymphoplasmacytic clones that commonly secret monoclonal IgM, Rituximab is recommended. If no clonal cells or circulating monoclonal immunoglobulins are identified, an empiric regimen may be applied according to the class of monoclonal immunoglobulin deposition in the kidney. Daratumumab, an anti-CD38 monoclonal antibody, is under evaluation. The treatment aim at complete elimination or significantly reduction of the pathogenic monoclonal paraproteins.

Conclusion

MGRS disorders encompass a wide spectrum of diseases caused by monoclonal gammopathy, with PGNMID being a relatively rare type. PGNMID is characterized by glomerular involvement only, predominantly MPGN pattern, non-organizing monoclonal immunoglobulin depositions in mesangial, subendothelial and subepithelial areas. Clinical presentations include heavy proteinuria, nephrotic syndrome, microscopic hematuria, renal insufficiency and hypertension. Patient with PGNMID need thorough hematological evaluation, including monoclonal paraprotein surveillance and bone marrow biopsy. Clone-directed therapy like bortezomib- or rituximab-based regimens improve renal and patient survival. Specific treatment for PGNMID remains underdeveloped due to limited data from studies with small population. Long-term monitoring of hematological malignancies is guaranteed in this population.

病例報告　112_C 138

困難定位的二尖瓣裂

Difficult diagnosed mitral cleft lesion, a case report

王思翰 蔡惟全 李文煌
國立成功大學附設醫院心臟血管內科

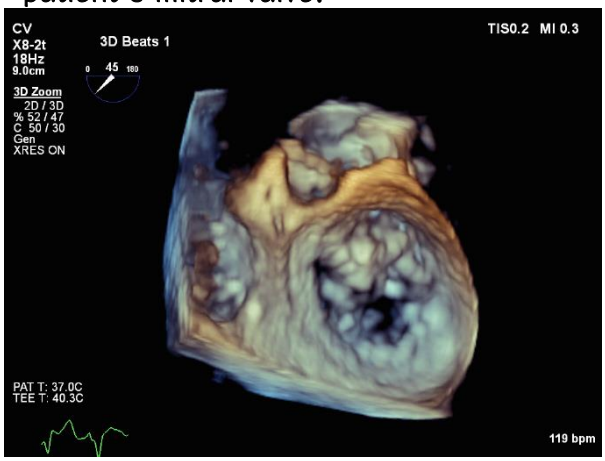
Introduction

Mitral cleft is a rare disease, which is often congenital heart disease associated. Endocardial cushion defect often contains ostium primum atrial septal defect, absence of the membranous septum and an anterior mitral leaflet cleft.[1] Mitral cleft often lead to congenital mitral regurgitation and need surgical repair or Mitraclip intervention.[2] 3D transesophageal echocardiography is believed to be the most accurate method to be done for assessment of the mitral valve structure.[3]

Case presentation

This was a 53-year-old woman with hypothyroidism, permanent atrial fibrillation, endocardial cushion defect, which was repaired 42 years ago and severe mitral valve regurgitation, which was regularly followed up at cardiologist's outpatient clinic. Surgical intervention was suggested after follow-up echocardiography revealed decline of left ventricle ejection fraction(69.6%→57%), elevation of left ventricular end systolic internal diameter(3.29→3.81) and increase of pulmonary artery systolic pressure(30 → 67mmHg) within 1 year. Transesophageal echocardiography was then performed for preoperative assessment and revealed severe mitral regurgitation and a mitral cleft at P2P3 with a posterior eccentric jet concomitant with A2 prolapse with a concentric jet and pulmonary vein systolic flow reversal. A severe tricuspid regurgitation with annulus dilation and a centric jet, dividing into two jets was also revealed. However, the patient hesitated about surgical intervention and the surgical plan was postponed.

Figure 1 3D reconstruction image of the patient's mitral valve.



Nevertheless, ascites developed with bilateral lower limbs edema and exacerbated dyspnea developed after 4 months of observation. Mitral valve repair with annuloplasty and tricuspid annuloplasty was thus performed. Unexpectedly, the mitral cleft was discovered to be at the patient's anterior leaflet(A2) during the operation. The patient tolerated the operation and followed up at cardiovascular surgeon's outpatient clinic and the follow-up echocardiography revealed residual mild mitral regurgitation.

Discussion

Cleft mitral valve is a rare disease, which was often associated with congenital heart disease and is the most common etiology of congenital mitral regurgitation.[4] Mitral cleft could be detected and located with 2D transthoracic echocardiography through parasternal short axis view.[1] 3D echocardiography provide higher prevalence of mitral cleft and was suggested to

be used to confirm the diagnosis of mitral cleft.[3,4] 3D transesophageal echocardiography using matrix array technology allows the examiner to display the beating heart instantaneously in real-time from any spatial angle, was likely to provide more accurate diagnosis and information of the mitral cleft lesion.[5]

We presented a case of mitral cleft associated with atrioventricular septal defect. Former transthoracic 2D echocardiography located the cleft at the anterior leaflet. However, transesophageal echocardiography suggested that the mitral cleft was at posterior leaflet between P2 and P3 through 3D reconstruction model. The mitral cleft was thus considered to be at the posterior leaflet until surgical intervention was done, which confirmed the location of the mitral cleft to be at the anterior leaflet. The reason of misinterpret of the cleft location was since the posteromedial commissure was mistaken as the mitral cleft.

Inclusion of aorta and left atrial appendage into the 3D reconstruction model and well angle of the 3D model help with correct interpretation of the location of the mitral cleft. 3D transesophageal echocardiography is subjected to the same problem of artifacts encountered on 2D echocardiography. The artifact might even appear more realistic after displayed with a 3D format.[6] The artifact of 3D reconstruction echocardiography will also obstruct accurate interpretation of the mitral valve structure. Some artifacts could be avoided by asking patients to stay still, suspend breath for a while, tuning gain setting or slightly change probe position, however, some artifact is inevitable. [6] Decreased artifact shall lead to more accurate assessment of the valve.

With 2D echocardiography under parasternal short axis view, transverse view of the mitral valve could be acquired. Mitral cleft could be detected with separation of the leaflet during diastolic phase and appearance of thin linear echoes at the defective leaflet during systolic phase.[1]

With above maneuvers and careful interpretation of the mitral valve image, accuracy of the diagnosis of mitral cleft anatomy is expected to improve.

Conclusion

We provided a rare case of mitral cleft, interpretated with 3D transesophageal echocardiography, the most accurate contemporary device to check structural defect. However, with inappropriate 3D image acquisition and the effect of echocardiography artifact, the valve structure could be misinterpreted. This could be possibly avoided by more carefully acquisition of the valve structure with less artifact, reference of 2D echocardiography and more closely interpretation of the adjacent anatomy structures. Accurate anatomy information leads to better pre-operative assessment and possibly better clinical outcome of the patient.

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病例報告　112_C 139

罕見疾病的罕見表現:以餐後嘔吐及腹痛為初始症狀的雙重抗嗜中性白血球細胞質抗體及抗腎小球基底膜抗體陽性疾病

An Unusual Presentation of an Unusual Disease: Abdominal Pain and Postprandial Vomiting as Initial Presentation of Dual ANCA and Anti-GBM Positive Disease

陳常胤[1] 陳盈妊[2] 蔡宏名[3] 吳忠泰[4] 林威宏[1,4]
國立成功大學附設醫院[1]教學中心 [2]病理部 [3]影像醫學部 [4]內科部

Introduction

Anti-neutrophil cytoplasmic autoantibody (ANCA) associated vasculitis (AAV) is a rare disorder affecting predominantly small-sized arteries with an incidence of 1.2 to 2.0 cases per 100,000 individuals.1 Anti-glomerular basement membrane (anti-GBM) disease is another small vessel vasculitis approximately 10 times rarer than AAV.2 Besides these two distinct diseases, dual ANCA and anti-GBM positive disease is diagnosed in patients who exhibit ANCA and anti-GBM antibody simultaneously. Double positive patients (DPP) only account for one third of patient with positive anti-GBM antibody and 6.9% of patient with positive ANCA. Here, we described a patient with dual ANCA and anti-GBM positivity presenting with unusual initial symptoms, abdominal pain and postprandial vomiting.

Case Presentation

This 55-year-old woman had a history significant for hypertension, dyslipidemia, and type II diabetes mellitus with medication control. One month before she presented to our hospital, she noted diffuse abdominal dull pain. She also complained about postprandial nausea and vomiting. Moreover, dry cough developed at the same time that abdominal pain started. She noted intermittent fever at home. She denied numbness, respiratory symptoms other than cough, blurred vision, decreased amount of urine, hematuria, dysuria, or bubbles in the urine. She visited NCKUH emergency department (ED) one week ago. Fever was documented. Creatinine was 0.98 mg/dL with a baseline at 0.64 mg/dL. Urinalysis showed microscopic hematuria, pyuria, and proteinuria. Antibiotics were provided. While dry cough resolved spontaneously after discharge from the ED, fever, nausea, and vomiting worsened in the following days.

The patient visited the ED again two days prior to admission due to frequent vomiting unrelated to oral intake and persistent high fever. Leukocytosis with neutrophilia was noted. Creatinine was 1.49 mg/dL. Worsened hematuria, pyuria, and proteinuria were observed. Urine and blood cultures were negative. Abdominal computed tomography (CT) showed bilateral nephromegaly and poor perfusion in the bilateral kidneys. Increase in mesenteric fluid infiltration was noted. The patient was then admitted for further evaluation. Immunofixation electrophoresis of urine and serum revealed no monoclonal gammopathy. Bone marrow biopsy did not find evidence of hematologic malignancy. Gallium scan revealed diffusely and symmetrically increased radioactivity in the bilateral kidneys. Mild degree of increased radioactivity over small bowels was observed. Nausea and vomiting subsided spontaneously after admission. Nevertheless, high fever persisted and rapidly progressive glomerular nephritis was diagnosed.

Titer of anti-nuclear antibody was 1:40. Titer of ANCA with a perinuclear pattern reported

1:640 while anti-GBM antibody was 12.6 U/mL. Renal biopsy later confirmed crescentic glomerulonephritis with concurrent presence of ANCA and anti-GBM antibody. Cyclophosphamide 400 mg was infused and fever disappeared immediately. Plasma exchanges for five times were performed. Methylprednisolone 40mg IV BID for two weeks followed by prednisolone 15mg PO BID were given. Hematuria and proteinuria improved gradually during treatment. Creatinine decreased from the peak at 3.76 mg/dL to 2.68 mg/dL before discharge. The patient is on regular outpatient follow-up. Cyclophosphamide will be infused monthly and prednisolone is continued.

Discussion

Dual positive disease, characterized by the presence of both ANCA and anti-GBM antibody, is an uncommon disorder that manifests clinical features resembling both AAV and anti-GBM disease. In contrast to anti-GBM disease, DPP experiences a more prolonged prodromal phase, akin to individuals diagnosed with AAV. During this prodromal period, systemic symptoms such as fever, general malaise, and weight loss are commonly reported.[3] However, the presenting symptoms of DPP was closer to those of anti-GBM disease instead of of AAV. These symptoms primarily revolve around renal and/or pulmonary manifestations. Renal involvement is observed in the majority (91.6%) of patients upon presentation. Pulmonary involvement is also frequently observed, affecting 63.2% of DPP. Furthermore, 42.1% of DPP exhibit a combination of renal and pulmonary manifestations. Extrarenal and extrapulmonary manifestations as presenting symptoms are relatively uncommon in DPP, accounting for one third of patients. Among these cases, only 2.7% of DPP exhibited gastrointestinal (GI) involvement.[4]

While the existing literatures on DPP did not specify the symptoms and mechanisms of GI involvement, it is logical to compare GI involvement in DPP with that in AAV, as anti-GBM disease typically presents only with renal and/or pulmonary symptoms. In AAV, GI involvement is thought to occur due to mesenteric ischemia resulting from inflammation of the arteries supplying the intestines and other GI organs.[5,6] The most common symptoms of GI involvement in AAV were abdominal pain (79%) and rectal bleeding (50%). Nausea and vomiting were reported in 33% patient while 27% had diarrhea. The abdominal CT findings of AAV with GI involvement included diffuse or multifocal bowel wall thickening with or without bowel distension. Ascites and bowel perforation had been reported.[7,8]

In our case, the patient exhibited symptoms commonly observed in chronic mesenteric ischemia. Namely, postprandial vomiting and diffuse abdominal pain. Abdominal CT images confirmed the presence of increase mesenteric infiltration, indicating mesenteritis. Additionally, increased radioactivity in the intestinal area on Gallium scan of our case could be a hint for active mesenteritis although Gallium scan was not able to pinpoint the precise location of the inflammation due to its technological limitation.

Diagnosis of GI involvement of vasculitis is challenging. Biopsy of GI tract are difficult to obtain. Moreover, superficial mucosal biopsies endoscopically obtained have a low yield. In one study, only 8 of 124 patients showed vasculitis findings histologically.[9] Most diagnosis for GI vasculitis relies on imaging. In small vessel vasculitis such as AAV, angiography seldom detects visible microaneurysm or arterial stenosis as observed in patients with polyarteritis nodosa.[8] In our case, increased mesenteric fluid infiltrate on abdominal CT is a radiologic manifestation similar to that in AAV patients with GI involvement.[7] Given the abdominal CT findings in combination with Gallium scan result and symptoms similar to those of mesenteric

ischemia, it is reasonable to speculate that GI symptoms in our case result from mesenteric inflammation related to dual ANCA and anti-GBM positive disease.

Conclusion

We presented a unique case of DPP manifesting abdominal pain and postprandial vomiting. Moreover, vasculitis-induced mesenteritis as the cause of gastrointestinal symptoms in DPP is an unusual presentation that requires careful approach for concise treatment.

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病例報告　112_C 140

Catheter-related thrombosis in a patient with sickle cell disorder

葉立浩 柯呈諭
成大醫院心臟內科

Introduction

In Taiwan, sickle cell disease (SCD) is not prevalent and rarely encountered in clinical practice. This may lead to physician's lack of understanding and awareness of this disease. SCD causes significant morbidity and mortality if untreated. In this report, we present a case of a patient who developed catheter-related thrombosis and acute myocardial infarction that eventually diagnosed with sickle cell disorder.

Case

A 26-year-old woman presented to the emergency department with chief complaints of chest tightness for days. This patient is an African descent in Saint Vincent and the Grenadines, studied in Taiwan as an international student. She had the past medical history of type 2 diabetes mellitus, hypertension, dyslipidemia, morbid obesity (BMI 41.6) and anterior ST-elevation myocardial infarction (STEMI) post primary PCI and stenting at left anterior descending artery (LAD) about 18 months before this admission.

This time, she had intermittent chest tightness with radiation to left neck and shoulder. Electrocardiogram (ECG) showed sinus rhythm and right bundle branch block, similar to previous ECG. Creatine kinase myocardial band (CK-MB) and high sensitivity troponin-T (hs-TnT) were within normal range. With the impression of unstable angina, coronary angiography was performed and showed no significant in-stent restenosis or thrombus over LAD. However, thrombosis was frequently noted over her vascular access (radial and brachial arteries) during hospitalization. On the next day after cardiac catheterization, she had intermittent attacks of chest pain again. ECG (Figure 1A) showed no notable ST-T change. Laboratory testing (Table 1) showed that the levels of CK-MB and hs-TnT were dynamically elevated.

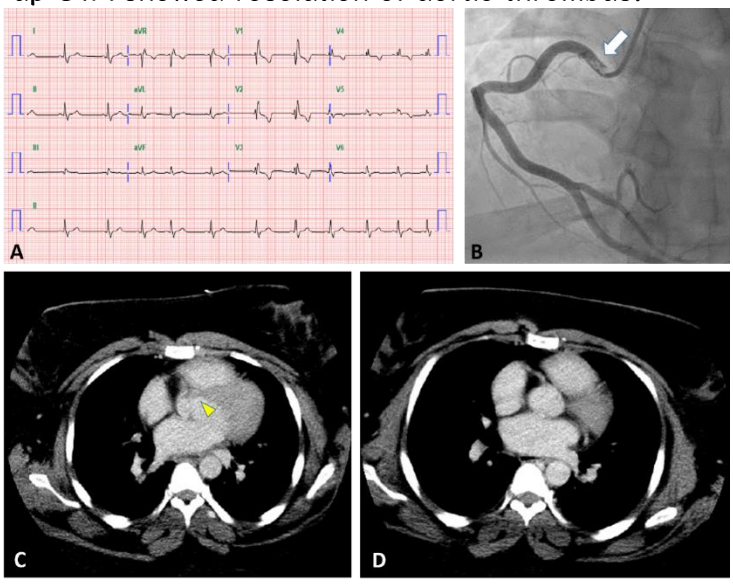

Figure 1. (A) The 12-lead ECG showed sinus rhythm, right bundle branch block, precordial lead T-wave inversion, similar to baseline. (B) Coronary angiography disclosed huge thrombus over ostium and proximal segment of RCA (white arrow). (C) Aortic CTA revealed thrombus at RCA ostium and right coronary cusp (yellow arrowhead). (D) Follow-up CTA showed resolution of aortic thrombus.

With the impression of non-ST-elevation myocardial infarction (NSTEMI), she underwent coronary catheterization (Figure 1B), which showed thrombus formation over ostium and proximal part of right coronary artery (RCA). Aspiration thrombectomy or other coronary intervention were not performed due to high embolic risk. Heparin and tirofiban infusion were administered. To clarify thrombus burden, aortic computed tomography angiography was performed, revealing filling defect in sinus of Valsalva, particularly right coronary cusp (Figure 1C), compatible with acute thrombosis over RCA ostium extending to aortic root.

Table 1. Important laboratory findings of the patient during hospitalization

	Result	Reference range
WBC (cells/μL)	7600	3300-9900
Hb (g/dL)	13.9	11.0-15.0
Hct (%)	42.7	33.3-44.4
MCV (fL)	80.4	80-100
RDW (%)	13.7	11.6-15.6
Plt (cells/uL)	371000	157-392
0hr CK-MB (ng/mL)	1.7	≤3.6
3hr CK-MB (ng/mL)	12.8	
0hr hs-TnT (ng/L)	21.3	99 percentile: 14.0
3hr hs-TnT (ng/L)	99.5	

RBC Morphology
Microcytosis (1+), normochromic

Hb Electrophoresis		
Hb form	Result	Normal range
Hemoglobin A (%)	55.7%	96.8-97.8%
Hemoglobin F (%)	0%	<0.5%
Hemoglobin A2 (%)	3.4%	2.2-3.2%
Hemoglobin S (%)	40.9%	0%

As multiple thrombotic events developed, testing for thrombophilia was done. The levels of protein C, protein S, antithrombin III, homocysteine, antinuclear antibody (ANA), lupus anticoagulant, anti-cardiolipin antibody, anti-β 2-glycoprotein I antibody were within normal limits. Considering her ethnic group, sickle cell disorder should be excluded. Hemoglobin (Hb) electrophoresis was performed (Table 1), expressing HbS (40.9%), HbA (55.7%) and HbA2 (3.4%), confirming that this patient had sickle cell trait. Given that she had recent exposure to cardiac catheterization, acute thrombosis of RCA ostium and coronary cusp may be contributed by catheter-related thrombosis and underlying sickle cell disorder.

During hospitalization, intravenous heparin was switched to warfarin. After receiving one-week course of anticoagulation, follow-up aortic computed tomography angiography showed that thrombus size was markedly reduced (Figure 1D). The patient was discharged in good condition with outpatient follow-up at cardiovascular and hematology department.

Discussion

Sickle cell disease is an inherited group of red blood cell disorders, resulting from the presence of a mutated form of hemoglobin, hemoglobin S (HbS). SCD affects millions of people, particularly common among those whose ancestors came from sub-Saharan Africa, South America, Central America, the Caribbean, Saudi Arabia, India and Mediterranean countries. SCD may cause significant morbidity and mortality, particularly in people of African ancestry. The distinctive features of SCD are vaso-occlusive phenomena and hemolytic anemia. Sickled red blood cells have markedly reduced deformability, increased adhesion to vascular endothelial cells, which lead to intravascular hemolysis, inflammation and activation of hemostatic mechanisms, causing vaso-occlusion crisis, organ ischemia and other systemic complications.[1]

The term of sickle cell disorders was used to refer to all conditions in which a person carries the sickle cell variant. Sickle cell disorders may be resulted either from homozygosity for the sickle mutation (Hb SS) or compound heterozygosity with another beta globin variant (for example, sickle-beta thalassemia, Hb SC disease). If the other beta globin gene is normal, the individual has sickle cell trait, a relatively benign carrier condition that is usually free from symptoms of sickle cell disease.[2]

Diagnosis of the sickle cell disorder can be made with gel electrophoresis, high performance liquid chromatography, isoelectric focusing, polymerase chain reaction or DNA sequencing.

In Taiwan, the most available diagnostic method is Hb electrophoresis. If Hb electrophoresis reveals that there is 0% Hb A, <2% Hb F, normal Hb A2, and the remainder Hb S, then the diagnosis of sickle cell anemia (HbSS) is confirmed. The diagnosis of sickle cell trait can be made by the pattern of >50% Hb A, 35 to 45% Hb S, and <2% Hb F by Hb electrophoresis.[3] People with sickle cell trait do not have an increased mortality rate or shortened life expectancy compared with the general population. However, sickle cell trait may exert a significant increased risk of exertional rhabdomyolysis and venous thromboembolism. In rare cases, splenic sequestration and infarction can develop at high altitude.[2] In comparison, arterial thrombosis in individual with sickle cell trait was rarely reported. In this case, RCA ostium and aortic thrombosis could be hardly explained by traditional cardiovascular risk factor of atherosclerosis, thus additional thrombophilia survey was warranted, revealing sickle cell disorder as a potential risk factor. In addition, recent exposure to coronary intervention may increase the risk of catheter-related thrombosis.

Conclusion

We reported a young female with sickle cell trait who developed catheter-related thrombosis and NSTEMI. Although sickle cell trait is thought to be relatively benign, increasing evidence suggests that individuals with sickle cell trait may have an increased risk of thrombosis. Future rigorous, evidence-based studies are warranted to address the causal relationship between sickle cell trait and vascular complications, providing potential way of risk modification.

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病例報告　112_C 141

一位重症病患之短暫極度胰島素阻抗現象

Transient Extreme Insulin Resistance in a Critically Ill Patient

魏秀育[1] 沈修年[2]
財團法人台南奇美醫學中心 [1]內科部 [2]加護醫學部

Background

Insulin resistance is a common feature in critically ill patients. However, the occurrence of transient extreme insulin resistance (EIR) requiring exceptional high-dose insulin is rare.

Case Report

A 68-year-old woman with type 2 diabetes, treated with oral anti-diabetic drugs, was admitted to the ICU due to pneumonia-induced sepsis presenting with out-of-hospital cardiac arrest. Her latest HbA1c level was 9.3%. Her initial glucose level was 574 mg/dL, osmolality was 328 mOsmol/kg, and ketone bodies were normal. After fluid, insulin and antibiotic therapy, her hemodynamics improved. Enteral feeding was started. The daily insulin requirement decreased from 108 units on day 1 to 22 units on day 3, maintaining a target glucose level of 150-200 mg/dL. However, hyperglycemia recurred after an episode of urinary tract infection with *Candidemia* on day 4. Her glucose level continued to rise despite an increasing rate of insulin infusion (1 unit/ml). The glucose level reached a maximum of 850 mg/dL on day 13 despite an insulin infusion rate of 155 units/hour. To avoid fluid overload, the infusate of insulin was changed to 20 units/ml. A reversal of insulin resistance was noticed on day 16 when the insulin infusion rate reached a maximum of 960 units/hour (a total dose of 18,224 units on that day) and then was rapidly tapered down to zero within 12 hours. There were 24 episodes of mild to moderate hypoglycemia during hourly monitor between day 17 and 20, even when hydrocortisone was given for vasopressor-dependent septic shock since day 17. Small doses of insulin were needed again since day 21. Despite the control of hyperglycemia, she eventually died of recurrent sepsis on day 25.

Discussion

Exceptional high-dose insulin infusion may be required in critically ill patients with stress-related EIR, which is typically transient. The highest reported insulin dose for critically ill patients with transient EIR was 91,580 units within 25 hours, including a maximal infusion rate of 20,000 units in a 2-hour period, administered to a patient with shock associated with diabetic ketoacidosis, targeting a reduction of the glucose level from 1,241 mg/dL to below 300 mg/dL. Clinicians should be aware of the phenomenon and cautious to avoid fluid overload and hypoglycemia during the steep titration of high-dose insulin infusion.

病例報告　112_C 142

Klebsiella pneumoniae 模仿隱球菌之中樞神經感染: 病例報告

Klebsiella pneumoniae mimicking Cryptococcus neoformans Infection in the Central Nervous System: Case Report

翁寧駿[1] 湯宏仁[2] 余文良[3]
奇美醫療財團法人奇美醫院 [1]內科部 [2]感染科 [3]加護醫學部

Introduction

Klebsiella pneumoniae(K.pneumoniae) can cause various can cause various infections like pneumonia, urinary tract infections, wound infections, and bloodstream infections. Instances of K.pneumoniae leading to central nervous system(CNS) infections are rare. As for CNS infection or meningoencephalitis, the analysis of cerebrospinal fluid(CSF) is crucial. The India ink staining of CSF is a sensitive for detecting Cryptococcus neoformans, which is surrounded by a thick capsule. In this report, we present a case where K.pneumoniae sepsis led to CNS infections. The patient's altered mental state and seizures prompted CSF analysis, showing positive India ink result, but culture identified K.pneumoniae. This established the diagnosis of K.pneumoniae-related sepsis complicating CNS infections.

Case presentation

A 47-year-old man was admitted due to general weakness and fever, associated with dizziness and headache. He had a history of alcoholic pancreatitis. Upon arrival at the emergency department(day 0), his vital signs included a temperature of 37.2°C, a heart rate of 116 beats per minute, a respiratory rate of 17 breaths per minute, and a blood pressure reading of 104/70 mmHg. Physical examination revealed drowsiness and distended abdomen. Laboratory tests indicated leukocytosis, elevated lactate levels, and hyperbilirubinemia. Brain CT scan revealed a subarachnoid hemorrhage (SAH). Blood culture growth confirmed K. pneumoniae infection. Further abdominal CT disclosed a well-enhanced 6 mm nodule in liver. Given the impression of sepsis, K.pneumoniae bacteremia, jaundice, and SAH, he was admitted for management and treatment. During his stay, he received treatment with Cefoperazone/Sulbactam. Seizures occurred twice after a fever episode on day 2. Then, his level of consciousness worsened, and muscle strength also decreased. An emergent brain CT showed an escalation of brain edema. As a result, he was transferred to the intensive care unit (ICU) on day 3.

In the ICU, he shifted infection control to Meropenem. A LP was performed, and the CSF analysis indicated a positive result for India Ink stain. However, Cryptococcus antigen tests were reported negative in CSF and serum. Filmarray of CSF did not detect Cryptococcal gene, either. Two days later (day 5), the CSF culture revealed K. pneumoniae. The thick capture also led to wrong reading to yeast in Gram stain. Following the antibiotics treatment, his consciousness improved, and his neurological status was closely monitored. Subsequently, he was successfully extubated on day 13 and transferred to the ordinary ward for following care.

Discussion

Analyzing CSF is crucial for identifying pathogens in acute CNS infections. Standard CSF

tests include cell count, protein levels, glucose concentration, Gram stain, special stains like India ink and acid-fast bacillus stain, VDRL test, and bacterial, fungal, and mycobacterial cultures. India ink staining plays a significant role by identifying capsule-covered microorganisms, particularly useful for distinguishing encapsulated yeast like Cryptococcus. These encapsulated yeasts manifest a halo-like appearance. Despite its traditional use for fungi, it's noteworthy that the bacterium K.pneumoniae, with a capsule shielding it, can also be detected using India ink staining. The polysaccharide structure capsular variants in K.pneumoniae are linked to disease severity. India ink staining showed no obvious differences in capsule between other pathogens. Thus, other methods like culture or antigen detection are essential for accurate diagnosis.

Conclusion

In Taiwan, there's a noticeable rise in community-acquired bacterial meningitis cases caused by K.pneumoniae. This case highlights the need to recognize this uncommon disease and underscores the importance of not disregarding routine lab data. Treating K.pneumoniae infections is becoming harder due to antibiotic resistance, including carbapenems and extended-spectrum β-lactamases. Survivors of K.pneumoniae meningitis have been treated with third-gen cephalosporins plus pefloxacin, gentamicin, or amikacin. Meropenem was used in one case, but sensitivity results weren't provided. Innovative treatment strategies are urgently needed for these recurring, severe healthcare-associated infections. Effective antimicrobial targets should ideally be species-specific, minimally toxic, and lack existing resistance mechanisms.

病例報告　112_C 143

由變性淋巴瘤激酶(ALK)抑制劑誘發的重度肌炎:病例報告

Severe Myositis Induced by Anaplastic lymphoma kinase (ALK) inhibitors : A Case Report

林湀宸[1]　郭雨萱[1,2]
[1]奇美醫院內科部　[2]奇美醫院腫瘤內科

Introduction

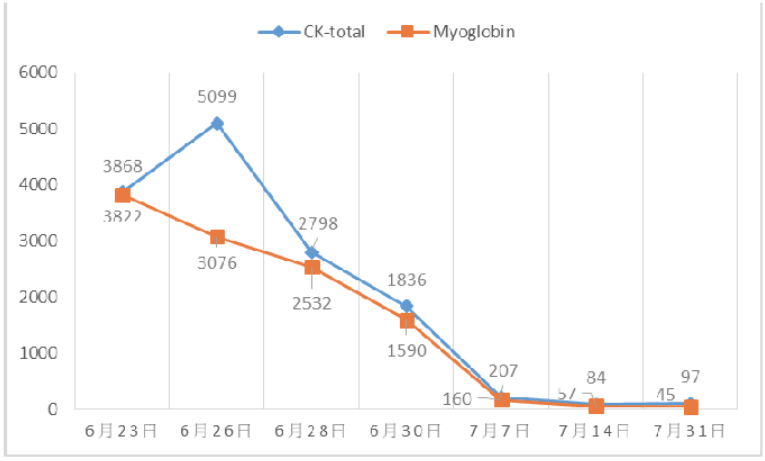
ALK (Anaplastic Lymphoma Kinase) inhibitors have been utilized in patients diagnosed with non-small cell lung cancer (NSCLC) harboring the EML4-ALK fusion gene. Infrequently, ALK inhibitors have been linked to notable muscular issues, such as muscle weakness, as reported in a small number of instances. In this case study, we describe a patient who encountered severe myositis after starting alectinib, an ALK inhibitor. Notably, the patient's condition significantly improved with hydration and discontinuation of the medication.

Case presentation

A 66-year-old woman with a medical history of stage I adenocarcinoma of the rectosigmoid colon (pT1N0M0) underwent laparoscopic low anterior resection and enterolysis on July 18, 2022. Following this, she was diagnosed with stage IIIA mucinous adenocarcinoma of the lung in the right upper lobe (pT2bN2M0) and underwent video-assisted thoracoscopy surgery for right upper lobe lobectomy and lymph node dissection on September 6, 2022.

She underwent six cycles of chemotherapy with Navelbine plus cisplatin, starting in October 2022 and completing in January 2023. However, a subsequent chest CT on March 30, 2023, revealed a persistent enlargement of the right subvascular lymph node, suggestive of possible metastasis. This finding was subsequently confirmed by a PET scan and pathology. Genetic sequencing identified an ALK mutation, leading to the initiation of Alectinib treatment at a dose of 600 mg twice daily, commencing on May 26, 2023.

Unfortunately, one month after the initiation of this new treatment, the patient began experiencing numbness in all four limbs, unsteadiness, and ataxia. She sought medical attention at our oncology and neurology outpatient department on June 23, due to persistent discomfort and weakness that had progressed to the point where she was unable to walk. During her visit to the emergency room (ER), laboratory tests revealed elevated levels of myoglobin and total creatine kinase (CK). Serum creatine kinase (CK) levels were notably elevated at 5099 U/L (normal: <168), and serum myoglobin levels were elevated at 3076 ng/ml (normal: <106).



While hospitalized, the treatment of ALK inhibitor was discontinued, and the patient received hydration. Subsequent laboratory tests indicated a declining trend in these markers, and her clinical condition significantly improved. After discharge, Alectinib was reduced to 300 mg once daily and then gradually titrated back up to 450 mg twice daily.

Serum creatine kinase (CK) levels were closely monitored and remained within normal ranges.

Discussion

This patient, diagnosed with advanced non-small cell lung cancer (NSCLC), experienced significant muscle weakness following treatment with ALK inhibitors, notably resulting in an inability to walk. According to reports from the United States Food and Drug Administration (FDA), severe muscular issues, such as grade 3 myalgia or musculoskeletal pain and elevated creatine kinase (CK) levels, occurred in 0.7% and 4.0% of patients treated with alectinib, respectively. While severe adverse muscular events leading to noticeable muscle weakness are rare, the current case underscores the potential of ALK inhibitors, especially alectinib, to induce such effects.

Conclusion

Many of the side effects linked to alectinib remain incompletely understood, such as myalgia, peripheral edema, and bradycardia. A deeper comprehension of the underlying mechanisms responsible for these effects would greatly assist in their effective management.

病例報告　112_C 144

無症狀鹿角結石之糖尿病患，同時併產氣性腎盂腎炎、輸尿管炎及膀胱炎

Silent staghorn stone complicated with coexisting emphysematous pyelonephritis, ureteritis and cystitis in a diabetic patient

簡志強 [1] 吳梓甄 [2]
[1] 奇美醫院腎臟內科 [2] 奇美醫院

Introduction

Emphysematous urinary tract infection (UTI), which are accompanied by gas formation, may involve the bladder, renal pelvis, ureter, or kidney. The most common pathogen of emphysematous UTIs are *Escherichia coli* and *Klebsiella pneumoniae*, and the most important risk factors include diabetes mellitus (DM) and obstructive uropathy. Emphysematous pyelonephritis (EPN), emphysematous cystitis (EC) or emphysematous ureteritis (EU) is uncommon type of complicated UTI. EPN, EU, and EC rarely coexist despite possessing similar mechanisms. Herein, we present a rare case of silent bilateral staghorn stone complicated with coexisting EPN, EU, and EC.

Case presentation

A 49-year-old woman without any underlying disease presented to our emergency department. The patients had experience general weakness and dysuria for days, accompanied by poor appetite and lower abdominal distension. The body weight reduced from 48 to 28 kg within the preceding 6 months and occasional consciousness disturbances were noted.

Physical examination revealed cachexia and a distended lower abdomen. Laboratory test revealed leukocytosis with left shift (white blood cell [WBC] count: 19,100/uL), impaired renal function with hyperkalemia (BUN 129 mg/dL, creatinine 4.94 mg/dL, and K 7.75 mmol/L), and hyperglycemia with hyperosmolarity (glucose 1046 mg/dL, blood osmolality 356 mOsm/kg, glycated hemoglobin 15.7%). Urinalysis exhibited pyuria (WBC count>10,000/uL) and bacteriuria (9,000/uL).

Abdominal computed tomography revealed bilateral complete staghorn stones, severe hydronephrosis with thinning of the renal cortex, and gas formation in the urinary tract. The images show involvement of left real, calyx, and pelvis; beaded stream-like gas in the left ureter; and extension of the urinary bladder (UB) by gas in the UB lumen, UB wall and perivesical fat. Severe emphysematous UTI is associated with the coexistence of pyelonephritis, ureteritis, and cystitis.

Under the impression of newly-diagnosed type 2 diabetes mellitus (DM) with hyperosmolar hyperglycemia, and complicated UTI with impaired renal function, the patient was treated with antibiotics, bilateral percutaneous nephrostomy, and sugar control. After 13 days of treatment, the clinical conditions improved and patients was discharged.

Discussion

DM and urinary tract obstruction are the major risk factors for emphysematous UTIs. Various hypotheses exist regarding the pathogenic mechanisms underlying EPN, including high glucose levels in tissues, host immune impairment, gas-producing organisms, impaired tissue perfusion and urinary tract obstruction. High glucose levels affect immunity in patients with

DM by negatively regulating the functions of neutrophils, macrophages, natural killer cells, and the complement system. High glucose levels in adjacent tissues act as metabolic or fermentation substrates for bacteria, forming gases (CO2, H2, N2, O2, and NH3). Renal hypoperfusion prevents gas elimination, resulting in gas accumulation in the parenchyma and lumen.

Three factors potentially contribute to the development of coexisting emphysematous UTIs: (1) the presence of gas-forming bacteria, (2) high local-tissue glucose levels, and (3) impaired tissue perfusion. Patients with poorly controlled blood sugars easily meet the above conditions, possibly explaining why DM is a major risk factors for emphysematous UTIs.

In addition to complicated emphysematous UTIs involving the kidney, ureter, and bladder, the patient also presented with bilateral complete staghorn stones. This was the first time the patient experience mild urinary discomfort and required medical assistance, without any known underlying DM, urinary calculus, or symptomatic UTIs before. The severe staghorn stones indicated recurrent UTIs with a urease-forming pathogen, although the patient had no known UTI history or symptoms before this course. The patient was believed to have been exposed to the risk factor over long periods of hyperglycemia, frequent asymptomatic UTIs, and obstructive uropathy of unknown duration.

Health examinations are important because of their sensitivity in screening for DM, pyuria, proteinuria, hematuria, and other silent diseases. Image studies should be performed if required, especially in those with DM, impaired renal function, and immunosuppression. Sonography is a relative inexpensive and safe examination that enables rapid scanning of patients' kidneys.

Conclusion

In conclusion, silent bilateral staghorn stone complicated with coexisting emphysematous pyelonephritis, ureteritis and cystitis should be considered in patients with DM. More attention should be paid to awareness of regular health examinations and image studies when treating these high-risk patients.

病例報告　112_C 145

瑞癌寧成功誘導治療 RET 基因重排的乳突性甲狀腺癌

Successful induction treatment with Selpercatinib for advanced RET mutated papillary thyroid cancer — A case report

許佑如[1]　郭雨萱[1,2]
[1]奇美醫院內科部　[2]奇美醫院血液腫瘤科

Introduction

Radioactive iodine I-131 (RAI) is a crucial component of adjuvant treatment for patients facing high-risk differentiated thyroid cancer (DTC). However, resistance to RAI is noted in 5% to 15% of DTC cases and 50% of metastatic DTCs. Recent progress in understanding the oncogenic pathways involved in thyroid cancers and the causes of RAI resistance has led to the development of targeted therapies, which are showing promising results. Moreover, these kinase inhibitors have demonstrated potential in redifferentiation therapy. RET fusion accounts for approximately 6% of papillary thyroid cancer cases. In this context, we present a case illustrating the promising effects of Selpercatinib on advanced RAI-refractory papillary thyroid carcinoma with RET rearrangement, including redifferentiation effects.

Case presentation

A 48-year-old woman, without a history of systemic disease, arrived at the emergency room (ER) with a left thyroid mass that had been present for two years and worsening dyspnea over the past two days. Physical examination revealed a fixed, hard mass on the left side of her neck, measuring approximately 3 x 3 cm. She exhibited shallow and rapid breathing with stridor and accessory muscle use, necessitating emergency intubation. A contrast-enhanced neck CT scan performed on January 12, 2023 (Figure 1), showed a 3.4 x 3.5 x 3.6 cm soft tissue mass with calcifications in the left thyroid gland, invading adjacent tissues, including the left vocal cord, left trachea, and metastasis in left neck levels III and IV. Pathology confirmed papillary carcinoma. A FDG-PET scan on January 20, 2023 (Figure 2), revealed FDG uptake in the left thyroid cancer, metastatic lymph nodes in left neck levels III and IV, classifying it as cT3aN1bM0 and hinting at RAI-refractory thyroid cancer. While surgery was recommended, the patient hesitated due to the potential need for a laryngectomy. As a result, a tracheostomy was performed first. Molecular analysis using the Amoy assay revealed RET gene rearrangements. Archer FusionPlex confirmed the RET rearrangement as CCDC6(E1)-RET(E12). Starting on February 21, 2023, the patient began treatment with Selpercatinib, 80 mg twice daily. After six months of treatment, follow-up CT scans showed a significant

Figure 1

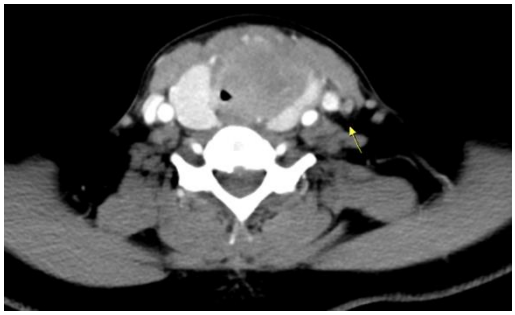
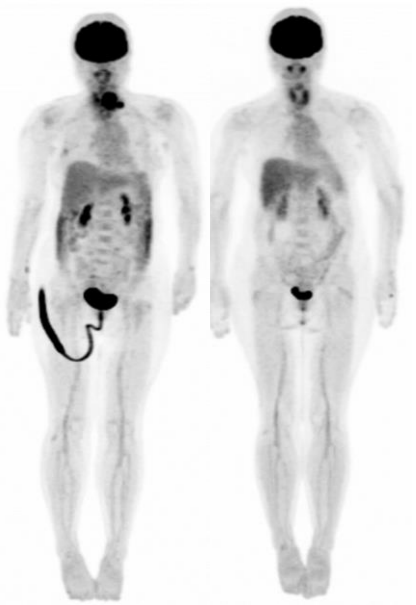
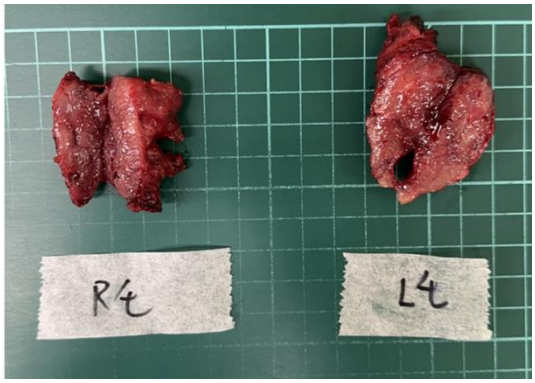


Figure 2　　Figure 3



reduction in the tumor size with no compression of the trachea. An FDG-PET scan on July 14, 2023 (Figure 3), demonstrated nearly a complete response to therapy in the left thyroid. Previously observed lesions in left neck levels III and IV either resolved or were too small to exhibit FDG uptake, suggesting re-differentiation after Selpercatinib treatment. Successful radical thyroidectomy was performed on September 11, 2023. Follow-up I131 scans and I131 treatment will be arranged in the future.

Figure 4



Discussion

Papillary thyroid cancers often carry genetic mutations and rearrangements that activate the mitogen-activated protein kinase (MAPK) pathway, promoting cell division. Sequentially, RET and NTRK1 rearrangements, BRAF activating mutations, and RAS activating mutations lead to MAPK activation. In adults, approximately 90 percent of sporadic papillary cancers exhibit these rearrangements, with the BRAF V600E mutation being the most prevalent. Therefore, molecular profiling should be considered for patients with aggressive papillary thyroid cancer that does not respond to conventional therapies. RET fusion accounts for 6% of papillary thyroid cancer cases. For patients with RET fusion-positive radioiodine-refractory thyroid cancer, selpercatinib and pralsetinib have received FDA approval as second-line treatments after disease progression on sorafenib, lenvatinib, or both. In this context, the phase 1/2 LIBRETTO-001 trial reported an overall response rate of 79% to selpercatinib. Similarly, in the phase 1/2 ARROW trial, pralsetinib also demonstrated an overall response rate of 89%. In our patient, the large tumor with airway invasion initially posed challenges for surgery. We chose selpercatinib due to its high response rate. After six months, the tumor responded very well, and the patient underwent successful surgery, avoiding the reduced quality of life associated with total laryngectomy. Initially, high FDG uptake indicated lower radioiodine avidity, making the use of selpercatinib more reasonable. After treatment, there was almost no FDG uptake by tumor cells, hinting at the possibility of redifferentiation. Several case reports and ongoing clinical trials have explored the role of kinase inhibitors that target the MAPK or PI3K pathways in redifferentiation therapy.

Conclusion

We reported a case in which a patient with RET-fusion locally advanced RAI-refractory papillary thyroid cancer responded well to selpercatinib, a RET fusion inhibitor. The favorable response led to successful curative surgery and redifferentiation of the thyroid cancer. Next-generation sequencing should be considered for all thyroid cancer patients who cannot undergo curative treatment. Whether these targeted drugs can be moved to the front line in certain conditions remains to be further explored in clinical trials.

病例報告　112_C 146

由環磷酰胺誘發的急性胰臟炎：一個罕見的病例報告

Drug-Induced Acute Pancreatitis (DIAP) Associated with Cyclophosphamide: A Rare Case Report

黃博裕[1] 楊畯棋[2] 許銘仁[2]
[1]永康奇美醫院內科部 [2]永康奇美醫院胃腸肝膽科

Introduction

Drug-Induced Acute Pancreatitis (DIAP) is a rare but significant adverse effect that can be triggered by various medications. The diagnosis is often challenging due to its rarity and the lack of comprehensive literature. This case report aims to shed light on DIAP as an uncommon but serious adverse effect of Cyclophosphamide, a medication commonly used in the treatment of nephrotic syndrome, autoimmune disorders, and certain cancers.

Case Presentation

A 49-year-old male was admitted to the internal medicine ward with complaints of left upper quadrant (LUQ) and left lower quadrant (LLQ) abdominal pain that had been ongoing for weeks, but had aggravated over the past 24 hours. He reported that the abdominal pain was constant and dull. His symptoms were associated with nausea and a decreases appetite. The patient has a history of nephrotic syndrome and has been taking prednisolone for the past three months from nephrologist in our hospital. He initiated Cyclophosphamide one month ago as part of his treatment regimen for nephrotic syndrome. In addition on previous mentioned medication, he also took famotidine, furosemide, aspirin, amlodipine/olmesartan, pravastatin/fenofibrate, and potassium gluconate in this month. The patient reported a brief history of alcohol exposure only a few months, and he has been abstinent for the past 20 years. There is no family history of pancreatic diseases. He denied taking any other medications or herbal medication except those prescribed by our hospital.

The initial vital signs indicate a normal sinus rhythm of 96 beats per minute, a blood pressure of 163/99 mmHg, and a saturation of 95% on ambient air. Upon physical examination, the patient's breath sounds were clear bilaterally and he displayed no pitting edema. Abdominal examination revealed localized tenderness upon palpation in the left lower and upper quadrants, with an absence of rebound tenderness and a negative Murphy's sign. On review of systems, he denied any constitutional symptoms (fever or chills, weakness or fatigue, weight loss or gain, night sweats), cardiovascular, respiratory, neurological, musculoskeletal, hematological or endocrinological problems.

Laboratory studies revealed an elevated white blood cell count (12,200/μL), marked elevated lipase level (307 U/L). Liver function tests and coagulation profile were within the normal range. The Lipid profile was also within the normal range, indicating no hypertriglyceridemia or hypercalcemia. There is no history of recent abdominal procedures or trauma. Further laboratory tests were negative for seromarkers of IgG4-related disease. Abdominal computed tomography showed signs consistent with acute pancreatitis, including necrotic tissue in the pancreatic tail and the presence of peripancreatic fluid collection. Otherwise, there was no evidence of choledocholithiasis on CT scan. A follow-up abdominal ultrasound revealed the presence of gallbladder sludge, but no bile duct dilatation was observed. His symptoms and

condition improved after discontinuation of cyclophosphamide, combined with treatments that included aggressive intravenous hydration, Gabexate mesilate, and pain management. The patient was subsequently diagnosed with drug-induced acute pancreatitis, which was attributed to his recent use of Cyclophosphamide and soon subsided after discontinuing the medication. No other identifiable causes or triggers for pancreatitis were found.

Discussion

Acute pancreatitis (AP) is predominantly attributed to choledocholithiasis and alcohol consumption. Additional etiological factors of clinical significance encompass hypertriglyceridemia, hypercalcemia, physical trauma, and infections. Additionally, post-ERCP (endoscopic retrograde cholangiopancreatography) and autoimmune conditions can also contribute to the onset of AP. However, once common causes have been excluded, DIAP should always be considered by clinicians.

DIAP represents up to 5% of all acute pancreatitis cases, making it the third common cause of acute pancreatitis after alcohol and choledocholithiasis have been excluded[1]. The worldwide incidence of DIAP ranges from 5 to 80 per 100,000 adults and is reported to be higher in patients with inflammatory bowel disease (IBD), children, geriatric population, and the immunocompromised individuals[1].

DIAP is a diagnosis of exclusion, often requiring an extensive workup to eliminate other potential causes. The Badalov classification system is widely employed to categorize DIAP as class I to IV, based on the available existing supporting evidence[2,3]. Class I is defined as having at least one case report indicating that the drug caused AP after rechallenge. In contrast, Class IV drugs lack clear evidence regarding rechallenge or a "consistent latency", with less than two case reports been published on this topic.

Upon reviewing the patient's medication history, potential culprits for his DIAP include prednisolone and Cyclophosphamide. Although corticosteroids are classified as class I drugs, the patient continued to take prednisolone during his hospital stay[3,4]. Furthermore, previous studies did not provide a reasonable latency period for the exposure of steroids. A large-scale population-based nested case-control study investigated the association between oral corticosteroids and acute pancreatitis[5]. The study discovered an increased odds ratios of AP only in cases of exposure within the recent 30 days, whereas the patient had already initiated steroid use 2 months prior to experiencing symptoms. On the other hand, the patient developed symptoms just several days after starting Cyclophosphamide treatment. Although Cyclophosphamide is classified as a class IV drug[3], but it remains the most probable cause of his DIAP on the timeline of symptom onset. However, the specific mechanism by which cyclophosphamide causes pancreatitis is still unclear to date.

Conclusion

This case report highlights the importance of considering DIAP as a potential cause of acute pancreatitis, especially in patients with a history of relevant drug exposure. As DIAP is actually becoming an increasing cause, it should be considered after alcohol and gallstones are ruled out. The Badalov classification provides estimates and relevant references for assessing the likelihood of drug-induced pancreatitis. Early recognition and management are crucial to prevent irreversible damage and complications.

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病例報告　112_C 147

病例報告：癌症免疫療法造成之急性肝炎

Immunotherapy related adverse effect(irAE)- acute hepatitis: a case report

吳庭瑋[1]　陳威宇[2]
[1]奇美醫院內科部　[2]奇美醫院血液腫瘤科

Introduction

The introduction of immunotherapy, particularly checkpoint inhibitors, in cancer treatment has led to unforeseen adverse events, including the activation of the immune system, which can precipitate autoimmune diseases. One such complication is immune checkpoint inhibitor(ICI)-induced acute hepatitis, which can manifest as elevated liver enzymes, jaundice, and, in severe cases, present with a prolonged INR, resembling acute liver failure.

Case presentation

A 42-year-old man with no prior history of HBV or HCV was diagnosed with buccal squamous cell carcinoma, stage IVa (cT4aN2cM0), on November 1, 2021. He underwent a wide excision of the left buccal mucosa, partial maxillectomy, marginal mandibulectomy, and selective neck dissection involving left levels I to III and right level IA. Additionally, he received a left free anterolateral thigh flap transfer and a tracheostomy on November 3, 2021. Adjuvant concurrent chemoradiotherapy (CCRT) with cisplatin was administered for six cycles and completed by January 18, 2022. Unfortunately, the tumor recurred on August 22, 2022, leading to the initiation of immunotherapy with Nivolumab, administered at approximately 3 mg/kg for a total of 18 doses over 40 weeks. Following the course of immunotherapy, he presented to our emergency department with acute consciousness disturbance and hypoglycemia persisting for one day. Additional associated symptoms included poor appetite and lethargy, which had been ongoing for a few days. There were no febrile episodes, shortness of breath, nausea, vomiting, abdominal pain, or melena. Upon triage, the patient's consciousness improved to a Glasgow Coma Scale (GCS) score of E4V5M6 after the administration of glucose by emergency medical technicians (EMTs). His vital signs were recorded as follows: temperature 35.7°C, pulse rate 62 beats per minute, respiratory rate 20 breaths per minute, with a blood pressure reading of 116/101 mmHg. Laboratory results indicated acute hepatitis with markedly elevated AST/ALT levels (2875/1883 U/L), total and direct bilirubin of 2.73 mg/dL and 2.09 mg/dL, respectively, a prolonged INR of 1.78, and hypoalbuminemia of 2.6 g/dL. An abdominal CT scan revealed acute hepatitis. The patient was diagnosed with acute hepatitis complicated by acute liver failure, coagulopathy, and jaundice. Immediate treatment with intravenous solumedrol, approximately 1 mg/kg/day, was initiated. The patient responded well to treatment in the ward, with a rapid improvement observed in liver enzyme levels, resolution of jaundice, and

Table 1. Labaratory data

Variable	At ER	Hospital Day 4
Blood		
WBC (per μl)	4600	1700
Hb (g/dl)	10.2	8.9
Platelet count (per μl)	159000	54000
AST (U/liter)	2875	245
ALT (U/liter)	1883	794
Bil-Total (mg/dL)	2.73	1.36
Bil-Direct (mg/dL)	2.09	0.89
INR	1.78	1.37
Albumin(g/dL)	2.6	nil

correction of coagulopathy.
To investigate other potential etiologies of hepatitis, a comprehensive viral hepatitis panel was conducted, including tests for HAV, HBV, HCV, CMV, EBV, and HSV, all of which yielded negative results. Additionally, autoimmune markers including ANA, AMA, and anti-sm antibodies were tested and found to be negative. Given the favorable response to steroids, a liver biopsy was deemed unnecessary, and the patient was discharged with a prednisolone dosage of 2 tablets per day as part of his ongoing treatment plan.

Discussion

Immune checkpoint inhibitors (ICI) can trigger immune-related adverse events due to heightened T cell activation and associated cytokine or autoantibody effects. Hepatitis as an immune-related adverse event (irAE) can result from lymphocyte infiltrative lobular necrosis, with or without granulomatous formation.
The overall incidence of immune checkpoint inhibitor-induced hepatitis with monotherapy ICI therapy is approximately 5-10%, accounting for 3-6% of all Nivolumab-induced irAEs. According to current studies, the median time from initiation to presentation with Anti-PD-1/PD-L1-induced hepatitis is approximately 14 weeks, with a wide range of 2-49 weeks. The diagnosis of irAE hepatitis is made by exclusion, involving initial history-taking, physical examination, medication history review, and a comprehensive survey by laboratory tests to rule out viral and autoimmune hepatitis. Imaging studies with CT or ultrasound may be conducted, and a biopsy may be considered in refractory or severe cases.
Nivolumab-induced irAE hepatitis typically presents as hepatocellular type with a self-limited pattern. However, in rare cases, it may progress to Grade 3 or Grade 4 according to CTCAE (1-4%). Currently, the management of irAE hepatitis is based on its severity as per CTCAE grading:
In Grade 1 cases, discontinuation of ICI may not be necessary, and liver enzyme monitoring every 1-2 weeks may suffice.
For Grade 2 cases, a short-duration pause in ICI treatment is recommended, and treatment may be resumed once symptoms subside to Grade 1. Corticosteroids at a dose of 0.5-1 mg/kg/day may be administered if improvement does not occur spontaneously.
Grade 3 to 4 patients should immediately discontinue ICI treatment, and corticosteroids at a dose of 1-2 mg/kg/day are suggested. A second-line of immunosuppressants may be reserved for refractory cases. The tapering of steroids may span 4-6 weeks, with a reduction of 10 mg per week, while closely monitoring for associated side effects and opportunistic infections. Regarding rechallenge, current guidelines advise against reinitiating treatment with ICI in patients who have experienced Grade 4 hepatitis.

Conclusion

Immunotherapy-related adverse effects, including hepatitis, can develop after the initiation of immunotherapy, and they exhibit diverse timing and disease courses. This case illustrates the importance of regular liver enzyme monitoring for patients receiving immune checkpoint inhibitors. In severe cases, treatment discontinuation with steroids should be considered.

病例報告　112_C 148

肺炎克雷伯氏菌所致肝膿瘍併發脊椎硬腦膜外膿瘍– 病例報告

Klebsiella pneumoniae primary liver abscess associated epidural abscess: a case report

李承翰[1] 陳宏睿[1,2] 嚴世島[3]
奇美醫院 [1]內科部 [2]感染科 [3]神經外科

Background

Patients with *Klebsiella pneumoniae* primary liver abscess in Taiwan have been reported to have a relatively higher rate of developing metastatic infections, most commonly presenting as endophthalmitis and/or meningitis. In this case, we present a patient with a K. pneumoniae liver abscess, which led to hematogenous metastatic infections in the form of a prevertebral abscess and an epidural abscess, resulting in neurological deficits.

History

A 58-year-old man with a history of hypertension presented to the emergency department (ED) in August 2023, after experiencing fever for five days. He also complained of sore throat, dysphagia, and generalized muscle soreness. A COVID-19 Ag test performed by a local practitioner returned negative results. Additionally, tests for Influenza virus A/B Ag, Dengue NS1 Ag, as well as virus IgG and IgM, were all negative. The serum white blood cell (WBC) count, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were elevated. Abdominal sonography at the ED revealed a 17x24 mm heterogeneous nodule on the liver (S7). Abdominal computed tomography revealed a 3.7 cm liver abscess on S6/7 of the liver. The patient was administered empirical antibiotics, including Ceftriaxone 1g every 12 hours and Metronidazole 500mg every 8 hours, which led to a resolution of the fever. After admission, an 8 Fr. pigtail drainage catheter was inserted into the liver abscess under sonographic guidance. Three milliliters of pus was aspirated and sent for culture. Both the blood and pus cultures yielded *Klebsiella pneumoniae*, prompting a de-escalation of antibiotics to Cefuroxime 1500 mg every 8 hours in accordance with the sensitivity report. However, despite the use of painkillers, the patient continued to experience persistent neck pain and left shoulder discomfort. A neck magnetic resonance imaging (MRI) was arranged to investigate the suspicion of C-spinal metastatic infection. The MRI revealed a rim-enhancing cystic lesion measuring 8.2x3.7x2.1 cm in the C4-7 prevertebral region, suggestive of abscess formation. In light of this finding, we transitioned the patient's antibiotics to Cefoperazone/Sulbactam 4 g every 12 hours, taking into consideration the potential inoculum effect. We initially planned to perform image-guided drainage, but after discussing with the radiologist, it was determined that no safe route was available. Therefore, we proceeded with an anterior cervical approach for debridement and removal of the prevertebral abscess. During the operation, we discovered and removed infected disc fragments in the anterior C5-6 region. However, post-operation, muscle power in the bilateral upper limbs decreased to 3/3 and muscle power in the lower limbs decreased to 1/1. Additionally, no sensation below the C4 dermatome was detected. Subsequent C/T-spine MRI revealed an epidural abscess from C3 to T1, causing severe central stenosis, spinal cord compression, and edema at the C4-C7 levels, without involvement of the T-spine. The following day, we performed a cervical posterior laminoplasty of C4-7. After the operation,

with rehabilitation, the patient's muscle power mildly improved to RUL/LUL: 4/3 and RLL/LLL: 2/2. We maintained treatment with Cefoperazone/Sulbactam and de-escalated to Ciprofloxacin 400 mg every 12 hours to complete the course. The patient's inflammation markers, including WBC and C-reactive protein, gradually decreased. The pigtail drainage of the liver abscess was removed. He was subsequently discharged to another hospital for further rehabilitation

Discussion

Metastatic infection of *Klebsiella pneumoniae* primary liver abscess is relatively common in Taiwan. While endophthalmitis and meningitis are the most common complications, epidural abscess is less frequently encountered. Early identification of an epidural abscess is essential to prevent further complications. The degree of neurologic recovery after surgery is correlated with the duration of the neurologic deficit, underscoring the importance of timely surgical intervention. In our case, the patient initially presented with fever, dysphagia, and generalized soreness. Antibiotic treatment, percutaneous drainage, and surgical drainage were performed. However, lower limb weakness developed post-surgery, leading to the discovery of an epidural abscess. After prompt surgical intervention, the patient's muscle power showed mild improvement.

Conclusion

Klebsiella pneumoniae primary liver abscess-associated metastatic infections should be considered, especially given the higher incidence in Taiwan. While epidural abscess is a relatively rare metastatic site, early treatment is crucial to prevent further complications.

病例報告　112_C 149

罕見的肋膜腔內惡性單發性纖維瘤

Ruptured solitary fibrous tumor with hemothorax

許閔智[1] 楊思雋[2]

[1]郭綜合醫院內科部 [2]成功大學附設醫院胸腔內科

Introduction

Solitary fibrous tumor (SFT) is a rare mesenchymal tumor. Ruptured SFT is less common. We reported a case with a SFT, which ruptured and was complicated with hemothorax.

Case presentation

A 62-year-old woman without specific past medical history presented to the emergency department with acute right chest pain for one day. In addition to chest pain, dyspnea on exertion was also noted. Physical examination revealed decreased breathing sound and dull percussion over the right lower lung. Contrast-enhanced chest computed tomography showed a 13 cm conglomerate rich in vascularization without invasion of the surrounding structures. Diagnostic pleurocentesis revealed a pleural fluid to serum hematocrit ratio of 86% and a percutaneous pigtail catheter was placed. After drainage of the hemothorax, a well-defined and convex-to-lung mass emerged, symbolizing a pleural tumor. Core needle biopsy of the mass showed strong nuclear expression of signal transducer and activator of transcription 6 (STAT6)—a specific marker for SFT. She underwent en bloc resection of the tumor and adjuvant radiation therapy. The tumor did not recur over 6 months of follow-up.

Discussion

SFT is a rare mesenchymal tumor most commonly occurs in the pleural cavity. Its etiology is still unclear. Most of the symptoms can be attributed to local mass effects, such as dyspnea, chest tightness. Patients presented with acute chest pain were uncommon. Chest radiograph and computed tomography usually show a
well-circumscribed tumor with hypervascular and necrotic regions within the lesion.
Histologically, SFTs are composed of cells with ovoid to spindle shaped nuclei.
Some cases might show a " staghorn" vascular pattern, which symbolizes hypervascularity with perivascular sclerosis. STAT6 immunochemical staining is highly specific for SFTs. Current treatment strategies for SFTs are similar to those for soft tissue sarcomas. Complete resection of SFTs is associated with lower rates of local recurrence and metastasis. Radiotherapy is recommended for malignant SFTs. The use of chemotherapy is scarce.

Conclusions

Ruptured SFT may present with acute chest pain. Due to a lack of established treatment, each case should have an individualized plan after surgery.

病例報告　112_C 150

可利舒 Cholestyramine 引起嚴重不可逆高血氯代謝性酸中毒死亡：兩個相關病例的研究報告
Cholestyramine-associated with severe, irreversible, hyperchloremic metabolic acidosis mortality: two related case studies

蔡文仁[1] 盧慶祥[2] 王堯顯[3] 張淑芬[4] 陳呈堯[5]
[1]健仁醫院腎臟內科 [2]健仁醫院胸腔內科 [3]健仁醫院感染科 [4]健仁醫院檢驗科
[5]台北醫學大學醫學檢驗暨生物技術學系

Introduction

Cholestyramine is a positively charged resin that binds bile acids to form a non-digestible complex in gastrointestinal tract. It is commonly used to treat diarrhea associated with bile acid malabsorption, pseudomembranous colitis and pruritis of partial biliary obstruction. The connection between cholestyramine treatment and severe hyperchloremic metabolic acidosis (HCMA) remains unclear. However, the side effect of cholestyramine-associated severe HCMA is rarely fatal and can be alleviated by sodium bicarbonate ($NaHCO_3$) supplementation.
We reported two cases of elderly patients under chronic ventilator dependence (CVD), who rapidly developed severe HCMA after a short course of cholestyramine treatment. The conditions of these two patients were refractory to aggressive $NaHCO_3$ resuscitation and rapidly deteriorated by the oliguric acute renal failure (ARF) and sepsis, which eventually caused the death of these two patients.

Case presentation

Case 1.

A non-diabetic, 86-year-old female patient had had cerebrovascular accident with bedridden. Her body mass index (BMI) was at 14.1 (ideal range, 18.5-24 kg/m^2). She had been under CVD for 4 months before she was infected with *Clostridium difficile*-related pseudomembranous colitis. Cholestyramine powder 4g tid and metronidazole 250mg q8h were given per oral for 7 days to treat diarrhea associated with pseudomembranous colitis.
After cholestyramine treatment, laboratory results showed serum Na^+ value was 140.5 mEq/L (normal range, 135-148 mEq/L), K^+ was 5.34 mEq/L (normal range, 3.5-5.5 mEq/L), Cl^- was 121.3 mEq/L (normal range, 98-110 mEq/L), HCO_3^- was 8.7 mEq/L (normal range, 22.0-24.0 mEq/L) and base excess was -13 (normal range, -2 to 3 mmol/L). All these data suggested that the patient was in severe HCMA. During metabolic acidosis, the positive [2.37 mEq/L] urine anion gap ($UNa^+ + UK^+ - UCl^-$), urine pH value at 6.5 (> 5.0) and low urine osmolal gap at 19.6 mOsm/kg H_2O (<150 mOsm/kg H_2O) indicated low level of renal acid and urine NH_4^+ secretion. The estimated total body HCO_3^- deficit [0.5×body weight×(24-serum HCO_3^-)] was 252 mEq. Aggressive resuscitation treatment with 238 mEq of HCO_3^- didn't improve the patient's condition of severe HCMA. Hemodialysis was suggested, but was declined by the patient's family. Consequently, the patient developed urosepsis in conjugation with oliguric ARF (BUN: 142 mg/dl; Cr: 5.04 mg/dl), which caused the death of the patient.

Case 2.

A non-diabetic, 88-year-old male patient had had complications of chronic obstructive pulmonary disease, old pulmonary tuberculosis, stage 4 chronic kidney disease, old myocardial infarction and status post cholecystectomy. The patient had been under CVD for

11 months and had a BMI value at 18.5 kg/m^2. Cholestyramine powder 4g bid was given per oral for 22 days to treat chronic diarrhea caused by bile acid malabsorption.
After administration of cholestyramine, laboratory data showed serum Na^+ was 145.4 mEq/L, K^+ was 3.68 mEq/L, Cl^- was 123.5 mEq/L, HCO_3^- was 8.2 mEq/L and base excess was -14. All these numbers suggested that the patient was in severe HCMA. During metabolic acidosis, the positive [54.1 mEq/L] urine anion gap and urine pH value at 6.0 (> 5.0) indicated low urine acid secretion. The estimated total body HCO_3^- deficit was 413 mEq. Aggressive HCO_3^- supplement with a total amount of 765 mEq was prescribed for the treatment of severe HCMA, but not effective. Hemodialysis was suggested, but was refused by the patient's family. Later, the patient developed nosocomial pneumonia and oliguric ARF (BUN, 133 mg/dl; Cr 5.2 mg/dl), which ultimately led to the death of the patient.

Discussion

The daily biliary secretion is about 1 L containing ~3 g of total bile acids pooling from 4~12 cycles of enterohepatic circulation. The cholestyramine resin contains the binding sites of chloride (Cl^-), which can be exchanged with bile acids in the duodenum to form an irreversible and non-absorbable complex. The release of Cl^- from cholestyramine resin can further be exchanged with HCO_3^- through Cl^-/HCO_3^- antiport and results in duodenal HCO_3^- loss and Cl^- gain. Each gram of cholestyramine contains 4 mEq of Cl^-. In the present study, the calculated overall Cl^- load was 336 mEq and 704 mEq in Case 1 and 2, respectively.
In colon, malabsorption of bile acids can cause diarrhea via several mechanisms: (1) increase of intracellular mediator [cAMP] to enhance Cl^- secretion, (2) reduction of occludins to increase permeability and motility, (3) stimulation of cholingergic neurons via neurocrine-mediated secretion, (4) increase of serotonin release to increase mucus and fluid secretion and (5) decrease of Na^+/K^+-ATPase activity to reduce salt and water reabsorption. The cholestyramine-bile acid complex obstructs the above mechanisms and leads to anti-diarrhea effect.
The duodenal loss of HCO_3^- can be compensated in normal renal function. The chronic respiratory alkalosis in CVD patients impairs the regeneration of HCO_3^- in renal proximal tubules and collecting ducts. In our present study, the two patients under CVD and chronic respiratory alkalosis showed gain of Cl^- in conjunction with duodenal loss of HCO_3^- in oliguric ARF of chronic kidney disease, likely induced by cholestyramine, may impede renal regeneration of HCO_3^- as well as secretion of H^+ and Cl^-, which gives rise to severe HCMA and eventually irreversible clinical complications.
Cholestyramine-associated severe HCMA attributes to several risk factors: renal failure, concurrent spironolactone use, volume depletion, low BMI or small body weight, chronic respiratory alkalosis, impaired renal HCO_3^- regeneration, impaired urinary acidification and impaired Cl^- secretion.

Conclusion

The elderly patients in long-term bedridden condition usually have multiple organ disorders and are at higher risk for ARF, therefore, are more prone to development of severe metabolic acidosis in septicemia. Geriatric CVD patients with oliguric ARF when receives a short-term treatment of cholestyramine can promptly lead to severe HCMA. Our study suggests that cholestyramine treatment should be avoided or carefully monitored in patients at higher risk for prevention of the unwanted fatal outcomes.

病例報告　112_C 151

轉移性腹膜癌擬似胰臟炎

Intraperitoneal carcinomatosis mimicking acute pancreatitis

陳繼豪[1] 陳文誌[2] 余憲忠[2] 蔡維倫[2] 蔡峯偉[2] 呂家名[2]
[1]高雄榮民總醫院內科部 [2]高雄榮民總醫院胃腸肝膽內科

Introduction

The diagnosis of acute pancreatitis typically requires two of three criteria: typical epigastric pain, elevated serum lipase or amylase levels (three times above normal), and characteristic findings on imaging[1,2]. Gallstones and alcohol are common causes. Less common causes include hypercalcemia, hypertriglyceridemia, toxins, and anatomical anomalies. In some cases, acute pancreatitis can be idiopathic. This case report highlights a case where a patient met diagnostic criteria but was later diagnosed with intraperitoneal carcinomatosis.

Case presentation

A 52-year-old man with advanced gastric cancer, lymph node and peritoneal carcinomatosis, and prior treatment underwent operation of subtotal gastrectomy, D2 lymph nodes dissection, Roux-en-Y reconstruction, extended right hemicolectomy and concomitant hyperthermic intraperitoneal chemotherapy (HIPEC). He presented to the emergency department with acute abdominal pain in the epigastric region, radiation to back, along with nausea and vomiting for past few days. He reported anorexia and significant body weight loss over the past three months.

Upon arrival at the ER, vital signs were stable. Physical examination revealed diffuse tender abdomen with muscle guarding. Laboratory tests revealed an amylase level of 344 U/L (normal 29-103 U/L), a lipase level of 762 U/L (normal 11-82 U/L) and normal liver enzymes, total bilirubin and C-reactive protein (CRP) level without presence of leukocytosis. Transabdominal ultrasound (Fig. 1) showed mild dilatation of common bile duct (CBD) with maximal diameter of CBD about 0.89 cm in size, some gallbladder (GB) sludges, pancreatic duct about 0.22 cm in diameter, and no intra-hepatic ducts (IHDs) dilatation.

Under the suspicion of acute pancreatitis, the patient was initially managed with fluids challenge, analgesics, bowel rest and the administration of Gabexate Mesilate and then admitted. For persisted vomiting, even under liquid diet, Panendoscopy was performed to exclude gastric outlet obstruction, and it reported Reflux esophagitis, Los Angeles grade A and one protruding polyp 1 cm in size near anastomosis. Biopsy was done and pathology reported

Fig 1. Fig 1A (Left showed pancreatic duct 0.22cm in size. Fig 1B(Right) showed mild dilatation of common bile duct(CBD) with maximal diameter of CBD about 0.89 cm in size.

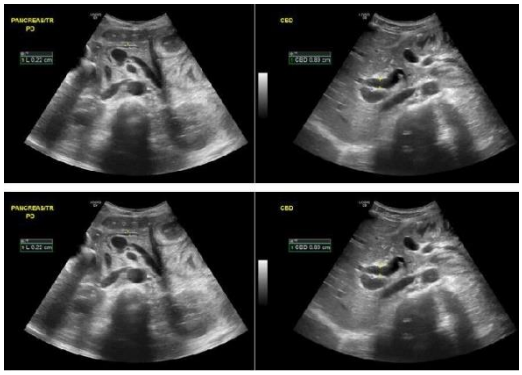
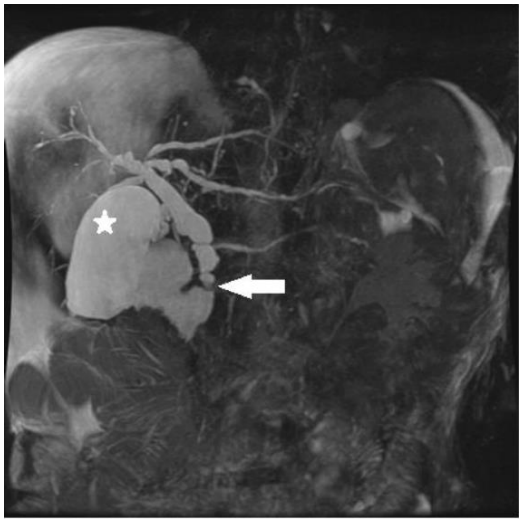


Fig 2. 3D-MRCP revealed mild dilated biliary tree and gallbladder(star) with narrowing over distal CBD (arrow) without filling defect identified

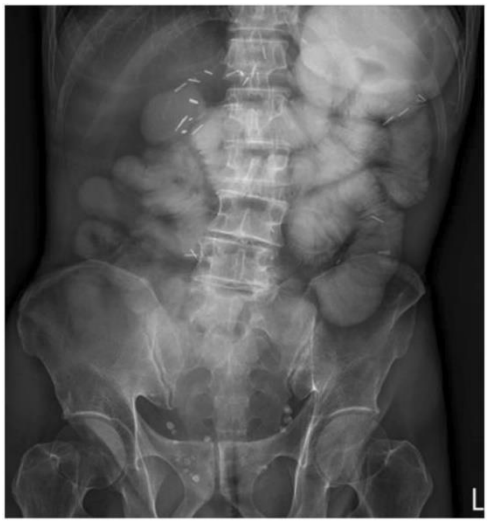


hyperplastic polyp with ulcer.

Magnetic resonance cholangiopancreatography (MRCP) was arranged as survey for CBD dilatation and showed mild biliary dilatation without definite peripancreatic head lesion (Fig. 2). Bowel wall thickening and distension noted, suspect due to bowel adhesion or carcinomatosis. Small ascites, small hepatic cysts and mild hydronephrosis of the bilateral kidney were noted. No other focal lesion in the upper abdomen.

Oral urografin administration was followed by plain abdomen X-ray examination, which revealed no enhancement over colon, indicating bowel obstruction (Fig. 3). Explore laparotomy was done. During operation, enterolysis was done but bypass cannot be performed due to extreme severe adhesion of all intra-abdominal organs. Instead, biopsy of some abdominal wall and intestinal tissue was performed. The patient's postoperative stay went uneventful but still suffered from symptoms of abdominal distention, nausea and vomiting. The patient, after understanding the severity of his medical condition decided to receive palliative care. The patient was discharged on the 5th postoperative day.

Fig 3. Plain film of abdomen after iodinated contrast showed the contrast medium accumulated in stomach and small intestine without enhancement over colon, indicating bowel obstruction.



The surgical specimen, including specimen from small bowel nodule. Pathological examination showed presence of scant tumor cells, favor metastatic carcinoma.

Discussion

V V Gumaste et al found serum lipase, with 100% sensitivity and 99% specificity at three times the upper normal limit, to be a superior diagnostic marker for acute pancreatitis compared to amylase[3]. However, another study reported lower sensitivity (55%) for lipase using the same cutoff[4]. Serum lipase and amylase elevation can occur in diverse conditions, necessitating consideration of clinical context and additional diagnostic factors in acute pancreatitis diagnosis. Ahmer M. Hameed's systemic review identified multiple scenarios with significant lipase elevation, including renal impairment, hepatobiliary, gastrointestinal, and neoplastic issues, as well as critical illness, alternative pancreatic diagnoses, and miscellaneous factors, highlighting the complexity of interpreting these enzyme levels[6]. Peritoneal carcinomatosis, originating from diverse primary tumors, presents with non-specific symptoms, including abdominal discomfort, pain, ascites, and palpable mass, observed in up to 85% of cases, making diagnosis challenging[7,8].

Metastasis from ovarian, gastric, and colorectal cancers is the leading cause. Bowel obstruction in this setting can be either mechanical or functional and occur in 10%–28% of all colorectal cancers and in 20%–50% of all ovarian cancers[7,9].

Small bowel obstruction (SBO) is a known complication after laparoscopic Roux-en-Y gastric bypass (RYGB), with an incidence ranging from 1.27% to 5%[10-16]. A specific type of SBO, known as afferent loop bowel obstruction, is an uncommon complication after gastrojejunostomy and lead to afferent loop syndrome (ALS) with typical symptoms of epigastric pain, abdominal distention, nausea, and potentially bilious vomiting. An associated elevation of the serum amylase, liver function tests, and even pancreatitis has been well documented[17-21].

A retrospective analysis of 99 operations for SBO in 80 patients after RYGB revealed that 48% of all patients had elevated levels of amylase or lipase at the time of operation. The rates of elevated enzymes were higher in cases of acute obstruction compared to those with chronic symptoms and especially in obstructions involving the biliopancreatic limb[22].

Simultaneous acute pancreatitis secondary to an ALS is possible and reported by Elpidio Manuel Barajas-Fregoso et al in an old male after subtotal gastrectomy and RYGB due to antecedent gastric adenocarcinoma. In that case, pancreatic enzymes were significantly elevated with Amylase 1246 U/L and lipase 3381 U/L. Abdomen CT also demonstrated pancreas with diffuse enlargement, which is diagnostic for acute pancreatitis[23].

SBO in gastric bypass patients may lead to the accumulation of digestive secretions, elevating pressure in the afferent limb and causing pancreatic inflammation. Therefore, when these patients with abdominal pain and elevated enzyme levels arrive at the ER, SBO should be considered.

In conclusion, while serum lipase is more reliable than amylase in diagnosing acute pancreatitis, but clinical context, other diagnostics, and potential alternate causes of elevated lipase should be considered. Additionally, in post-RYGB surgery patients with abdominal pain and high pancreatic enzymes, small bowel obstruction should be investigated as a possible association.

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病例報告　112_C 152

克隆氏症伴隨著瀰漫性膿皮症的腸道外表現-病例報告

A case report of Crohn's disease with extraintestinal manifestation of diffuse pyoderma gangrenosum

張維哲 [1] 蔡騂圳 [1,2] 蔡峯偉 [1,2] 方華章 [1,2]
[1] 高雄榮民總醫院內科部 [2] 高雄榮民總醫院肝膽腸胃科

Introduction

Crohn's disease (CD) is a chronic inflammatory disorder primarily affecting the gastrointestinal tract. It often presents with various extraintestinal manifestations, including pyoderma gangrenosum (PG), a rare neutrophilic dermatosis. We describe a unique case of Crohn's disease with extensive cutaneous involvement and lower gastrointestinal bleeding, highlighting the diagnostic and therapeutic complexities encountered in managing such cases.

Case Presentation

A 22-year-old male with a history of thalassemia presented with intermittent bloody stool and progressive skin erosions and necrosis over the face, scalp, and both legs for one month. The patient denied any recent abdominal pains or change in bowel habits. He was treated initially at a regional hospital where colonoscopy showed large colon ulcer with suspected recent bleeding. Argon plasma coagulation was performed. Due to persistent bleeding and progression of the skin lesions, he was transferred to the medical center for further management.

The patient's body height was 175cm and body weight was 52 kilogram. The body mass index was 17. His conscious was clear, and vital signs were body temperature 37.8 ℃, blood pressure 121/81 mmHg, pulse rate 75 beat per minute, and respiration rate 15 per minute. Upon physical examination, mark pale conjunctiva was noted, and palpation of the abdomen was soft and non-tender, without mass lesions. Digital rectal exam showed bloody stool content without palpable mass. Neither external hemorrhoid nor anal fistula nor fissure were seen. Several nodules and pustules over anterior chest wall and scalp were seen, and some large skin ulcers with necrosis on both legs.

Laboratory findings included profound anemia (Hb 2.4 g/dL) along with leukocytosis (WBC: 15.56K) with neutrophil predominance. Autoimmune laboratory examinations including Anti-Nuclear Antibodies (ANA) and Antineutrophil Cytoplasmic Antibodies (ANCA) were negative. A series of diagnostic examinations were performed.

the sigmoidoscopy showed numerous skipped and punched-out ulcers which were 0.5~1.5cm in size. Neither typical longitudinal ulcer nor cobble stone appearance were seen. Biopsy was done and pathology result showed basal plasmacytosis, crypt distortion, and crypt abscess. The acid fast stain for tuberculosis, PAS stain for amoeba and immunohistochemical stain for cytomegalovirus and herpes simplex virus were negative. according to the clinical history, skin manifestations, endoscopic finding and biopsy result, Crohn's disease with pyoderma gangrenosum was diagnosed.

The dermatologist was consulted and skin biopsy was done with consistent pyoderma gangrenosum.

Magnetic Resonance Enterography (MRE) was arranged for evaluation of the extent of

Crohn's disease, which revealed multifocal colonic wall thickening and hyperemic changes, which was particularly pronounced in the descending and sigmoid colon, and therefore consistent with Crohn's disease. No evidence of small intestinal stricture or obstruction was found.

The patient received intravenous corticosteroid and intravenous infliximab treatment combined with immunosuppressive agent (azathioprine), resulting in dramatic improvement of both gastrointestinal and cutaneous symptoms. The skin lesions resolved and scarring was noted after one month of treatment. Oral steroids were taper off gradually in the following three months. Follow-up colonoscopy 6 months after treatment showed residual ulcers at the sigmoid colon. The patient was on scheduled intravenous infliximab infusion with oral azathioprine for maintenance therapy for Crohn's disease and pyoderma gangrenosum.

Discussion

Crohn's disease (CD) is a chronic inflammatory bowel disease that can affect any part of the gastrointestinal tract[1]. It is characterized by transmural inflammation, which can lead to complications such as strictures, fistulas, and abscesses. The clinical case presented involves a 22-year-old male with Crohn's disease and an extraintestinal manifestation of diffuse Pyoderma Gangrenosum (PG), a rare skin condition characterized by painful ulcers[2-4]. In a recent meta-analysis, the prevalence of extraintestinal manifestation in inflammatory bowel disease patients was 24%, and pyoderma gangrenosum in Ulcerative Colitis (UC) and CD patients were both 0.01%[5]. In a Taiwanese cohort study, 11.9% of the IBD patients had extraintestinal manifestation. No CD patients had PG, while 0.4% of the UC patients had PG[6]. While PG is a rare EIM in IBD patients, it is more common in UC patients than in those CD.

The standard of care for Crohn's disease involves steroids, immunosuppressive agents and biologics or small molecules therapies. In this case, the patient was initially treated with steroid and azathioprine, follow up by intravenous infliximab. Infliximab is a monoclonal antibody that binds to tumor necrosis factor alpha (TNF-α), a pro-inflammatory cytokine. A previous investigation showed a 92% response to either Infliximab or another biologic agent[7]. In our case, the use of Infliximab led to an improvement in the patient's symptoms of hematochezia.

According to the ECCO Guidelines on Extraintestinal Manifestations in Inflammatory Bowel Disease, treatment with TNFα antagonists, particularly infliximab, is recommended for the treatment of pyoderma gangrenosum in Crohn's disease. Early use should be considered, particularly for severe manifestations. Other treatments that may be considered include systemic steroids, ciclosporin, ustekinumab, dapsone, metronidazole, and tetracyclines. For milder disease, topical steroids and topical calcineurin inhibitors may be considered. It is also recommended to involve a dermatologist early in the management of Pyoderma Gangrenosum[8].

While Infliximab has shown effectiveness in this case, other biologic agents such as Adalimumab or Vedolizumab could also be explored for their potential benefits and side effects in treating Crohn's disease with extraintestinal manifestations[9]. Further understanding of the pathogenesis of Pyoderma Gangrenosum in Crohn's disease and the underlying mechanisms linking these two conditions could lead to targeted therapies that address both the intestinal and extraintestinal manifestations of the disease.

Conclusion

This case report presents a 22-year-old patient with Crohn's disease and extraintestinal manifestations of pyoderma gangrenosum with successful treatment with steroid and infliximab. Further investigations into the pathophysiology of pyoderma gangrenosum and treatment with new biologic agents is warranted.

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病例報告　112_C 153

A 44-year-old man with emphysematous liver abscess and hemolytic anemia caused by *Clostridium perfringens*

劉峯銘[1] 陳瑞光[2]
[1]高雄榮民總醫院內科部 [2]高雄榮民總醫院內科部感染科

Abstract

Clostridium perfringens, a rare pathogen in liver abscess cases with a high mortality rate, was identified as the causative agent in a case involving a 44-year-old man who presented with fever and abdominal pain, subsequently developing hemolytic anemia. Abdominal computed tomography (CT) revealed a 4.8 cm emphysematous liver abscess in Segment 6 of the liver, accompanied by multifocal pneumo-portals in the right lobe of the liver. The patient underwent CT-guided drainage and received antibiotics treatment, including Clindamycin and penicillin G, based on blood culture results that confirmed the presence of *Clostridium perfringens*. The patient required intensive care, including mechanical ventilation and hemodialysis. Fortunately, after 48 days of treatment, the patient was discharged.

Presentation

A 44-year-old man presented with right lower quadrant (RLQ) pain. He was a carrier of HBV without regular follow-up. Only two days prior, he had visited our emergency department due to epigastric pain, accompanied by nausea and vomiting. These symptoms had developed shortly after attending a wedding banquet where he consumed sashimi and sticky rice. Laboratory investigations and imaging studies revealed no abnormal findings except for hyperglycemia and an elevated glutamic pyruvic transaminase (GPT) level (80 U/L). Consequently, he took some medication to relieve his symptoms and subsequently returned home.

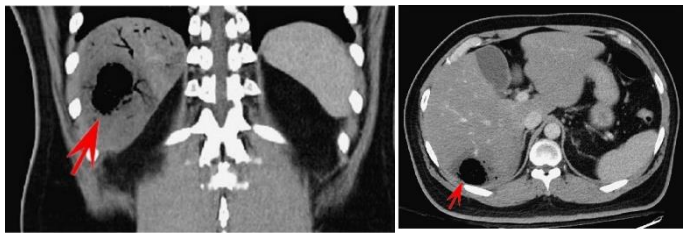
Table 1. Laboratory data summary

	Day 1	Day 2	Day 3	Day 5	Day 10
WBC (/μL)	11370		14000	12220	17140
Hemoglobulin (g/dL)	15.9		10.7	8.9	6.9
Platelet (K/μL)	211		118	67	234
GOT (U/L)	163		776		32
GPT (U/L)	119	354	444		38
Total bilirubin (mg/dL)	8.7	13.0	24.3		2.7
C-reactive protein (mg/dl)	9.57		47.47		
Lactate (mmol/L)		8.73	2.28		
Creatinine (mg/dL)	1.35		7.59		14.68

However, two days later, the patient developed right lower quadrant (RLQ) pain, jaundice, and fever, with temperatures reaching up to 39 degrees Celsius. Physical examination revealed RLQ tenderness and jaundice. Laboratory investigations showed elevated levels of C-reactive protein (9.57 mg/dL), leukocytosis (11.37 K/microliter, with neutrophils accounting for 85.9%), increased lactate concentration (8.73 mmol/L), glutamic oxaloacetic transaminase (GOT, 163 U/L), GPT (119 U/L), glutamic pyruvic transaminase (GGT, 85 U/L), total bilirubin (8.7 mg/dL), acute kidney injury (Creatinine 1.35 mg/dL) and diabetic ketoacidosis (blood sugar 328 mg/dL, blood ketone 4.1 mmol/L, pH 7.244, and HCO3- 14.4 mmol/L).

Due to the clinical presentation suggesting acute appendicitis, an abdominal CT scan was performed, revealing a 4.8 cm emphysematous liver abscess in Segment 6 of the liver with multifocal pneumo-portals in the right lobe of the liver. Empiric antibiotic therapy with ceftriaxone and metronidazole was initiated. The CT-guided drainage was performed for source control. Subsequent culture reports confirmed the presence of *Clostridium perfringens* bacteremia. Consequently, the patient was started on antibiotics with Clindamycin and penicillin G.

Figure 1 . Abdominal computed tomography: a emphysematous liver abscess, accompanied by multifocal pneumo-portals.



Following admission, the patient's jaundice continued to worsen (with total bilirubin levels as high as 24.3 mg/dL), and normocytic anemia developed (with hemoglobin levels as low as 6.9 g/dL). These conditions were likely related to intravascular hemolysis caused by *Clostridium perfringens*.

The patient required intensive care for complications including septic shock, acute hypoxemic respiratory failure necessitating mechanical ventilation, and acute kidney injury requiring hemodialysis. Fortunately, the patient was successfully weaned from ventilation, discontinued hemodialysis, and discharged after 48 days of treatment.

Discussion

In East Asia, liver abscesses are primarily attributed to *Klebsiella pneumoniae*, which has been identified in up to 79.9% of cases in Taiwan[1]. Other commonly encountered pathogens include *Escherichia coli*, *Streptococci*, and *Entamoeba*. Conversely, *Clostridium perfringens* is an infrequent culprit in the development of liver abscesses.

Clostridium perfringens can cause soft tissue infections, and occasionally pyogenic liver abscesses. The alpha toxin produced by this bacterium is a hemolytic toxin that plays a crucial role in its pathogenesis. Active immunization of mice with the C-domain of α-toxin has been shown to provide protection against Clostridium perfringens infection[2]. Notably, massive intravascular hemolysis occurs in 7 to 15% of cases of *Clostridium perfringens* bacteremia, and this condition carries a high mortality rate, which can be as high as 80%[3]. Prompt treatment, which includes source control through surgery [4] and CT-guided drainage [5] is imperative. Clindamycin, metronidazole, tetracycline, and rifampin have been reported to suppress alpha toxin production, a crucial factor in the pathogenesis[6]. Additionally, the combination of penicillin and clindamycin has been shown to be associated with improved survival [7].

In this case, the patient received prompt intervention, including CT-guided drainage, and appropriate antibiotic treatment with the combination of penicillin and clindamycin. This approach may have contributed to the patient's survival, despite the high mortality documented in the literature for *Clostridium perfringens* septicemia with massive intravascular hemolysis.

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病例報告　112_C 154

懷孕相關血栓性微血管病：一位年輕孕婦產後多重器官衰竭

Pregnancy-associated thrombotic microangiopathy: a case of multiple organ failure in a young woman after delivery

王靖堯[1] 康盈盈[2,3] 陳信佑[1]
[1]高雄榮民總醫院內科部腎臟科 [2]高雄榮民總醫院藥學部 [3]高雄醫學大學公共衛生學系

Introduction

Pregnancy-associated, complement-mediated thrombotic microangiopathies (TMAs) are rare, occurring in about 1 in 25,000 pregnancies. These TMAs may be associated with specific diseases such as hemolytic uremic syndrome (HUS), characterized by prominent renal involvement, or thrombotic thrombocytopenic purpura (TTP), characterized by hematologic and neurologic manifestations.

TMA reflects an endothelial injury syndrome marked by HELLP (hemolysis, elevated liver enzymes, low platelet count syndrome) or pre-eclampsia that requires urgent attention. Complements involved in pregnancy-associated TMA include C3, C4, C3a, and C4a because of their important role in implantation and placental development.

We present a case to address pregnancy-associated TMA disorders, including the commonly misdiagnosed TTP and atypical HUS, and to emphasize the importance of timely diagnosis and treatment.

Case presentation

This 26-year-old woman, with no prior medical conditions, had a normal spontaneous delivery before. This time, she was 33 weeks pregnant and had two prenatal check-ups. The first at 8 weeks' gestation showed no abnormalities, but the second at 28 weeks raised concerns about pre-eclampsia, including diabetes, hypertension and proteinuria.

She was admitted to Tri-Service General Hospital Penghu Branch due to vaginal bleeding and bilateral flank pain. Initially, placental rupture and fetal demise were suspected, leading to an emergency cesarean section with substantial blood loss of 1600 ml. However, the following day, signs of multiple organ failure emerged, leading to her transfer to the Intensive Care Unit (ICU) at Kaohsiung Veterans General Hospital.

Her initial symptoms suggested glomerulonephritis, but further laboratory investigations were negative. Laboratory findings revealed microangiopathic hemolytic anemia with thrombocytopenia, acute kidney injury (AKI), and liver enzyme abnormalities, consistent with TMA. The patient received hemodialysis since admission to date. A complete 5-day cycle of plasmapheresis was also initiated until testing ruled out TTP with an ADAMTS-13 activity level of 81%. While in the ICU, postpartum hemorrhage and septic shock occurred. She was intubated and then successfully extubated, but her blood urea nitrogen and creatinine levels remained elevated. A kidney biopsy revealed TMA, and genetic testing revealed membrane cofactor protein (MCP) mutations, confirming atypical HUS. Her current treatment with eculizumab has resulted in a gradual improvement in kidney function and overall health.

Discussion

Suspicion of pregnancy-associated TMA is raised by specific indicators: thrombocytopenia,

AKI, anemia, lactate dehydrogenase >1.5× the upper limit of normal, negative direct antiglobulin test, and mechanical hemolysis on the blood smear. The first priority is to rule out TTP in case its life-saving use of plasma exchange is indicated. The second goal is to diagnose pregnancy-associated HUS, although this is a clinical diagnosis of exclusion. Urgent management often includes plasma exchange, especially in cases of severe neurologic or cardiac complications or profound thrombocytopenia ($<30\times10^9$/L). However, plasma exchange should only be continued if TTP is confirmed. Complement inhibitor therapy with eculizumab is recommended for patients with pregnancy-associated HUS, with possible dose adjustments and individualized duration of use.

On the other hand, pregnancy-associated TTP is characterized by severe ADAMTS-13 deficiency (<20%) and tends to manifest in the second and third trimesters due to decreased ADAMTS-13 activity and increased von Willebrand factor. When ADAMTS-13 levels are above 10%, plasmapheresis provides minimal benefit, making rapid ADAMTS-13 testing not only essential for diagnosis, but also cost-effective by avoiding unnecessary procedures. In addition, testing for ADAMTS-13 activity serves a triple purpose: rapid diagnosis or exclusion of TTP, exploration of alternative disorders with TMA features (e.g., pre-eclampsia/eclampsia, HELLP syndrome, antiphospholipid syndrome), and finally, diagnosis by exclusion of complement-mediated atypical HUS.

Whether TMA occurring before, during, or after pregnancy is associated with different maternal and neonatal outcomes was investigated in a cohort study of 28 women with a history of complement-mediated TMA and 74 pregnancies. Mixed models were used to account for repeated pregnancies within the cohort. Women whose pregnancies occurred after a diagnosis of TMA had better pregnancy and neonatal outcomes than women whose pregnancies occurred before TMA or were complicated by pregnancy-associated TMA. Neonatal development was excellent in all three pregnancy conditions.

Conclusion

The management of pregnancy-associated TMA involves two main pillars. The first is urgent ADAMTS13 activity testing to diagnose or rule out TTP, given its life-threatening potential and need for continuous plasmapheresis. The second is the rapid exclusion diagnosis of complement-mediated atypical HUS in order to initiate specific complement inhibitor treatments.

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病例報告　112_C 155

第四期肝細胞癌病患接受 Pembrolizumab 治療後出現疑似免疫治療引發嗜血症候群 - 個案報告

Suspicious of immunotherapy induced hemophagocytic lymphohistiocytosis after Pembrolizumab treatment in a stage 4 hepatocellular carcinoma patient

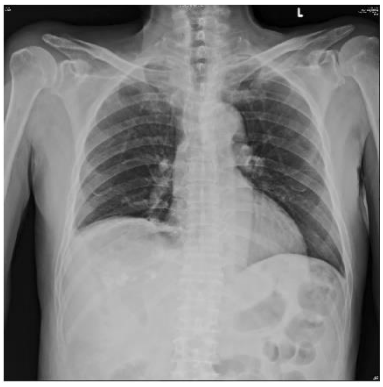
黃冠輔 [1] 吳鎮琨 [1,2] 胡琮輝 [1,2]
高雄長庚醫院 [1] 內科部 [2] 內科部肝膽胃腸科

Introduction

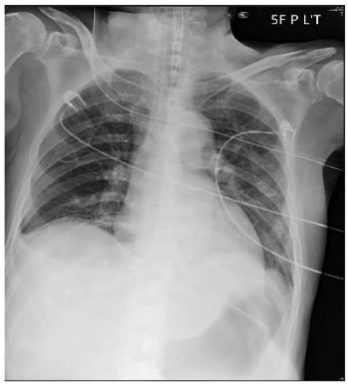
Immunotherapy, such as immune checkpoint inhibitors (ICIs), has been widely usedin the past decade in the treatment of malignancies. Despite good therapeutic results, some side effects, referred to as immunotherapy-related adverse events (irAE), have been widely reported. Hemophagocytic lymphohistiocytosis (HLH) is one of the more serious irAEs, which may lead to a high mortality rate once diagnosed[1]. There have been some case reports and reviews dealing with the relationship between ICIs and HLH, including all kinds of ICIs[2].

Case presentation

Chest X-ray on 6/22



Chest X-ray on 6/27



A 71-year-old male suffered from abdominal pain for one week, accompanied with fever, nausea, vomiting, poor appetite and general malaise. He had a medical history of stage IV hepatocellular carcinoma (HCC) with lung and bone metastasis. He has received transcatheter arterial embolization (TAE), spinal radiotherapy, and tyrosine kinase inhibitor (Sorafenib and Regorafenib) therapies in the past year. Recently, he received his first dose of immunotherapy with Pembrolizumab a week before hospitalization. A fever of 38.2 degrees was recorded at triage. The physical examination revealed no jaundice, no peritoneal sign or abdominal muscle guarding. Complete blood count and biochemistry profile showed leukocytosis(13000/μL), thrombocytopenia (3000/μL), acute kidney injury (BUN 53.4mg/dL, Creatinine 1.77mg/dL, eGFR 38; baseline eGFR measured 99.5), abnormal liver biochemical tests of AST/ALT (109/41 U/L) and jaundice (total bilirubin 7.1mg/dL), elevated CRP (255.44 mg/L) and lactate (21.2 mg/dL). Chest X-ray revealed no pneumonia patch in addition to previous metastasis. Empiric antibiotics were given soon after his arrival at ER. He was admitted under the tentative diagnosis of suspicious sepsis. After admission, he developed rapid onset of tachypnea and shortness of breath which progressed to acute respiratory failure in one day. Then after, the patient was intubated for ventilation support. Norepinephrine line was also used for hemodynamic maintenance. Emergent abdominal CT for infectious focus survey showed no specific finding except previously existing liver cirrhosis and liver tumors. Follow-up lab data during admission revealed progressive anemia (8.9 g/dL), thrombocytopenia (3000/μL), acute kidney injury (BUN 103.8mg/dL, Creatinine 4.44mg/dL, eGFR 13), abnormal liver biochemical tests of AST/ALT (384/374 U/L), as well as jaundice (total bilirubin 10.5 mg/dL). Highly elevated ferritin (22674 μg/L) was also found after admission. Due to cytopenia (2/3 lineage) with very high ferritin levels, we consulted a

hematologist for suspicious HLH. The hematologist suspected septic shock and decompensated liver function to be the cause of cytopenia and suggested treating sepsis first. Bone marrow examination may be indicated if persistent cytopenia after sepsis is controlled. However, the clinical condition progressed and deteriorated rapidly with profound hypotension. Patient was eventually discharged against medical advice on the fifth day of hospitalization.

	6/22	6/27
WBC(1000/μL)	13.0	14.0
RBC(million/μL)	4.48	2.83
Hemoglobin(g/dL)	14.0	8.9
Hematocrit(%)	42.0	26.5
MCV(fL)	93.8	93.6
MCH(pg/cell)	31.3	31.4
MCHC(gHb/dL)	33.3	33.6
RDW-SD(fL)	56.3	66.8
Platelets(1000/μL)	3	3
RDW-CV(%)	16.9	22.7
PDW(fL)	9.5	-
MPV(fL)	8.5	-
Segment(%)	85.0	80.0
Band(%)	-	6.0
Lymphocyte(%)	5.0	5.0
Monocyte(%)	9.0	5.0
PT(sec)	13.8	13.9
APTT(sec)	37.3	31.0

	6/22	6/23	6/27
BUN (mg/dL)	53.4	-	103.8
Creatinine(mg/dL)	1.77	-	4.44
GPT(U/L)	41	-	374
GOT(U/L)	109	-	384
T.bil(mg/dL)	7.1	-	10.5
D.bil(mg/dL)	-	-	6.0
Na(mEq/L)	131	-	139
K(mEq/L)	3.9	-	3.7
CRP(mg/L)	255.44	-	121.79
Ammonia(ug/dL)	35	122	-
Lactate(mg/dL)	21.2	94.9	53.9
Ferritin(μg/L)	-	22674	-
Triglyceride(mg/dL)	-	85	-

Discussion

Several reports have indicated that the onset of Pembrolizumab-related HLH varies widely, ranging from 1 week to 9 months after initiation of immunotherapy[2]. The present case had only received Pembrolizumab treatment once 1 week before admission. Currently, diagnosis of HLH-2004 requires meeting at least 5 of 8 criteria. Our patient fulfilled 3 of 8 criteria (fever, increased ferritin, cytopenia) by the data available during his hospitalization. Unfortunately, the patient is too ill to receive further studies for definite diagnosis of HLH. According to a large observational study in 2623 critical care adult patients, a ferritin level above 9,083 μg/L revealed a sensitivity of 92.5% and specificity of 91.9% for diagnosis of HLH[3]. Another study, by using a higher ferritin cutoff level of 50000 μg/L, revealed that marked hyperferritinemia may not be specific to HLH in adults, because it might also be related to variable conditions such as infection, renal failure and hepatocellular injury[4]. In our patient, HLH should still be taken into consideration regarding the markedly elevated ferritin level and recent history of immunotherapy, without evident results of sepsis (both a negative blood culture and image study). Nevertheless, more prompt action should be taken for such a patient with similar clinical manifestations.

Conclusion

We report a 71-year-old male, who had stage IV hepatocellular carcinoma, just received one

Pembrolizumab treatment a week before admission, presenting with fever, cytopenia and a high ferritin level. Due to a rapid progression of clinical course and very high ferritin level, HLH should be strongly considered for differential diagnosis. Further survey and management of HLH could be conducted simultaneously with other possible causes of a fatal condition.

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病例報告　112_C 156

以下肢靜脈血栓與水腎表現的 IgG4 相關原發性後腹腔纖維化

Deep vein thrombosis and hydronephrosis secondary to IgG4 related idiopathic retroperitoneal fibrosis

王振宇[1]　吳柏融[2]
高雄長庚醫院[1]內科部　[2]內科部腎臟科

Introduction

Idiopathic retroperitoneal fibrosis (IRF) is a rare disease with fibrous tissue encircling abdominal organs. Symptoms include abdominal pain, venous thrombosis and hydronephrosis.

Case presentation

A 61-year-old man suffered from fever and left ankle swelling for 2 months. Left leg deep vein thrombosis (DVT) was diagnosed by ultrasound 1 month ago. Due to elevated liver enzymes, abdomen Echo. was arranged revealing left hydronephrosis. CT of abdomen found a soft tissue lesion over left iliac region. Biopsy reported lymphoplasmacytic infiltration composed of T cells and scattered IgG4 positive B cells. Prednisolone was prescribed and serum IgG4 declined. The size of retroperitoneal fibrosis decreased on follow-up CT.

Discussion

This patient is diagnosed with DVT but serum D-dimer is within normal range. When thrombosis and hydronephrosis occur, we should arrange CT or MRI of abdomen to exclude retroperitoneal fibrosis.

Conclusion

Although IRF is a rare disease, it should be taken into consideration if no known etiologies could explain hydronephrosis and thrombosis. Steroids are the first-line therapy with good response rate.

病例報告　112_C 157

柏格氏症造成手部嚴重缺血於手指小動脈的血管介入治療

Endovascular Treatment of Critical Hand Ischemia in Small Digital Arteries with Burguer's Disease

龔天佑[1]　薛書凱[1,2]
高雄長庚醫院　[1]內科部　[2]內科部心臟內科

Introduction

Burguer's disease (also known as thromboangiitis obliterans) has been identified as a vasculitis affecting small and medium arteries in upper or lower extremities. This arterial occlusive disease initiated as highly cellular and inflammatory intraluminal thrombus formation with relative sparing of vessel wall. Subsequent organization of thrombus and progression to vascular fibrosis were resulted[1]. The onset of symptoms is typically before the age of 45 years, and male smokers predominate. The presentations are intermittent claudication and critical limb ischemia, including rest pain, ulcerations, and digital gangrene in more advanced disease. The treatment for Burguer's disease is avoidance of exposure to firsthand or secondhand tobacco so that disease progression and further amputation could possibly be prevented[2]. However, Raynaud's phenomenon, which is presented in > 40% of patients, may be continued even after complete discontinuation of tobacco use[3]. Symptoms of vasospasm can be attenuated by vasodilator therapy including calcium channel blockers, nitrates, prostacyclin and phosphodiesterase inhibitors[4,5]. Intravenous form prostacyclin is more effective in relief of pain and improving ischemia[6].

In advanced disease, surgical revascularization is usually not feasible and patency rate is low due to the distal and diffuse nature of Buerger's disease[7]. Endovascular therapy has potential role in critical limb ischemia related to thromboangiitis obliterans, but only limited reports mainly in treating femoro-popliteal disease and below-the-knee arteries are available. Till now there is no case report of intervening occluded small palmar arteries and tiny digital arteries. Here we present a non-smoker young female of severe hand ischemia caused by Buerger's disease. Successful recanalization for occluded digital arteries was finally achieved with modified endovascular therapy.

Case presentation

A 38-year-old Taiwanese woman has past history of hypertension and type II diabetes mellitus under Metformin control with HBA1c 5.0%. She was sent to emergency department for sudden left thumb cold cyanosis and pain. No coagulation disorder except weak positive lupus anticoagulant test is diagnosed. Arterial doppler and Computed tomography of angiography showed patent left radial and ulnar artery, but palmar artery is difficultly assessed. Symptoms persisted under Rivaroxaban, Cilostazol and synthetic prostaglandin E1 (Alprostadil) treatment for more than 10 days. Thus, we performed left forearm angiography which showed occluded 1st digital artery without visualization of collaterals. Recanalization was tried with 0.014 inch guidewire under the support of microcatheter but no flow was observed even after repeated 1.5mm balloon dilatation. Fortunately, right thumb was preserved with attenuation of pain and cyanosis although relatively coldness and numbness still existed. Unknown cause of vasculitis with concomitant Raynaud's phenomenon is impressed. After 10 months away from previous admission, she sought medical aid at our ER for similar symptoms at right 2nd

fingers for few days. Catheterization was performed on the 4th day of admission. Thromboangiitis obliterans is impressed due to the characteristic multiple occlusions of small digital arteries with appearance of corkscrew collaterals by the angiogram[6]. Occluded right 2nd digital artery underwent local thrombolysis with intra-arterial infusion of Urokinase total 12000 units via a 0.018 inch microcatheter. Subsequent balloon angioplasty with 1.5x15mm balloon achieved partial recanalization of proximal 2nd digital artery. Right 2nd finger cyanosis was immediately improved, and she was discharged within 1 week. However, symptoms relapsed over right ring finger one months later. This time, urgent catheterization was performed within 48 hours. The 3rd catheterization indicated occluded right 4th digital artery of which diminished caliber and flow has been shown at previous angiogram. Urokinase total 12000 units was injected into proximal occlusion of digital artery and also palmar artery via the 0.018 inch microcatheter. Soft-tipped wire (Fielder X-TR, Asahi) cautiously passed the diffuse diseased and occluded digital artery to finger tip followed by repeated 1.5mm balloon dilatation. Furthermore, thrombosuction of digital artery was attempted with the microcatheter ten minutes after Urokinase infusion. Successful recanalization with restoring flow of 4th digital artery was obtained, and relief of cyanosis and pain was immediately observed at end of the procedure. Although this female patient is a non-smoker, exposure to secondhand smoke from her father since childhood and then her husband after the marriage is considered the major cause.

Discussion

In our case, the typical presentation of diffuse disease or occlusion of multiple right digital arteries ensure the diagnosis of Buerger's disease at 2nd time of admission. Her disease progressed within one year to cause cyanosis, peripheral neuropathy and superficial gangrene change at bilateral fingers. Attempt of endovascular intervention was not so satisfied at 2nd time, but successful recanalization for occluded right 4th digital artery was achieved with urgent procedure within 48 hours at 3rd catheterization. Combination of local thrombolysis, balloon angioplasty and modified thrombosuction by the microcatheter also lead to the success.

General studies showed there was little progress has been made in the treatment of Buerger's disease. Endovascular therapy for lower extremity arteries of Buerger's disease emerges in recent few years, and only small series of studies were reported. Technical successful rate ranged from 80% (40/50) in Dae-Hoon Kim's series to 95% by Graziani et al. and amputation-free survival rate is high with 3-year follow-up[8,9]. However, there was no report of endovascular intervention to small palmar artery or further tiny digital arteries till now. In our case, occluded digital artery of the young lady is successfully recanalized by endovascular intervention at 3rd attempt. To such small and diffusely diseased digital arteries, prevention of further vessel injury and worsen symptoms is essential. Careful wiring with soft-tipped wire is a better choice in early stage of arterial thrombosis. Adjunctive intra-arterial thrombolytic therapy into occluded arterial segments will be helpful due to poor distal run-off of the disease nature. Thrombosuction can be considered for removal of thrombus, but the peripheral or coronary thrombosuction catheters seem too large for the diseased digital artery. We used microcatheter alternatively for aspiration to diminish thrombus burden. Moreover, early intervention is recommended because organized thrombus with further fibrotic change raises the difficulties of passing soft-tipped wire. Thus, endovascular therapy is feasible for small palmar and digital arteries, and the promising result could be achieved

with urgent , cautious and aggressive intervention.

Conclusion

Buerger's disease is identified as an arterial occlusive disease possibly leading to distal limb pain, cyanosis, gangrene, and subsequent limb loss. There is no standard treatment has been established, and small series of endovascular treatment are limited to lower extremity diseases. Our case report showed the feasibility and safety of urgent recanalization to occluded and thrombotic tiny digital arteries of Buerger's disease presenting as critical limb ischemia.

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病例報告　112_C 158

肺放線菌病——一種罕見且困難診斷的疾病

Pulmonary actinomycosis: a rare and diagnostically challenging disease

黃紹維 [1]　王逸熙 [2]　林耕樓 [3]
高雄長庚紀念醫院 [1]一般科內科組 [2]內科部胸腔科 [3]內科部感染科

Introduction

Actinomycosis is a rare chronic disease caused by Actinomyces spp., anaerobic Gram-positivebacteria found in human mouth, digestive, and genital tracts. Actinomyces israelii is the most common species causing infections. It can affect various body sites. Pulmonary actinomycosis, often infected due to aspiration, is the third common type. Risk factors include poor oral hygiene, pre-existing dental disease, and alcoholism. Diagnosis is challenging due to similarity with other conditions. We present a case of successful treatment of pulmonary actinomycosis in a 50-year-old male with prolonged antimicrobial therapy.

Case presentation

This is a 50-year-old male who was a teacher in Cambodia for seven years. He returned to Taiwan in October 2022 and currently resides in a bungalow in Pingtung County. He is currently unemployed and keeps chickens and dogs at home. He denied any recent history of the cluster. He was a smoker with one pack per day. He had drunk about one liter of Kinmen kaoliang liquor and twelve bottles of Paolyta-B per week. He had medical history of type 2 diabetes mellitus with poor adherence of antidiabetic drugs, recurrent gingivitis, and tooth decay status post bilateral lower molar denture in the recent two years.

He had cough for one month. Some dark red and yellowish sputum was noted for one week. He denied fever, heartburning sensation, dysphagia, dyspnea, chest pain, body weight loss recently, night sweating. Therefore, he went to our emergent department for help.

At the emergent department, his vital signs were stable. Physical examination disclosed a smooth breathing pattern, bilateral clear and symmetric breathing sound. Laboratory data revealed leukocytosis (13800/uL) with neutrophil predominant (82.9%), and elevated C-reactive protein: 106.37 mg/L. Chest x-ray revealed one cavitary lesion at the left upper lung field (Figure 1). Computed tomography disclosed an ill-defined cavitated mass with ground-

Figure 1 The initial chest x-ray showed one cavitary lesion at the left upper lung field.

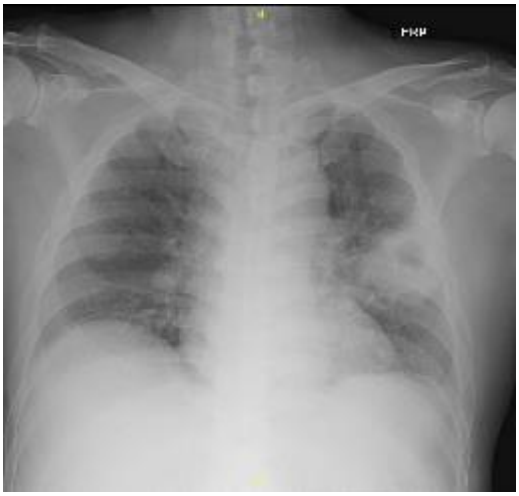
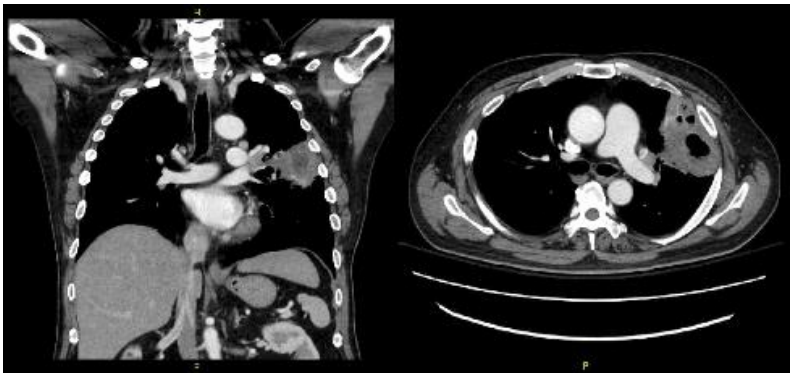


Figure 2 The initial chest CT scan showed an ill-defined cavitated mass with ground-glass opacities in the left upper lung field (91x44x50 mm).



glass opacities in the left upper lung field (91x44x50 mm) (Figure 2). Under the suspicion of lung cancer or mycoplasma tuberculosis, we checked the sputum culture, mycobacterial smear, and culture. We discussed with him for bronchoscopy for biopsy, but he refused our suggestion. However, blood cultures yielded Actinomyces oris. Besides, H&E stain found a colony of actinomyces and mixed inflammatory response at the periphery (Figure 3). Therefore, we started antibiotic treatment with the Penicillin G (12 million units per day) on May 2nd, 2023. The chest x-ray showed regressive change on May 25th, 2023. After finishing a one-month antibiotic course of Penicillin G, we switched it to amoxicillin 875 mg plus clavulanic acid 125 mg (Augmentin 1gm) and discharged him.

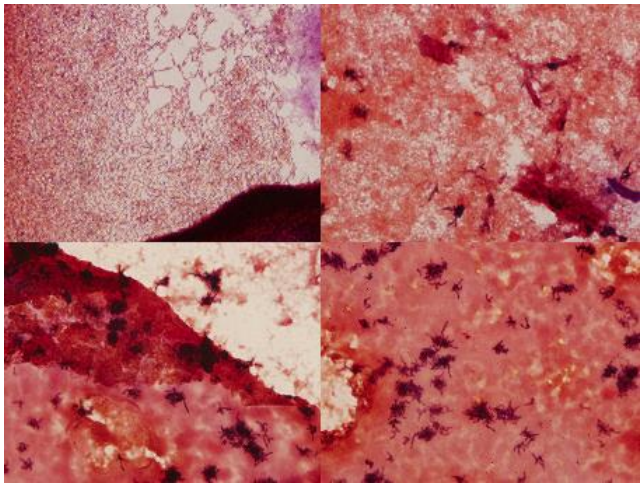
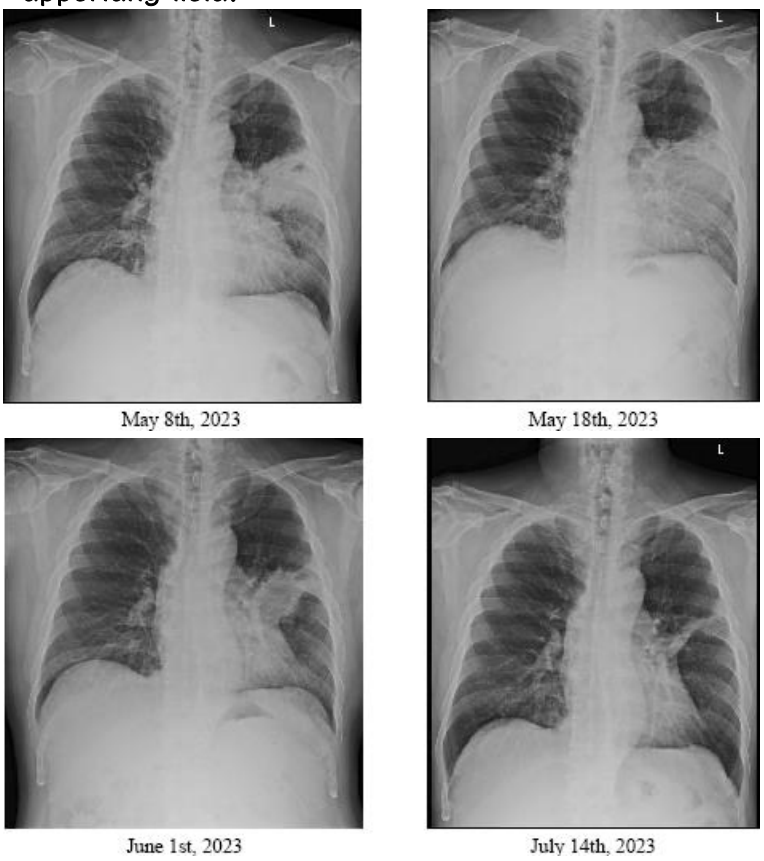


Figure 4 A series of chest x-ray showed regressive change of the patchy consolidation over the left upperlung field.

At the out-patient department, we kept Augmentin 1gm for the treatment. A series of chest x-ray showed regressive change of the patchy consolidation over the left upper-lung field (Figure 4). We also followed blood and sputum culture which didn't yield the Actinomyces oris. We will finish a oneyear treatment of the antibiotic later.



Discussion

Chronic lung diseases, alcoholism, diabetes, hematologic conditions, HIV infection, and immunosuppressive agent use are linked to pulmonary actinomycosis. In this case, the patient, though not immunocompromised and lacking chronic lung issues, had uncontrolled diabetes, and was a smoker and alcoholic. CT scans may reveal various features in pulmonary actinomycosis, such as airspace or lobar consolidation, ground glass opacification, pleural effusions, thickening, hilar lymphadenopathy, and necrotic masses. This similarity to malignancy, tuberculosis, or lung abscess often leads to misdiagnosis. The gold standard for diagnosing pulmonary actinomycosis is histological examination of a lung biopsy, as bacterial culture may be hindered by overgrowth of other bacteria or insufficient incubation time. Treatment with high doses of intravenous penicillin G (10–20 million units daily) over 2 to 6 weeks, followed by oral penicillin V or amoxicillin for 6 to 12 months is recommended. Ceftriaxone, doxycycline, and clindamycin are successfully used for severe infection or penicillin-allergic patients. On the other hand, metronidazole, aminoglycosides, co-trimoxazole, aztreonam and

fluoroquinolones have poor or no activity against actinomyces species. Treatment durations should over 3 months to prevent recurrence or local complications, including empyema, pleura, or mediastinal invasion. Extension of the duration to 12 to 18 months may be warranted for invasive cases and immunocompromised patients. Adequate surgical resection of infected tissues can shorten the treatment course, even for initially severe cases. Patients should be advised on maintaining oral hygiene, avoiding contaminated soil, and wearing protective clothing during agricultural or gardening activities.

Conclusion

Pulmonary actinomycosis, an uncommon infectious disease, often lacks specific symptoms and clear radiographic indications. It can be mistaken for malignancy, tuberculosis, or lung abscess. Definitive diagnosis relies on histological examination and bacterial culture of a lung biopsy. Treatment typically involves high-dose intravenous penicillin G (10–20 million units daily) for 2 to 6 weeks, followed by oral penicillin V or amoxicillin for 6 to 12 months. Duration of treatment should exceed 3 months for pulmonary actinomycosis. The prognosis for pulmonary actinomycosis may be less favorable compared to more common forms like cervicofacial and pelvic actinomycosis.

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病例報告　112_C 159

結核病用藥 Isoniazid 造成藥物誘導性紅斑性狼瘡，以免疫性血小板低下、自體免疫溶血性貧血、抗磷脂症候群為表現之案例報告

Drug-induced lupus erythematosus (DILE) caused by Isoniazid, manifesting as immune thrombocytopenia, autoimmune hemolytic anemia, and antiphospholipid syndrome: A case report

周侑俊 [1] 黃虹綾 [1,2]
[1] 高雄醫學大學附設醫院內科部 [2] 高雄醫學大學附設醫院胸腔內科

Introduction

There are many medications that have the potential to cause drug-induced lupus erythematosus (DILE), including traditional medications such as procainamide, hydralazine, quinidine, methyldopa, isoniazid, and others. New agents such as TNF-alpha inhibitors have also been reported to increase the incidence of DILE in recent years[1]. Among tuberculosis medications, isoniazid is the drug most commonly associated with drug-induced lupus erythematosus, presenting with a variety of symptoms.

Case presentation

The case is about a 90-year-old Asian male patient who has underlying diseases of hypertension, hyperlipidemia, gout, chronic kidney disease stage 3, and deep vein thrombosis (DVT) under direct oral anticoagulant (DOAC) use. He had been diagnosed with tuberculosis pleurisy in December 2022, and his right pleural effusion yielded Mycobacterium tuberculosis. Thus, he received HERZ treatment for tuberculosis immediately.

However, ethambutol was held due to blurred vision and pyrazinamide was held due to high uric acid level after treatment initiated for 1 month. He continuously received rifampin and isoniazid for another 1 month, but developed erythroderma at face, trunk and limbs, hence rifampin and isoniazid were held since drug-related eruption was suspected. After 2 months, the laboratory data showed severe thrombocytopenia, with platelet level below 5000/μL, and there was no improvement even after platelet transfusion.

A series of investigations, including of auto-immune profile, hematologic profile, virus infection screening, bone marrow examination, were performed. Bone marrow examination revealed immune thrombocytopenia pattern. Laboratory data result showed direct & indirect antiglobulin test, anti-IgG antibody positive, hence warm autoimmune hemolytic anemia (AIHA) was favored. Although anti-nuclear antibody, anti-dsDNA antibody, anti-histone antibody were negative, anti-bodies of antiphospholipid syndrome include anti-cardiolipin antibody, anti-β2-glycoprotein antibody, and lupus anti-coagulants were all positive.

Methylprednisolone was administered intravenously in a dose of 40mg every 12 hours, resulting in an increase in the platelet level. The steroid dose was gradually tapered down to prednisolone 10mg twice daily in oral form while monitoring the platelet level, which remained within normal range. For antiphospholipid syndrome, the patient maintained previous DOAC use, peripheral vessel sonography revealed no evidence of new thrombotic event. Rifampin and ethambutol were reintroduced, and moxifloxacin was added to the anti-tuberculosis regimen without including isoniazid. Throughout the treatment, the platelet levels remained within the normal range. Currently, the patient is being followed up at the outpatient

department with medications above.

Discussion

Numerous medications have been reported to be associated with drug-induced lupus erythematosus (DILE). Among them, isoniazid carries a lower risk of developing DILE compared to procainamide and hydralazine[1]. Most of cases present with joint and muscle involvement, account for 50% to 90% of cases. Cutaneous signs are present in 25% to 53% of cases, with rare visceral, central neurological, and renal involvement. Anemia, leukopenia, and thrombocytopenia are rarely observed[2,3].

Although most patients with drug-induced lupus erythematosus (DILE) have positive findings for anti-nuclear antibodies (ANA) and anti-histone antibodies, there are still some cases that exhibit negative results for these antibodies while still meeting the diagnostic criteria for systemic lupus erythematosus (SLE). A case report of a 53-year-old man with drug-induced lupus erythematosus (DILE) caused by hydralazine, presenting as cardiac tamponade, revealed negative findings for ANA and anti-histone antibodies. Similar cases were also mentioned[4].

Returning to this case, despite negative results for ANA and anti-histone antibodies, this 90-year-old male presents with immune thrombocytopenia, autoimmune hemolytic anemia, and antiphospholipid syndrome. Additionally, his condition improved after receiving steroid treatment. Based on the above findings, the patient is diagnosed with drug-induced lupus erythematosus (DILE) caused by Isoniazid.

Conclusion

In the HERZ regimen for pulmonary tuberculosis, each medication is associated with specific adverse effects. The common side effects of Isoniazid include peripheral neuropathy and acute hepatitis. However, we should be aware that among the medications in the HERZ regimen, Isoniazid has the highest possibility of causing drug-induced lupus erythematosus (DILE).

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病例報告　112_C 160

新冠病毒感染後C型肝炎再度活化

Hepatitis C virus reactivation after SARS-CoV-2 infection

張仲威[1]　張庭遠[1,2]
[1]高雄醫學大學附設中和紀念醫院　[2]衛生福利部屏東醫院

Introduction

An outbreak of coronavirus disease 2019 (COVID-19) caused by the Omicron variant occurred in Taiwan from April 2022. COVID-19 infection can cause liver injury in approximately 20% of infected patients.

Case presentation

In this report, we present a case suggesting that SARS-CoV-2 might cause hepatitis C virus (HCV)[1] reactivation after COVID-19 infection. A 46-year-old woman with a history of two conditions presented to our department. She had a human immunodeficiency virus infection and was receiving regular treatment with dolutegravir/abacavir/lamivudine for more than five years. In addition, she had a history of chronic hepatitis C (CHC) infection with spontaneous seroclearance and was attending regular follow ups for three years. This time, she presented with jaundice for one week. She experienced no abdominal pain, fever, or other symptoms. She had tested positive for SARS-CoV-2 based on a rapid test 1 month prior and was treated with Nirmatrelvir/Ritonavir (paxlovid) therapy for five days. During the period she experienced jaundice, the initial biochemical analysis results showed abnormal levels of alanine aminotransferase (914 IU/L) and bilirubin (8.0 mg/dL). Additionally, the concurrent HCV RNA titer was positive (52.9 IU/mL; Table 1). The following serological results were all negative: hepatitis A IgM, hepatitis B core IgM, hepatitis B surface antigen, antinuclear antibody, antimitochondrial antibody, anti-smooth muscle antibody, and thyroid-stimulating hormone. Computed tomography of the abdomen showed no evidence of obstructive jaundice, and she denied drug abuse. Subsequently, she received direct antiviral agent (DAA) therapy.

Table 1

	Before COVID-19	After COVID-19
AST(IU/L)	17.0	947.0
ALT(IU/L)	12.0	914.0
Creatinine(mg/dL)	0.6	0.7
Bilirubin(mg/dL)	0.8	8.0
Platelet count($\times 10^3 \mu$/L)	307.0	164
Anti-HCV	Positive	Positive
HCV RNA(IU/mL)	Negative	52.9

Discussion

HCV reactivation was defined as follows: (1)HCV RNA becoming positive after serocelarance or (2)an increase in the HCV RNA level by at least 1 $\log_{10}$IU/mL from baseline. HCV reactivation might occur after using immunosuppressants, such as corticosteroids, during COVID-19 infection[2]. However, the patient had not received any immunosuppressants before or during her COVID-19 infection[3]. Furthermore, CHC infection is prevalent between 3–5% of the population in Taiwan[4]. The interaction between the two viruses is crucial, especially for CHC patients who have previously had spontaneous seroclearance[5]. The mechanism of HCV reactivation after COVID-19 infection without immunosuppressant administration remains relatively unknown. The limitation of this study was that we could not completely

exclude the possibility of paxlovid-induced hyperbilirubinemia. However, HCV reactivation did occur in this case.

Conclusion

Therefore, we report this case to raise awareness among physicians about the potential risk of HCV reactivation after COVID-19 infection and to emphasize the importance of administering DAA treatment promptly.

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病例報告　112_C 161

以肌痙攣及呼吸困難表現的急性缺血性腦中風在一位患有阻塞性氣道疾患的患者

Uncommon presentations of jerky movement and dyspnea in an obstructive pulmonary disease patient with acute ischemic stroke

鄒沐容[1] 張揚沛[2] 黃虹綾[1,3]

[1]高雄醫學大學附設醫院內科部 [2]高雄市立大同醫院神經內科 [3]高雄市立大同醫院胸腔內科

Introduction

Stroke may result in respiratory abnormalities, which influence the central control of the respiratory drive, airway protection and maintenance, or the respiratory mechanics of inspiration and expiration. Herein, we presented a case of acute ischemic stroke in left cerebellar hemisphere with the initial presentations of dyspnea and jerky movement over left face and upper limb.

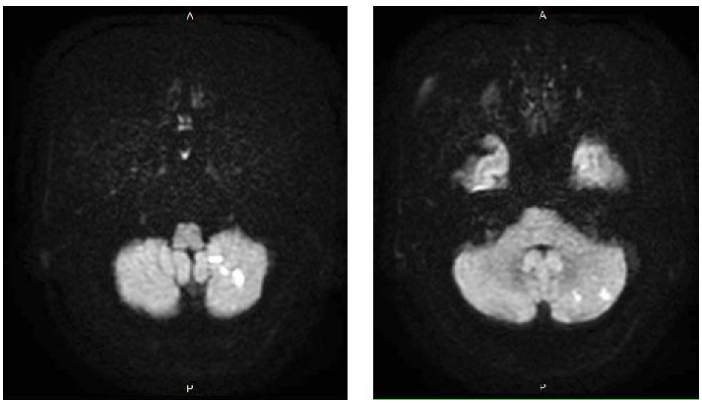
Case Report

A 75-year-old man presented to emergency department due to shortness of breath. He had underlying diseases including asthma-chronic obstructive pulmonary disease overlap syndrome and hypopharyngeal cancer post total laryngectomy with permanent tracheostomy. On physical examination, left hand stimulus-sensitive jerky movement, and left face twitching were found, which was noticed for a week before this admission according to the patient. He also mentioned about difficulty on phonation via tracheoesophageal speech. He denied fever, dizziness, blurred vision, progressive cough with sputum, nausea, vomiting, limbs weakness, numbness, or ataxia. The electroencephalography revealed normal cerebral cortical function but repetitive, irregular eye muscle artifacts on left frontal leads.. Magnetic resonance imaging of the brain disclosed recent infarcts in the bilateral thalami, left occipital lobe and left cerebellum. Carotid duplex revealed moderate stenosis of left common carotid artery but transcranial duplex did not reveal further abnormality. 24 Holter's EKG did not disclose evidence of cardiac arrhythmia or atrial fibrillations. Clonazepam was prescribed for symptom control of hemifacial spasm and aspirin was used for stroke treatment. After a week of treatment, the above symptoms were gradually improvement and the patient was able to have conversation via tracheoesophageal speech as usual.

Discussion

In our patient, shortness of breath was the initial presentation. Difficulty in phonation with tracheoesophageal speech and myoclonic movement appeared simultaneously, which make it arduous to reach early diagnosis of acute ischemic stroke.

Lesions of large cerebral hemispheres with or without mass effects and brain stem may result in central respiratory breathing, such as Cheyne-Stokes respiration, hypoventilation, hyperventilation and other periodic breathing changes, some of which may be associated



with poor outcome[1].Patients suffering from ischemic stroke of posterior circulation often present symptoms of dizziness, nystagmus, truncal and/or limb ataxia, hypotonia of one side, oscillopsia, or cranial nerve impairment[2]. Ipsilateral cerebellar infarction presenting with multifocal myoclonus was rarely reported[3].

Another possible explanation for the symptoms in our patient would be limb-shaking transient ischemic attack (TIA). Shaking-limb TIA, a rare and under-recognized stroke, often results from cerebral hypoperfusion due to contralateral carotid stenosis, which may represent as rhythmic or arrhythmic involuntary hyperkinesia affecting the hand, arm, leg, hand-arm, or hand-arm-leg unilaterally[4]. The involuntary movement would be mostly rhythmic, but choreic or tremor-like movements are also commonly reported[5]. Involuntary movement may recover after carotid stenting[6]. In our patient, his involuntary movement occurred ipsilaterally to the stenosis of carotid artery, which was excluded the possibility of shaking-limb TIA. Patients with focal motor seizure, secondary to stroke or other metabolic disorders may also represent clonic limb movement and abnormal respiratory patterns and electroencephalography may be helpful for differential diagnosis.

According to the image findings and clinical manifestations of the case, lesions in the Guillain-Mollaret triangle was considered, which causes palato – pharyngo – laryngeal myoclonus. The symptoms include dysphagia, dysphonia, or dysarthria. Synchronous myoclonus of branchial arch muscles, the diaphragm, facial muscles, or even the extremities was rarely reported[7]. Back to our case, flexible nasopharyngoscopy showed no obvious palatal myoclonus, which might be suppressed by clonazepam treatment.

In brief, it's important to consider cerebrovascular events in dyspneic patients with involuntary movement.

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病例報告　112_C 162

一位反覆感染巴斯德氏菌菌血症及蜂窩性組織炎的酒精性肝硬化病患：病例報告與文獻回顧

Recurrent *Pasteurella multocida* bacteremia and cellulitis in an alcoholic cirrhotic patient: a case report and literature review

黃奕翔 [1] 梁博程 [1,2] 葉明倫 [1,2] 黃釧峰 [1,2] 林子堯 [1,2] 戴嘉言 [1,2] 黃志富 [1,2] 莊萬龍 [1,2], 余明隆 [1,2]

[1] 高雄醫學大學附設醫院內科部 [2] 高雄醫學大學附設醫院肝膽胰內科

Introduction

Pasteurella are gram-negative, facultative anaerobic coccobacilli, which colonize in upper respiratory tract and gastrointestinal tract of domestic animals, especially dogs and cats. *Pasteurella multocida* is the most frequently reported species of zoonotic infection associated with animal bites and scratches. Licking over wounds, or inhalation were also considered as transmission routes.

Common presentations of *Pasteurella* infection are localized skin and soft tissue infection, including cellulitis and abscess formation. Invasive infections are rare, such as bacteremia, septic arthritis, pneumonia, infectious endocarditis, peritonitis, or meningitis. Severe systemic infections are more easily seen in immunocompromised patients, for instance, patients with histories of liver cirrhosis, solid tumors, hematologic malignancies, diabetes mellitus, chronic kidney disease, or chronic obstructive pulmonary disease.

Herein, we present a case of recurrent *Pasteurella multocida* bacteremia and cellulitis in an alcoholic cirrhotic patient.

Case Presentation

A 48-year-old man with alcoholic liver cirrhosis had a history of esophageal varices bleeding post ligation, and left pyriform squamous cell carcinoma post surgical excision. He was a heavy alcoholism (200ml whiskey per day), smoker (Cigarette 1 pack per day), and betel nuts user (100 pieces per day) for over thirty years.

In March, 2018, he was ever admitted to our intensive care unit for *Pasteurella multocida* bacteremia, community acquired pneumonia, esophageal varices bleeding associated with microcytic anemia, and transfusion associated circulatory overload related acute respiratory failure which required intubation. No evidence of skin and soft tissue infection was noted then. Transthoracic echocardiogram revealed no cardiac vegetation. He was discharged after a twenty-day course of antibiotics treatment with intravenous levofloxacin.

He presented to our hospital in November, 2019, due to a one-day history of fever and chills, associated with right lower leg erythema, swelling, and heat. There was an animal contact history of two pet dogs at home, and frequent licking was noted, without bites or scratches. Upon arrival, his vital signs were as follows: temperature of 42.2°C, heart rate of 129 beats/min, respiratory rate of 20 breaths/min, and blood pressure of 155/89mmHg. Initial blood test showed leukocytosis with neutrophilia (white blood cell count 13270/uL, neutrophil 84.2%), mildly elevated C-reactive protein level (5.65 mg/L), hyperbilirubinemia (bilirubin total/direct: 1.20/4.63mg/dL), and hyperammonemia (180 μg/dL). He was admitted with empiric antibiotics treatment of intravenous ceftriaxone.

Leukocytosis (white blood cell count 29260/uL) and C-reactive protein level (129.00 mg/L)

progressed in the following two days. Soon, blood culture drawn at emergent department yielded *Pasteurella multocida*. Antibiotics were shifted to Penicillin G accordingly, and transthoracic echocardiogram was checked again, with no cardiac vegetation seen. Leg erythema improved and patient was afebrile after a fourteen-day antibiotics treatment course. The patient was discharged on day 17.

The right lower leg cellulitis recurred and led to admission with intravenous antibiotics treatment in February, 2020, January, 2021, and May, 2021. Chronic scratching wounds due to generalized eczema were considered as the cause. No more positive blood culture result of *Pasteurella* was noted during these hospitalizations. The patient was still under our outpatient department follow up.

Discussion

Pasteurella multocida is the most common pathogen of zoonotic infection associated with animal bites and scratches. Exposure to host's secretion, namely animal licking over open wounds, and inhalation were also considered routes of transmission.

Several previous case reports demonstrated liver cirrhotic with invasive Pasteurellosis presented as spontaneous bacterial peritonitis, infective endocarditis, enteritis, osteomyelitis and spondylodiscitis. Liver cirrhosis patients were considered immunocompromised and were susceptible to gram negative bacteria due to multiple plausible mechanisms, including impaired function of the reticuloendothelial system with altered mononuclear phagocyte function, and the presence of portosystemic shunts.

To the best of our knowledge, our case is the only reported in literature of liver cirrhosis patient with cellulitis associated with recurrent *Pasteurella multocida* bacteremia. Examining the patient's first infection in 2018 which *Pateurella* bacteremia was noted without obvious soft tissue infection, transmission from inhalation should be considered. Previous studies reported nasopharyngeal colonization with *Pateurella* with transient bacteremia, causing hematogenous seeding of the pathogen. As for the second infection in 2019, secretion exposure to chronic lower leg wounds due to licking by his pet dog was considered the acquisition route of the pathogen. Our case illustrates the importance to educate cirrhotic patient about avoiding close contact with animals.

Conclusion

In liver cirrhosis patients, who are in an immunocompromised status, *Pasteurella multocida* should be considered as one of the possible pathogens of bacteremia and cellulitis. Thorough history taking of any animal contacts are necessary, since the pathogen may be acquired by not only bites or scratches.

病例報告　112_C 163

以脛前靜脈執行經導管血栓治療急性廣泛靜脈血栓引起罕見症候群

Catheter-directed thrombolysis via anterior tibial vein for Phlegmasia Cerulea Dolens

陳沛蓉[1]　林子傑[2]

[1]高雄醫學大學附設醫院內科部　[2]高雄醫學大學附設醫院心臟內科

Introduction

Phlegmasia Cerulea Dolens (PCD) is a rare, but acute, critical and life-threatening form of deep vein thrombosis (DVT). When venous pressure rapidly increases due to simultaneously superficial and deep vein occlusion, arterial blood flow is obstructed, leading to distal limb ischemia. Catheter-directed thrombolysis (CDT) is an effective and widely used in DVT treatment. We reported a patient with Phlegmasia Cerulea Dolens and received emergent CDT via anterior tibial vein approach .

Case presentation

A 44-year-old woman, who presented with progressive dyspnea. Chest x-ray and bedside ultrasound examination showed massive pericardial effusion, bilateral lung masses, and pleural effusion. After series examination, a diagnosis of right upper lung adenocarcinoma with lung-to-lung, pleura, pericardium, liver-brain, bone, and adrenal metastases was made. She received her first cycle of chemotherapy with Alimta and cisplatin through the right femoral central venous catheter. However, progression of right lower limb ischemia occurred after chemotherapy, with progressive tenderness and swelling, and bluish discoloration, then gangrane of the right toes and soles. Computed Tomography Angiography (CTA) of the lower extremities showed partial deep vein thrombosis (DVT) in the femoral vein from the right thigh to the knee and the popliteal vein in the left knee, but patent arterial flow of right lower limb. Invasive angiography confirmed total occlusion of the right common femoral vein/superficial femoral vein/popliteal vein with massive thrombus. For poor response to anticoagulation with unfractionated heparin, emergent thrombolysis was indicated. We proceed with catheter-directed thrombolysis (CDT) via anterior tibial vein and percutaneous transluminal angioplasty

Fig 1 The sudden onset of limb cyanosis, decreased pulsation and swelling, which mimic peripheral arterial occlusive disease.

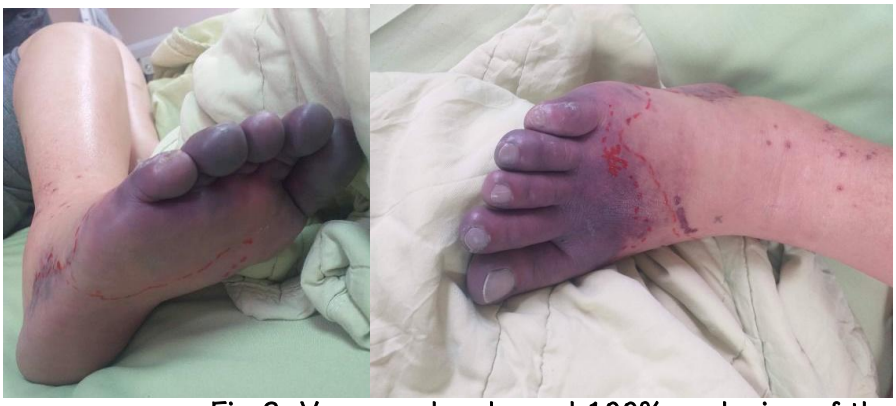


Fig 2. Venography showed 100% occlusion of the right common femoral vein/superficial femoral vein/popliteal vein with massive thrombus

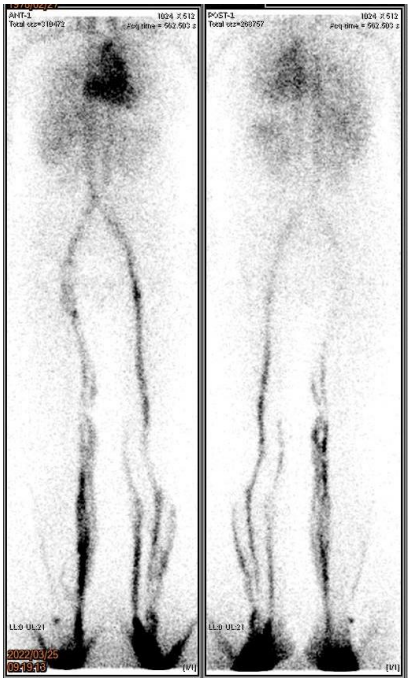


Fig 3. The arterial phase of lower limb CTA shows that the venous blood flow of the right lower limb is more obvious than that of the left lower limb. This indirectly proves that the venous return of the right lower limb is poor, causing arterial blood flow stasis.

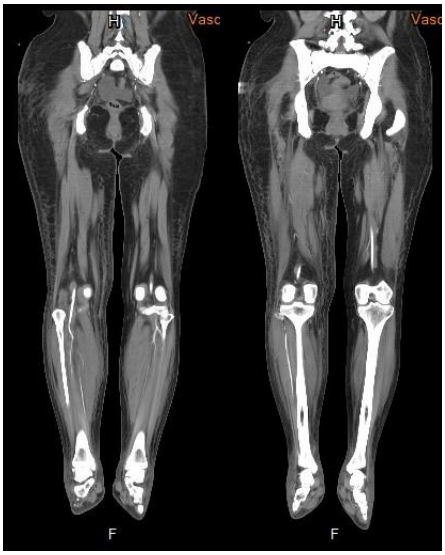
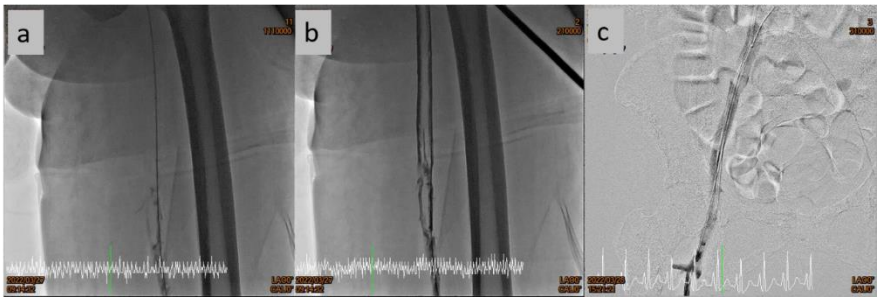


Fig 4a angiography before CDT showed total occlusion with massive thrombosis burden. b. showed improving venous flow after first CDT and PTA. After second CDT and high dose urokinase fibrinolysis and heparinization, the followed angiography showed much decreased thrombus burden.



(PTA). High-dose urokinase fibrinolysis (4400 IU/Kg bolus, then 500 IU/Kg/hr) with heparinization initially was administrated for 48 hours. In followed angiography, antegrade venous flow regain with much decreased thrombus burden, and then intravenous heparinization was maintained for residual thrombi. Finally, catheter-directed thrombolysis successfully preserved venous function and avoid of amputation.

Discussion

PCD is a rare but fatal form of DVT. As venous pressure increases due to superficial and deep vein thrombosis, arterial blood flow is obstructed, leading to gangrene and cyanosis. Clinical manifestation included pain, swelling, cyanosis, livedo reticularis and arterial ischemia with loss of distal pulses. As disease progresses, it may lead to shock, limb gangrene, amputation, compartment syndrome and death. Thus, early recognition and aggressive intervention are critical for PCD. Diagnosis of PCD is based on clinical diagnosis and there are no established diagnostic criteria. Four cardinal signs included edema, violaceous discoloration, pain and severe venous outflow obstruction. Risk factors included malignancy, femoral vein catheterization, heparin-induced thrombocytopenia, antiphospholipid syndrome, surgery, pregnancy and trauma[1]. Treatment strategy should be performed alone or combination, including anticoagulant, thrombolytic therapy and venous thrombectomy.

In addition, different from the traditional approach, this patient received CDT through anterior tibial vein. Compared with the retrograde approach, the antegrade venous approach via anterior tibial vein has the advantage of better preserving valve function. Yi et al studied calf vein anatomical considerations for CDT. The proximal and anterior tibial veins are ideal veins because of their less variability and larger surface area[2]. In previous studies, CDT through the anterior tibial vein approach was a safe and effective strategy for the treatment of acute deep vein thrombosis[3].

Conclusion

PCD is a rare but rapidly progressive and life-threatening form of DVT that requires urgent intervention to preserve the limb. Therefore, rapid recognition is very important in clinical situations. The clinical presentation included edema, violaceous discoloration, pain and

severe venous outflow obstruction. CDT is effective in PCD, has better thrombolytic effect, and requires less systemic urokinase dose. Besides, antegrade approach through anterior tibial vein is a newly effective approach with better preservation of valve function.

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病例報告　112_C 164

診斷時肝細胞癌直接侵犯胃

Hepatocellular carcinoma directly invaded the stomach at the time of diagnosis

陳沛蓉[1]　張庭遠[2]
[1]高雄醫學大學附設醫院內科部　[2]高雄醫學大學附設醫院肝膽內科

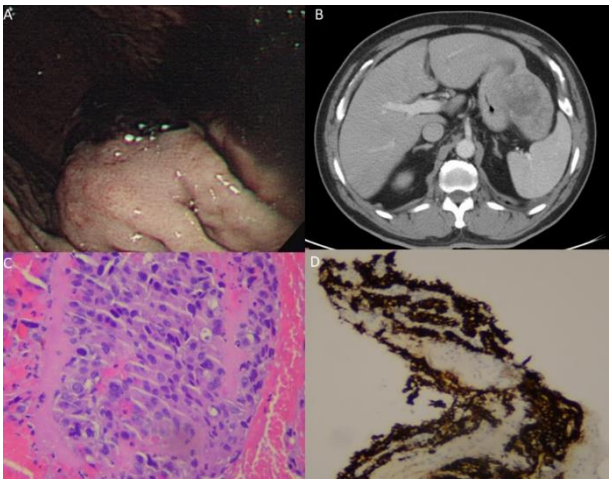
Introduction

Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third most common cancer death. Due to the high incidence and mortality rate, various curative and palliative treatment strategies have been developed. The most common extrahepatic metastatic site included lung, bone and lymph nodes. In contrast, HCC metastases to the gastrointestinal tract are rare, about 0.5-2%[1,2], and the mortality rate is quite high. HCC with gastrointestinal metastases should be considered when HCC patients present with gastrointestinal bleeding and anemia. Endoscope is the gold standard for diagnosing HCC with GI tract invasion.
We reported a patient with Hepatocellular carcinoma directly invaded the stomach at the time of diagnosis.

Case presentation

A 48-year-old man was admitted to our hospital because of melena for one month. The patient denied any systemic diseases before. Upper endoscopy showed an ulcerative mass at the gastric body, and the patient received endoscopic biopsy (Figure 1). Computed tomography showed liver tumours at bilateral hepatic lobes, and the left-lobe tumour directly invaded the stomach (Figure 2). Laboratory tests showed: haemoglobin 5g/dL and alpha-fetoprotein 2839.04 IU/mL. Hepatitis B surface antigen and antibodies to hepatitis C virus were both negative. The pathology of the gastric tumour showed metastatic hepatocellular carcinoma (Figure 3). An immunohistochemical study of the tumour tissue showed that the tumour cells were negative for CK7, CK20 and CDX-2 but positive for hepatocyte paraffin 1 (Figure 4) and glypican-3. After confirmation of metastatic HCC, he received trans-arterial chemoembolization (TACE) and lenvatinib therapy.

Fig A, endoscopic biopsy.
Fig B was the abdominal CT which revealed tumors in the bilateral hepatic lobes, and the left-lobe tumor directly invaded the stomach.
Fig C Pathologic report confirmed the diagnosis of HCC.
Fig D Immunohistochemical analysis showed positive expression for Hep par-1



Discussion

Hepatocelluar carcinoma (HCC) is the sixth most common cancer and the third most common cancer death according to GLOBAL CANCER OBSERVATORY 2020 data. Due to the high incidence and mortality rate, various curative and palliative treatment strategies have been

developed. The most common extrahepatic metastatic site included lung, bone and lymph nodes. In contrast, HCC metastases to the gastrointestinal tract are rare, about 0.5-2%[1,2], and the mortality rate is quite high. After being diagnosed with gastrointestinal metastases, the average remaining life is about 7.3 months[3]. Sohn, D et al reported the earliest case report of HCC metastasizing to the gastrointestinal (GI) tract in 1965. The HCC patient's tumor metastasized to the esophagus, and the tumor size was about 6cm and located in the left hepatic lobe with portal vein invasion[4]. Shiota, T et al reported the first HCC with stomach invasion, whose tumor located at both right and left hepatic lobe[5].

A systematic review study published by Urhut CM et al. in 2022 included 192 patients, most of whom were male, accounting for 87.3% [3]. According to the report, the most commonly gastrointestinal tract metastases were the stomach (27.9%) and duodenum (27.9%). Most of the route of metastasis are through direct invasion and hematogeneous metastasis. Thus, the risk factor of HCC with gastrointestinal tract metastases included growth mode, tumor size, tumor localization and portal vein invasion. Due to the close anatomical location, tumors located on the right side of the liver are more likely to invade the duodenum, while tumors located on the left side of the liver are more likely to invade the stomach[3].

The symptoms of HCC with gastrointestinal invasion included GI bleeding, anemia, abdominal pain, palpable mass, nausea and vomiting. Esophagogastroduodenoscopy and abdominal computed tomography (CT) with contrast are the most useful diagnostic tools. The most common endoscopic features include exophytic mass (15.73%), polypoid lesion (14.72%), ulcerative lesions (14.21%) and submucosal tumor (8.62%). Other features included ulcer, fistula and extrinsic compression. Histological evidence can help us to diagnose HCC with gastrointestinal invasion and differentiate the diagnosis of HCC and gastrointestinal cancer. Immunohistochemical evidence for diagnosing HCC included Hepatocyte paraffin-1 (Hep par-1), arginase-1, glypican-3 (GPC-3) and polyclonal carcinoembryonicantigen (pCEA)[6,7].

Conclusion

HCC with GI tract invasion is rare. However, HCC with gastrointestinal metastases should be considered when HCC patients present with gastrointestinal bleeding and anemia. Endoscope is the gold standard for diagnosing HCC with GI tract invasion. Although there are many treatment strategies for HCC, the prognosis of patients with liver cancer complicated with gastrointestinal metastases is poor, with mean survival 7.3 months.

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病例報告　112_C 165

非結核分枝桿菌肺病與慢性肺麴菌症的關係

The relationship between nontuberculous pulmonary disease and chronic pulmonary aspergillosis

倪世豪[1]　黃虹綾[1,2,3,4]

[1]高雄醫學大學附設醫院內科部 [2]高雄醫學大學附設醫院胸腔內科 [3]高雄市立大同醫院內科部 [4]高雄市立大同醫院胸腔內科

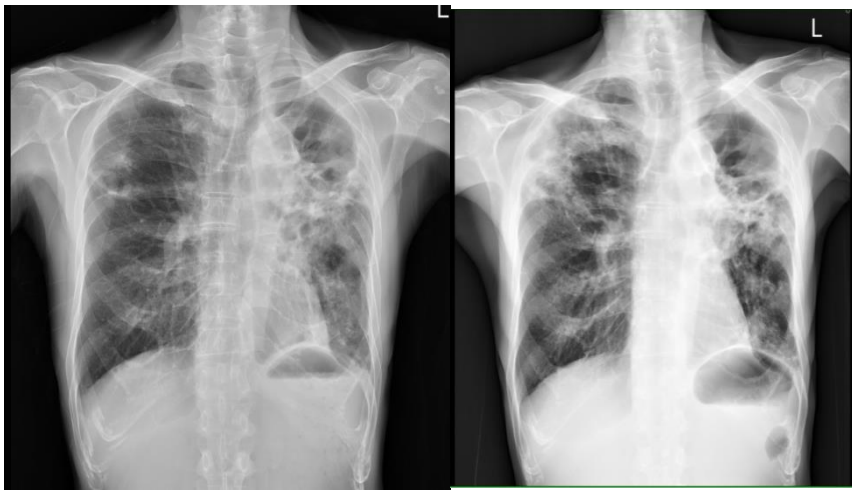
Introduction

Chronic pulmonary aspergillosis (CPA) is a common comorbidity in compromised patients with underlying structural lung disease such as chronic obstructive pulmonary disease (COPD), emphysema, and previous pulmonary tuberculosis (TB). In low TB endemic areas, patients with nontuberculous mycobacterial pulmonary disease (NTM-PD) will increase the risk CPA. We herein report a case of newly diagnosed CPA during his treatment of *Mycobactrium kansasii* (*M. kansasii*)-PD.

Case presentation

A 61-year-old heavy smoker man with old pulmonary TB history, presented with hemoptysis, productive cough and breathlessness for a month. The chest computed tomography (CT) showed fibrocavitary lesions, and 3 sputum cultures all yield *M. kansasii*, he was therefore diagnosed with *M. kansasii*-PD and received anti- *M. kansasii* therapy with rifampicin, ethambutol and azithromycin since then. Unfortunately, further deterioration of productive cough and hemoptysis during treatment, high resolution CT scan showed a ball-in-hole lesion over the right upper lobe lung, with positive serum Aspergillus IgG antibody test. Under the diagnosis of CPA and NTM co-infection, he received antifungal agent, voriconazole and anti-*M. kansasii* therapy simultaneously. During treatment, though the respiratory symptoms were improving, he suffered poor appetite and hyponatremia was detected. We prescribe symptom relief medication for him, monitor the serum concentration of voriconazole and follow up lab data regularly.

Figure 1. A serial of follow-up chest radiography during treatment of *M. kansasii*-PD
(A). Chest radiography at the initial diagnosis of *M. kansasii*-PD (Left) and (B). Follow up chest radiography after 4 months after treatment of *M. kansasii*-PD (Right), which showed progression of cicatrization atelectasis, fibrosis with cavitary lesion in right upper lobe.

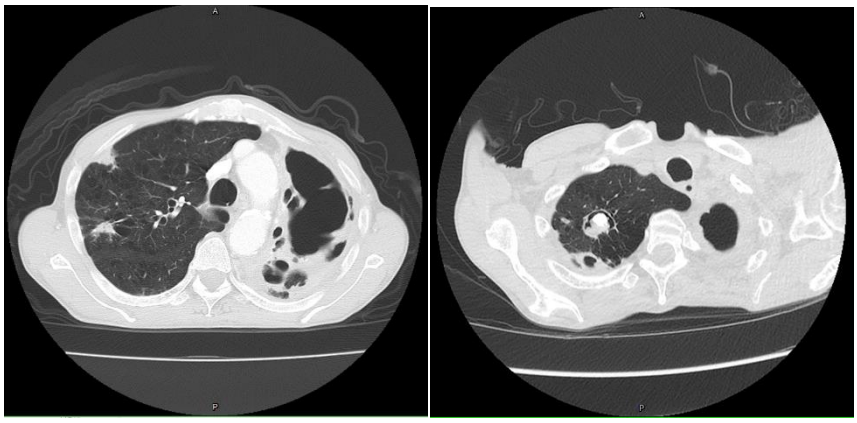


Discussion

The incidence of NTM-PD was gradually increasing in Taiwan in the past decade[1], which may be contributed by the previous endemic of pulmonary TB in Taiwan. The destructive lung disease is the major sequelae after TB treatment and increased the risk of subsequential development of NTM-PD. In TB-endemic countries, up to 93% of

patients with CPA were diagnosed in association with pre-existing pulmonary TB[2], whereas NTM-PD is the predominant risk factors for CPA in low TB endemic area, particularly in patients with fibrocavitary lesions, high dose steroid use and emphysema. Our case reminds clinicians that CPA development following NTM-PD or under effective NTM-PD treatment should be in caution while patients are encountering unexpected clinical deterioration. To treat CPA and NTM-LD simultaneously is a clinical concern due to the potential drug-drug interaction between triazole fungal agents and anti NTM medications, especially Rifampicin. Rifampicin is a strong CYP3A4 inducer which will accelerate breakdown of triazoles and lead to insufficient therapeutic concentration in blood. Therapeutic drug monitoring for triazole antifungal agents is recommended for patients under NTM and CPA treatment at same time.

Figure 2. A serial of follow-up chest CT during treatment of M. kansasii-PD
(A). Chest CT at the initial diagnosis of M. kansasii-PD (Left) and (B). Follow up CT after 4 months after treatment of M. kansasii-PD (Right), which showed a fungus ball lesion over right upper lobe lung



Conclusion

As CPA is one of the most common comorbidities for patients with NTM-PD, clinicians should keep in mind for their concomitance. Additionally, regular side effect monitor and therapeutic drug monitor for voriconazole during treatment should be conducted.

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病例報告　112_C 166

胰臟神經內分泌瘤經 177Lu-DOTATATE 胜肽受體—放射性核種治療後的少見肝毒性

Uncommon hepatotoxicity after peptide receptor radionuclide therapy(PRRT) with 177Lu-DOTATATE in pancreatic neuroendocrine tumor(pNETs)

嚴珮綺[1] 王耀廣[2,3] 吳宜珍[2,3] 沈延盛[4] 陳立宗[2,3]
[1]高雄醫學大學附設醫院內科部 [2]高雄醫學大學附設醫院胃腸內科 [3]高雄醫學大學醫學系
[4]國立成功大學醫學院附設醫院外科部

Introduction

The incidence of neuroendocrine tumor was 3.162 per 100,000 in 2015 in Taiwan[1]. 177Lu-DOTATATE had been approved by the US and Taiwan Food and Drug Administration for the treatment of SSTR(somatostatin receptor)-positive gastroenteropancreatic NET.

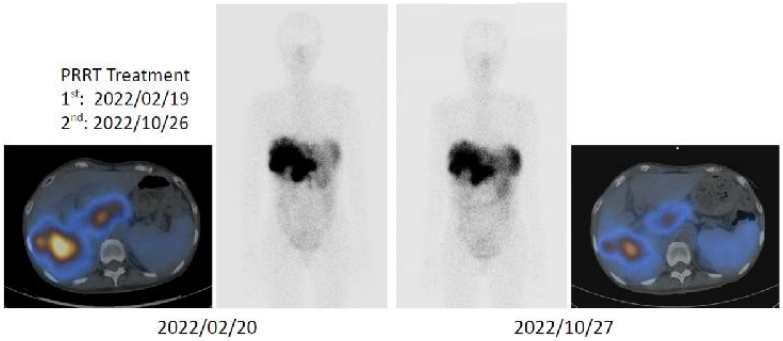
Case Presentation

A 53-year-old woman was diagnosed of G2 pNETs with multiple liver and retroperitoneal lymph node metastasis 13 years ago. The initial presentation included epigastralgia, diarrhea, poor appetite, body weight loss (4-5kg in one month), smaller caliber stool and bowel habit change (defecation 1 time per day to 2-3 times per day). Abdominal computed tomography (CT) revealed multiple hypervascular liver tumors at S5, S8 with thrombosis and multiple enlarged lymph nodes in the retroperitoneum. Biopsy of liver tumor disclosed metastatic NET (immunoreactive for INSM-1, synaptophysin and SSTR-2; Ki-67: 3-4% in liver). Abdominal magnetic resonance cholangiopancreatography confirmed 1.8cm NET in the body of the pancreas.

She received monthly Octreotide LAR 20mg for symptoms control. Everolimus was given in the following 1.5 years then shifted to Sunitinib 25mg daily after progressive disease but complicated with leukopenia (lowest WBC 1710/uL). Other medical history included thrombosis in superior mesenteric vein (SMV) and splenic vein, recurrent variceal bleeding, diabetes mellitus and uterine myoma post myomectomy. She received 68Ga-DOTATOC Imaging which showed Krenning score greater than 3 in tumors. The first and second PRRT with Lutathera were completed successively on 2022/02/19 and 2022/10/26, respectively. The post-treatment scan revealed regression of multiple metastasis (Fig. 1).

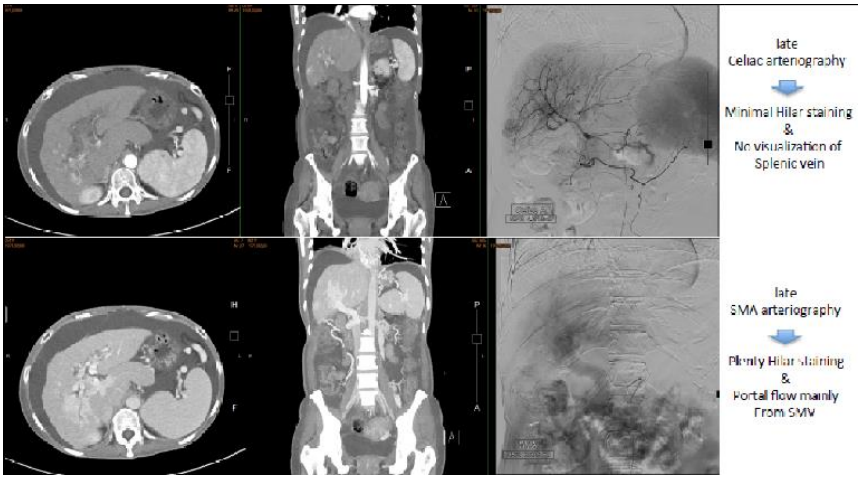
About two month later, she reported bloody vomitus and general weakness. Abdominal CT showed resolution of liver tumors but uneven liver surface and massive ascites. Celiac arteriography showed no obvious arterio-portal shunt, but high-grade portal hypertension with splenomegaly, remarkable hepatofugal flow and pronounced porto-systemic collaterals. Arteriography via superior mesenteric artery (SMA) contrast injection showed prominent dilatation of SMV, main portal vein (MPV) and advanced pruning of peripheral portal radicles (Fig. 2). The paracentesis pathology showed negative of malignancy.

Figure 1



She also suffered from recurrent hematemesis and severe abdomen fullness. Hyperbilirubinemia and hypoalbuminemia were noted. Proton pump inhibitor, somatostatin and prophylactic ceftriaxone were administered along with repeated esophagogastroduodenoscopy for band ligation for active gastric variceal bleeding. The patient received mesocaval shunt (SMV bypass to inferior vena cava) at National Cheng Kung University Hospital and the SMV pressure decreased from 17 to 5mmHg. Liver biopsy pathology disclosed compatible with non-cirrhosis portal hypertension. She was discharged 2 months later.

Figure 2



Discussion

PRRT, also known as a form of radiolabeled somatostatin analogue therapy, demonstrated promising effect[2-5] in SSTR-positive NET. The most common adverse events associated with ^{177}Lu-DOTATATE PRRT are renal and hematologic toxicity. CTCAE grade 3 or 4 renal toxicity, with renal protective agent prior to PRRT, was documented in <2% patients[4,5,6]. In the 2017 NETTER-1 randomized and controlled trial, the ^{177}Lu-Dotatate PRRT plus octreotide LAR 30mg group had 1-9% grade 3 or 4 cytopenia.

A retrospective cohort study of 95 patients of GEP-NETs with at least 1 hepatic metastasis from Hospital of the University of Pennsylvania reported a rate of hepatotoxicity 59% in the PRRT group and 31% in the standard treatment group ($p<0.001$). Of the pattern treatment-related hepatic toxic effects, ascites (6.5% vs 41%, $P<0.01$), death from treatment-associated liver failure (4% vs 18%, $P=0.01$) and hepatic encephalopathy (3.9% vs 18%, $P=0.07$) were documented.

Conclusion

Commonly reported side effects of PRRT included renal and hematology toxicity. Herein, we described a G2 pNETs patient suffered from rare complications of portal hypertension three months after two cycles PRRT. Her underlying thrombosis in SMV and splenic vein may be a risk factor.

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病例報告　112_C 167

以不明熱為初始表現的 MPO-ANCA 相關血管炎之重症病例

A critical case of MPO-ANCA-associated vasculitis presenting fever of unknown origin

鄧人豪[1] 莊政皓[3], 連培因[4] 陳冠亘[5] 吳秉勳[1,2]

[1]高雄醫學大學附設醫院內科部 [2]高雄醫學大學附設醫院腎臟內科 [3]高雄醫學大學附設醫院胸腔內科

[4]高雄醫學大學附設醫院病理科 [5]義大大昌醫院新陳代謝科

Introduction

Microscopic polyangiitis (MPA) is a type of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) that predominantly affects small-sized vessels, primarily affecting the lungs and kidneys. A broad spectrum of signs and symptoms may be present, such as fever, weight loss, peripheral neuropathy, cutaneous manifestations, and upper respiratory tract involvement. As we know, a fever of unknown origin (FUO) is defined as a fever with a temperature higher than 38.3°C for more than three weeks and unidentified the etiology within seven days of hospital evaluation. From the literature, the AAV disease demonstrated a classic FUO, as an initial presentation is limited. Herein, we report a case of MPA who presented FUO initially and was hospitalized in the intensive care unit and received adequate treatment by steroid, cyclophosphamide, and plasma exchange.

Case report

The 72-year-old patient was relatively healthy at baseline and presented insomnia, malaise, and loss of appetite around 3 months before hospitalization. Starting from one month before admission, he had a fever up to 37.8°C every afternoon, accompanied by chills and headaches. On examinations, the patient was alert and fully oriented. He presented no fever (body temperature was 37.0°C), adequate blood pressure (128/61 mm Hg), no tachycardia (pulse rate was 83 beats per minute), fair respiratory pattern (16 breaths per minute), and full oxygenation. His laboratory test showed leukocytosis with left shift (white blood cell count 11,130/L with 94.9% neutrophils), anemia (hemoglobin 6.3 g/dL), impaired renal function (blood urea nitrogen 55.3 mg/dl and creatinine 2.97 mg/dL), elevated inflammation markers (C-reactive protein 70.3 mg/L, procalcitonin 0.44 ng/mL, and ferritin 1636 ng/mL), and microscopic hematuria (urine microscopy 51-99 red blood cells in high power field). The chest radiograph showed bilateral lower lobe infiltrates. Because of fever, leukocytosis, and elevated inflammation markers, empirical broad-spectrum antibiotics were prescribed but still failed to control the fever. Five days after hospitalization, he presented a fever up to 38.2°C, dyspnea on exertion, bilateral lower leg edema, and a 3 kilogram-weight gain. Due to progress renal function decline and dyspnea, he was transferred from the local hospital to the medical center on the 7th day after hospitalization. However, no pathogenic bacteria were identified, including blood, urine, and sputum culture from the initial work-up for FUO. The following laboratory tests demonstrated a progress decline in renal function (creatinine 3.35 mg/dL), increased inflammation biomarkers (C-reactive protein: 143.3 mg/L), and proteinuria (4.59 g/24h). Immunologic biomarkers revealed a high titer of myeloperoxidase antineutrophil cytoplasmic antibody (>134 IU/mL) and normal value in serum Anti-proteinase-3 antineutrophil cytoplasmic antibody level, complement levels (C3 and C4), immunoglobulin level, antinuclear antibody titer (1:40), anti-dsDNA titer, anti-glomerular basement membrane antibody titer. Due to highly suspected AAV presenting rapid progress of glomerulonephritis,

a kidney biopsy was performed. The patient presented a dyspnea with desaturation after the blood transfusion for anemia correction. Orotracheal intubation was performed and the patient was transferred to the intensive care unit. After the interdisciplinary conferences with the rheumatologists, nephrologists, and intensive care physicians, the patient received pulse methylprednisolone therapy (500mg per day) for 3 days and cyclophosphamide(500mg) for one day. Five-dose plasma exchange therapy for the fulminant disease was also performed. Hemodialysis was administered simultaneously due to kidney injury and pulmonary edema status. The renal biopsy pathology demonstrated crescentic glomerulonephritis with moderate interstitial fibrosis and tubular atrophy. Moderate to marked vasculitis and intimal fibrosis of the medium-sized artery is appreciated. Immunofluorescence revealed the absence of immune-complex deposition in the basement membrane and mesangium. The pathological diagnosis was consistent with pauci-immune crescentic glomerulonephritis. The spiking fever resolved on the first day of pulse methylprednisolone therapy. The patient was extubated successfully 5 days after the high-dose immunosuppressive therapy, and the hemodialysis was discontinued due to a satisfactory urine output. The patient was discharged 35 days after hospitalization and was currently regularly followed up at a nephrology clinic with a stable renal function status (creatinine 1.88 mg/dL).

Discussion

FUO remains one of the most challenging diagnoses due to nonspecific clinical manifestations. Differential diagnosis often varies with age, immune status, geography, and environmental exposure. In our case, the 72-year-old patient presented with FUO for over 1 month and developed a critical illness. Elderly individuals exhibit a diminished immune response, leading to fever regulation and immune cell response alterations. Evaluation of elderly patients presenting FUO requires a different perspective from that needed for younger patients. Besides, the causes of FUO in the elderly are often associated with treatable conditions.[3, 4] Failure to promptly diagnose and commence appropriate treatment may increase morbidity and mortality in this vulnerable population. MPA patients are typically > 50 years old and predominantly men in most series (M/F: 1.5) and are more prevalent than granulomatosis with polyangiitis (GPA) in Asian populations.[5] For patients with active and severe GPA/MPA, the current guidelines do not recommend plasma exchange in all patients with active glomerulonephritis but still can be considered for patients at higher risk of progression to end-stage renal disease (ESRD).[6, 7] Our patient's serum creatinine level reached 6.23mg/dL upon admission to the intensive care unit, accompanied by anasarca and pulmonary edema. The patient underwent plasma exchange therapy while also receiving hemodialysis to eliminate excess fluid from the body, which might facilitate a quicker ventilator removal and transfer out of the intensive care unit. The patient did not experience any severe infection-related complications until discharge.

Conclusions

Among all the etiologies that cause FUO, MPA should be included in the differential diagnosis owing to its treatability and fatal outcomes. Prompt recognition and diagnosis may be warranted for elderly individuals with unknown fever and kidney injury due to their vulnerability. We demonstrate a case of MPA who presented with FUO, progressed to a critical condition, and achieved a favorable outcome following the interdisciplinary interventions.

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病例報告　112_C 168

末期腎臟病病人在 Denosumab 治療下仍呈現快速的骨質疏鬆惡化而導致腰椎骨折的系列變化

Rapid deterioration of osteoporosis leading to lumbar spine fracture in patients with end-stage renal disease despite Denosumab treatment

鄭仲廷 [1,2] 郭柏承 [4] 沈柏志 [1,3,4] 吳秉勳 [1,2,4]

[1] 高雄醫學大學附設中和紀念醫院內科部 [2] 高雄醫學大學附設中和紀念醫院腎臟內科 [3] 高雄醫學大學附設中和紀念醫院骨科部 [4] 高雄醫學大學醫學院醫學系

Introduction

Osteoporosis, which is a disease characterized by low bone mass, microarchitectural disruption, and skeletal fragility, results in decreased bone strength and an increased risk of fracture. It often co-exists with chronic kidney disease in older people and has become a complex problem for clinicians. Denosumab is a human monoclonal antibody targeting receptor activator of nuclear factor κ-B ligand (RANKL) that inhibits osteoclasts to decrease bone resorption and increase bone mineral density (BMD). Some studies showed the benefit of denosumab in dialysis people in increasing BMD. Here, we presented a case of osteoporosis in End-Stage Renal Disease(ESRD) under denosumab treatment and showed her serial changes in lateral spine imaging.

Case Presentation

This 75-year-old female had the underlying disease of ESRD under regular hemodialysis, bilateral legs peripheral artery occlusive disease post several times of percutaneous transluminal angioplasty with stent placement, old stroke, type 2 diabetes mellitus, hypertension, systolic dysfunction heart failure, and osteoporosis. Regular laboratory data was followed as our routine care protocol. Her osteoporosis was first diagnosed by dual-energy X-ray absorptiometry with T-score -3.5 in November, 2014. Denosumab 60mg subcutaneously every six months was given since December, 2014 for her severe osteoporosis. A fall episode occurred in October 2015, and an L2 compression fracture was found by lateral spine x-ray image and further confirmed by spine magnetic resonance imaging(MRI). Vertebroplasty was done for the L2 compressional fracture. Calcitriol and Cinacalcet were used for her secondary hyperparathyroidism. A sufficient supply of calcium and vitamin D was kept. A phosphate binder was also kept for her phosphate level control. The dose of medication was adjusted according to her regularly followed-up laboratory data. In this ESRD patient with standardized care, osteoporosis still progresses rapidly. An elevated parathyroid hormone and decreased circulating calcium levels were identified as expected. Using the Genant semi-quantitative method to measure the height of each lumbar vertebrae's anterior, middle, and posterior region. A progressed L4 compression fracture was identified in her serial lateral spine image. An apparent change in the lumbar vertebrae was identified in 2019. In this serial lateral spine image, a decreased vertebrae height was noted even under regular denosumab treatment, and a compression fracture occurred eventually.

Conclusion

This report illustrates the serial changes in lateral spine image in ESRD with osteoporosis,

even under scheduled denosumab treatment. Progressed compression fracture and decreased height of vertebra were noted. The treatment effect of denosumab on ESRDD patients may not be as effective as the general population without kidney disease. Further new medication or combination treatment strategies were still needed to prevent the fracture event among these high-risk groups of osteoporosis.

病例報告　112_C 169

一個憩室鈣化合併疝氣鈣化結節的案例報告

A case of Calcified Diverticula with concomitant Hernia with a calcific nodule

黃昱睿[1]　梁博程[1,2]

[1]高雄醫學大學附設醫院內科部　[2]高雄醫學大學附設醫院肝膽胰內科

Introduction

Diverticula is a phenomenon of the elderly, commonly affecting people over the age of 60. They are typically asymptomatic, unless accompanied by an infection or bleed. Diverticula and calcification of tissue are both relatively common processes; however, when occurring synergistically they present a rare phenomenon[1]. We reported a case presented with calcified diverticula and inguinal hernia with a calcific nodule.

Case presentation

A 78-year-old male with a history of chronic kidney disease stage 4, gouty nephropathy and hyperlipidemia. He came to our emergency room due to left lower quadrant abdominal pain for one day with mild diarrhea. After series examination, abdominal plain film disclosed two left pelvic region calcific nodule with rim-like periphery (Figure 1a.). The corresponding lesion on abdominal computed tomography (CT) without contrast demonstrated that the upper one was a diverticulosis of sigmoid colon with calcification, and the lower one was a calcific nodule in indirect left inguinal hernia (Figure 1b.). Also, CT exhibited diverticulosis of the descending and sigmoid colon with calcification (Figure 2.). The patient then received conservative treatment including analgesics. Symptoms relived and he was referred to urology clinic for further management due to suspicious of urolithiasis.

Figure 1. Two left pelvic region calcific nodule with rim-like periphery, upper one was a diverticulosis of sigmoid colon with calcification, lower one was a calcific nodule in indirect left inguinal hernia

figure1a　figure 1b

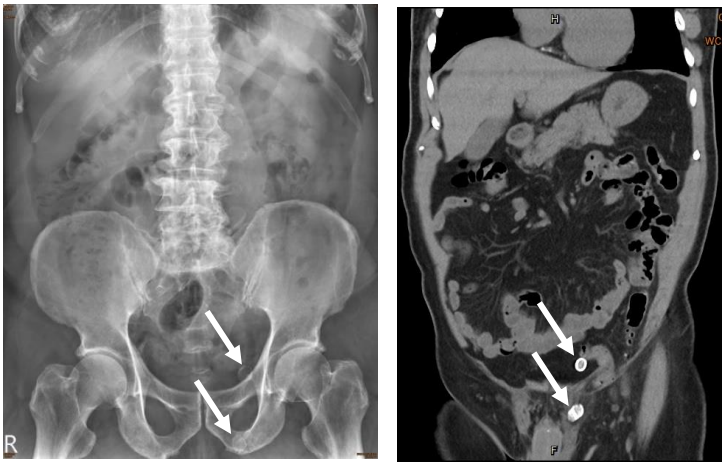
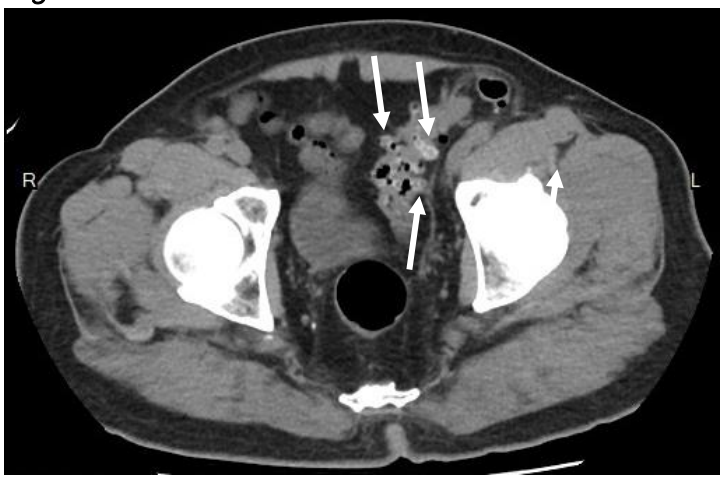


Figure 2. Diverticulosis of the descending and sigmoid colon with calcification



Discussion

Pathologic calcification may occur in any mesenchymatous tissue of low metabolism or decreased blood supply, or following the fibrosis of trauma or infection. Similarly the calcification of tumors is observed when the blood supply is so impaired that degenerative changes have appeared[2]. Cavernous

hemangiomas and vascular malformations are benign tumors of the colon. The presence of scattered punctate foci of calcification representing phleboliths can be used to confirm the diagnosis. Although rare, they usually present with bleeding, the most common location being the rectosigmoid junction. Calcification usually manifests in an amorphous heterogeneous pattern and is much more frequent in mucinous carcinoma owing to the abundant production of extracellular mucin by the tumor[3]. The presence of calcifications in a colon mass should therefore raise the possibility of mucinous or mixed mucinous–adenocarcinoma histology[4]. Calcification of diverticula could be due to dystrophic calcification, in which there is calcification of phosphate leaking from damaged, necrotic tissue which results in radiopaque opacity. This process is increased in an acidic environment despite a normal calcium level[5]. Previous case reported calcified diverticula with profuse blood loss. It should be monitored with dedicated surveillance to ascertain rebleeding rates for this particular phenomenon[1].

Conclusions

Physicians should be cautious of bowel calcification in abdominal images given the risk of bleeding in calcified diverticula and risk of malignancy in calcified colon mass.

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病例報告　112_C 170

晚期系統性類澱粉沉積症以心衰竭表現：病例系列

Late-Stage Systemic Amyloidosis with Presentation of Heart Failure: A case series

蔡曜宇[1] 黃天祈[2] 林楷傑[3] 余方榮[3] 卓士峯[4]
高雄醫學大學附設醫院 [1]內科部 [2]心臟血管內科 [3]內科部胃腸內科 [4]內科部血液腫瘤內科

Introduction

Amyloidosis is a group of rare diseases characterized by the deposition of abnormal protein fibrils in tissues. Amyloid deposits can occur due to the presence of abnormal proteins, excess abundance of normal proteins, or aging process. The most common type of amyloidosis in high-income countries is systemic light chain (AL) amyloidosis. Symptoms of amyloidosis depend on the organs involved and can be mistaken for manifestations of other diseases, including heart failure, nephrotic syndrome, gastrointestinal (GI) disorder or polyneuropathy.
We presented two cases of AL amyloidosis with multiple organ involvement. Both cases were diagnosed and treated on late stage of disease with clinical presentations of heart failure.

Case 1

The 62-year-old man had no previous underlying disease. He had progressive four limbs weakness, stiffness and numbness for 3-4 months. Yellowish patches over bilateral periorbital region and forehead also presented. Nerve conduction velocity (NCV) was done and demonstrated severe sensory and motor polyneuropathy. The skin biopsy showed amyloid deposition in the dermis and confirmed by positive Congo red stain. A monoclonal lambda light chain was identified in serum immunofixation electrophoresis (EP). Free light chain (FLC) assay displayed a significantly elevated lambda light immunoglobulin. 6 months later, the patient was hospitalized due to bilateral lower extremities edema and dyspnea. The patient's NT-pro BNP level raised to 3818.8 pg/ml and troponin I level of 0.03 ng/ml. The electrocardiogram (ECG) report showed low QRS voltage in limb leads and poor R wave progression. Transthoracic echocardiogram displayed hypertrophic left ventricle and restrictive left ventricular filling (E/A: 2.48 and E/E' in lateral wall). Cardiac Magnetic Resonance Imaging (MRI) showed diffused circumferential enhancement in left ventricle (LV) was noticed on late gadolinium enhancement (LGE) series. Little imaging evidence of Tc99m PYP avid myocardium distribution was noticed. Systemic AL amyloidosis with cardiomyopathy and polyneuropathy was impressed. Bone marrow examination revealed a small focus of atypical plasmacytoid cells with decreased cytoplasm. The final diagnosis of (1) multiple myeloma and (2) systemic AL amyloidosis with lambda light chain monoclonal gammopathy, revised Mayo stage IV was made. We initiated 1st treatment protocol with bortezomib via subcutaneous injection, cyclophosphamide twice daily for 3 days and dexamethasone daily for 2 days on day 1, day8, day 15 and day 22. However, the patient had limited improvement in symptoms. The patient refused further treatment after 1st cycle of chemotherapy of amyloidosis and accepted palliative care afterwards.

Case 2

The 70-year-old female had underlying disease of hypertension and thyroid cancer that was resected 20 years ago. She visited our hospital because of dyspnea on exertion for several months. The patient had associated symptoms of poor appetite, significant body weight loss and decreased urine output. ECG showed low voltage over limb leads. Hypertrophic LV with restrictive LV filling was noticed on echocardiogram. Diuretics was prescribed for symptom relief

initially. However, her symptoms progressed under 2 months of outpatient department follow-up. Dyspepsia, nausea, vomiting and tarry stool were noticed occasionally. She was hospitalized again. The patient had NT-pro BNP level of 8303.4 pg/ml and troponin I level of 0.1 ng/ml. Coronary angiogram revealed no significant coronary artery disease. Cardiac MRI of her demonstrated hypertrophic LV and diffused circumferential enhancement in LV on LGE series. Tc99m PYP cardiac amyloidosis imaging showed low probability of transthyretin (ATTR) amyloidosis. Esophagogastroduodenoscopy (EGD) and colonoscopy were arranged. Diffuse mucosal swelling with erosion and giant gastric folds at lower gastric body were noticed. Moreover, diffuse hyperemic and fragile mucosa found from rectum to sigmoid-descending colon junction was observed under colonoscopy. In both specimen of stomach and rectum, intense orange-red reaction under Congo red stain and apple green birefringence under polarized light were noticed. The findings suggested amyloid fibrils invasion of both upper and lower GI tract. Immunofixation electrophoresis of serum demonstrated monoclonal IgGκ. Bone marrow examination disclosed that plasma cells were increased focally (>10%) accompanied with some dysplastic changes. Final diagnosis of (1) multiple myeloma and (2) systemic AL amyloidosis with IgGκ monoclonal gammopathy, revised Mayo stage III, was made. We initiated 1st cycle of systemic therapy with attenuated regimen of with bortezomib via subcutaneous injection, cyclophosphamide and dexamethasone. However, shock status and respiratory failure developed on day 2 of therapy. The patient expired due to the above conditions.

Discussion

We presented two cases of multiple myeloma induced AL amyloidosis with multiple organ involvement. The initial presentation of the first case was polyneuropathy but developed heart failure in 6 months. The second case was characterized by initial presentation of heart failure and GI discomfort. Both cases terminated systemic therapy of amyloidosis early.

The cases remind clinicians of the importance of early diagnosis. A published survey showed a delay in the diagnosis of amyloidosis with a median time to diagnosis of 7 months. Symptoms that should trigger an appropriate workup include cardiac symptoms, peripheral neuropathy, and gastrointestinal organ involvement. More than half patients had multiple systems involvement. Increased awareness of symptoms and signs was crucial for early diagnosis of amyloidosis. Biomarkers such as NT-pro BNP, albuminuria, and alkaline phosphatase can be monitored to detect possible amyloid organ invasion. ECG and echocardiogram can act as key role in early detection of cardiac amyloidosis. Low voltage QRS complexes and conduction block were observed in ECG. Common findings in echocardiogram include thickening of the ventricular walls, particularly the left ventricle and diastolic dysfunction. Machine learning techniques can augment the diagnosis of cardiac amyloidosis, aiding in early detection.

Management of advanced amyloidosis involves sequential treatment with rapidly acting regimens. For AL amyloidosis, treatment options may include bortezomib-based therapy, high-dose melphalan with autologous stem cell transplantation, or daratumumab-based therapy. In advanced cardiac amyloidosis, cardiac transplantation may be considered. It can provide significant improvement in survival and quality of life for selected patients.

Conclusion

We presented two cases of advanced systemic AL amyloidosis with comprehensive diagnosis management, including laboratory, imaging, and pathologic study. This case series was meant to assist clinicians to understand and enhance awareness of systemic amyloidosis.

病例報告　112_C 171

以轉移性骨病灶表現的瀰漫性鳥型結核菌感染於一位成人後天性免疫缺失症患者-案例報告及文獻回顧

Disseminated Mycobacterium Avium Complex Infection Masquerading as Metastatic Bone Lesions in a patient with Adult-Onset Immunodeficiency

梁智瑋 蔡毓德
高雄醫學大學附設醫院感染內科

Introduction

Adult-onset immunodeficiency syndrome due to anti-interferon-gamma autoantibodies is a rare immunological entity, often manifesting in Southeast Asians. A hallmark of this syndrome is susceptibility to opportunistic pathogens, especially non-tuberculous mycobacteria (NTM). In certain instances, NTM can mimic metastatic bone disease, leading to diagnostic challenges. In this case, what was initially perceived as metastatic bone lesions was later identified as disseminated Mycobacterium avium complex (MAC) infection, leading to a conclusive diagnosis of adult-onset immunodeficiency syndrome (AOIS).

Case presentation

A 65-year-old man presented with a long-term cough, sputum production, and bone pain. Initial chest computed tomography (CT) showed consolidation in the right middle lobe (RML) of the lung. Bone scans indicated potential bone metastases. However, despite a CT-guided biopsy and video-assisted thoracic surgery (VATS) of the RML, malignancy findings were inconclusive. Another CT-guided biopsy of the left hip did not reveal malignant cells. Nevertheless, Mycobacterium avium complex (MAC) was detected in a sputum culture. He subsequently developed intermittent fevers. Considering his past positive NTM result, he began treatment for NTM pulmonary disease (PD). To investigate a primary source of the metastatic bone lesions, endoscopy of the upper digestive tract, colonoscopy, and oropharyngeal fiberscope were performed but unrevealing. Concurrently, due to noticeable hematuria, non-invasive papillary urothelial carcinoma was diagnosed via bladder tumor resection. After a combination therapy of rifampin, azithromycin, and moxifloxacin, his lung consolidation resolved. The antibiotics were discontinued after a year of NTM PD treatment. However, he soon exhibited fever, increased bone pain, and swelling in the right middle finger. A Positron Emission Tomography (PET) scan demonstrated progression in bone metastases. Surgical debridement on the swollen finger confirmed a mycobacterial infection, with MAC isolated from the abscess. Disseminated MAC infection was confirmed. The anti-human immunodeficiency virus antibody in this patient was negative. Crucially, testing revealed an auto-antibody positive for AOIS. Following renewed NTM treatment, his symptoms began to recede, accompanied by improved inflammatory markers.

Discussion

The adult-onset immunodeficiency syndrome due to anti-interferon-gamma autoantibodies is a nuanced immunological condition chiefly seen in Southeast Asians[1]. Its hallmark lies in heightened vulnerability to specific pathogens, with NTM being predominant1. The presentation of disseminated NTM infection as multiple bone lesions, as seen in our patient, is a unique clinical scenario that poses significant diagnostic challenges. While MAC

infections are known to manifest in various forms, bone involvement in NTM infection is relatively rare[2]. Some case reports have documented the presence of skeletal lesions in disseminated MAC, highlighting the importance of suspecting NTM in atypical bone lesions, especially in immunocompromised states[3].

Conclusion

The findings in our case emphasize the importance of maintaining a high index of suspicion for disseminated NTM in patients presenting with unexplained bone lesions, and investigating the etiologies of immunocompromised status.

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病例報告　112_C 172

進行性多發型腦白質病變: 一個在愛滋病患者身上具挑戰性的診斷

Progressive Multifocal Leukoencephalopathy: a Challenging Diganosis in Acquired Immunodeficiency Syndrome Patients

魏辰宇[1] 林尚儀[2] 尹莘玲[3] 郭欣慧[4]

[1]高雄醫學大學附設醫院內科部 [2]高雄醫學大學附設醫院感染內科 [3]高雄醫學大學附設醫院病理部法醫病理科 [4]高雄市立大同醫院感染內科

Introduction

Progressive multifocal leukoencephalopathy (PML) is a demyelinating neurological disorder attributed to the reactivation of the JC virus (JCV).[1] Overall, low incidence with non-specific neurological manifestation and lack of laboratory markers let clinicians easily miss the diagnosis.[2] Herein, we presented a human immunodeficiency virus (HIV) -infected man whose manifestation of proven PML was multiple brain abscesses.

Case presentation

A 38-year-old man who had untreated HIV for more than ten years presented to our hospital with a 2-week history of fever and progressive shortness of breath. His most recent CD4 cell count was 15 per microliter, and his HIV viral load was 190,948 copies per milliliter. Trimethoprim/sulfamethoxazole was administered for computed tomography (CT) of the chest, which showed diffused ground glass opacities with a sparing peripheral zone and favored *Pneumocystis jirovecii* pneumonia (PJP). Unexpectedly, bizarre behavior with progressive psychotic symptoms, including delusion and poor attention, were noted with frequent falls and left-side muscle weakness. CT and magnetic resonance imaging of the brain revealed multifocal ill-defined lesions with peripheral enhancement at the right frontal and parietal lobes and right centrum semiovale. (Figure 1A-C) Clear cerebrospinal fluid (CSF) was obtained. The highly active antiretroviral therapy (HAART) was initiated soon after the FilmArray Meningitis/Encephalitis panel, and the polymerase chain reaction (PCR) of the *Mycobacterium tuberculosis complex* showed unidentified pathogens. The brain biopsy was done due to multiple brain tumors with suspected abscesses precipitated by the uncommon pathogen. The pathology revealed areas of

Figure 1 MRI of the brain revealed multiple nodular lesions with hypointense on T1W (A) and hyperintense on T2W (B) with diffuse restriction (C) in the right centrum semiovale, bilateral frontal lobe, and right parietal lobe.

(A) (B) (C)

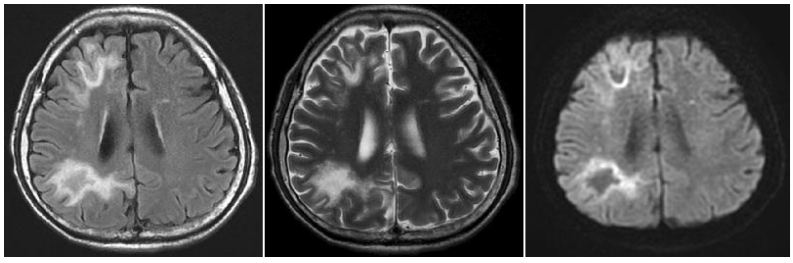
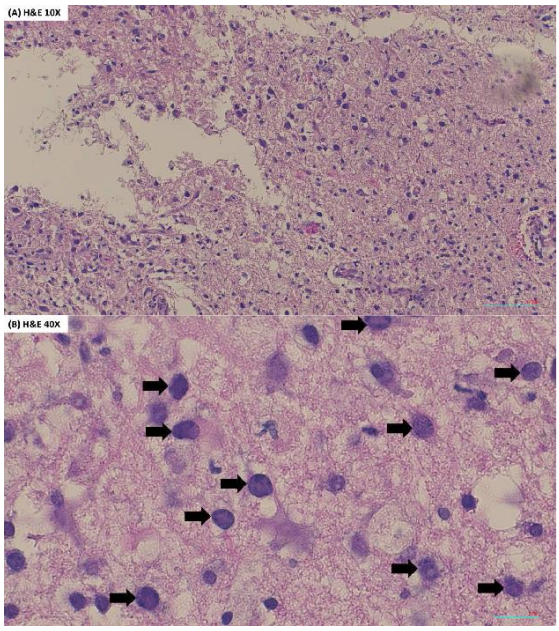
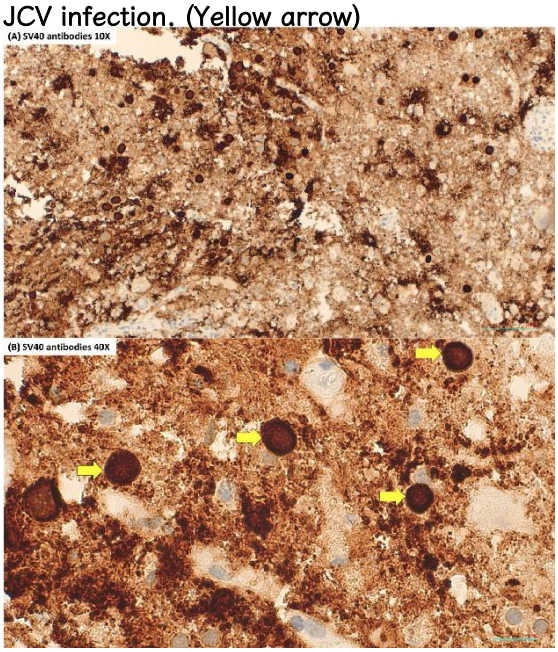


Figure 2 Areas of demyelination with abundant macrophages, enlarged oligodendroglial cells with dense chromatin, and viral inclusion bodies. (Black arrow)



demyelination with abundant macrophages, enlarged oligodendroglial cells with dense chromatin (H&E stain, Figure 2), and nuclei of infected oligodendrocytes were stained positive with Simian virus 40 (SV 40) antibodies, which represented evidence of JCV infection. (Figure 3) Therefore, the final diagnosis of progressive multifocal leukoencephalopathy was confirmed, and HAART was continued. However, neurological deficits persisted, including easy seizure attacks, left hemiplegia, and psychotic behaviors. Eventually, he died from another sepsis episode 4 months later.

Figure 3 Numerous viral inclusions were immunohistochemically positive for the SV40 antibody, representing evidence of JCV infection. (Yellow arrow)



Discussion

Chronic inflammatory disease, hematological malignancy, and HIV/AIDS were the leading predisposing conditions for PML[1,3]. Before the HIV/AIDS pandemic, PML was extremely rare and primarily exclusive in hematological malignancy[4]. However, even in the era of HAART, the overall occurrence of PML in HIV still reached 3-5%[3]. Besides, the growing concern of PML was also noted after the introduction of immunomodulatory therapy in various diseases, such as Natalizumab, with an overall incidence of 0.9%[5].

Early recognition and diagnosis of PML is difficult due to the physicians' unfamiliarity. According to the research, the median time of diagnostic delay from initial symptoms was 74 days with extended delay for more than three months in 39.7% of cases, even with the assistance of radiological, virological, and histological tests[2]. Most of the clinical manifestations were non-specific, including coordination, motor and language deficits, visual disturbance, and seizure[2]. Therefore, about 60% of PML was initially disregarded as vascular, tumoral, or other infectious diseases, regardless of HIV status[2]. With the recent development of the ultrasensitive PCR for JCV in the CSF, the frequency of detecting patient with PML had increased based on the Japanese nationwide study[3,6]. With this non-invasive diagnostic method, physicians might establish the diagnosis earlier without taking the risk of brain biopsy, such as in our patients.

Conclusion

This case reminded physicians of PML in the differential diagnosis list while facing HIV/AIDS patients who presented with neurological symptoms. Introducing more sensitive and less invasive tests is crucial in reaching the goal of early diagnosis and intervention.

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病例報告　112_C 173

內視鏡下酷似巨大黏膜下腫瘤的脾彎結腸腫瘤合併胃侵犯

Splenic Flexure Colon Cancer with Gastric Invasion Mimicking Huge Subepithelial Tumor under Endoscopy

林楷傑 [1,2]　張哲墉 [1,2]
[1] 高雄醫學大學附設醫院內科部　[2] 高雄醫學大學附設醫院胃腸內科

Introduction

Colorectal cancer is the third most common malignancy worldwide. Bedsides, in Taiwan, it has also become the most common cancer in male and the second-most common cancer in female. Approximately 10% of patients with locally advanced colorectal cancer presenting with T4 disease (T4a, peritoneal involvement; T4b, invasion of adjacent organs) at the time of diagnosis. We reported a case of a 55-year-old male with T4b colon cancer invasion to stomach, and presenting like a huge SET (subepithelial tumor) under endoscopy.

Case presentation

A 55-year-old male with underlying diseases of asthma and hypertension came to local clinic first because of progressive dyspepsia and easy bloating since 3 months ago. The symptoms progressed gradually and showed no obvious improvement after having medication treatment. Symptoms of epigastralgia, poor appetite, nausea, and caliber stool passage were also mentioned during the period. He was then referred to our emergency department because of tarry stool and progressive dyspnea for 3 days. At our emergency department, tachycardia (pulse rate: 137 beats/minute) and mild tachypnea (respiratory rate: 23 cycles/minute) were noted. His blood pressure and other vital signs remained stable. His laboratory data showed severe anemia (hemoglobin: 4.9g/dL). We soon let the patient NPO (Nil Per Os), and gave adequate intravenous fluid supplement and blood transfusion. For evaluation of UGI (upper gastrointestinal) bleeding etiology, we arranged an EGD (esophagogastroduodenoscopy) exam

Figure 1 EGD revealed huge subepithelial lesion at gastric body with central ulceration.

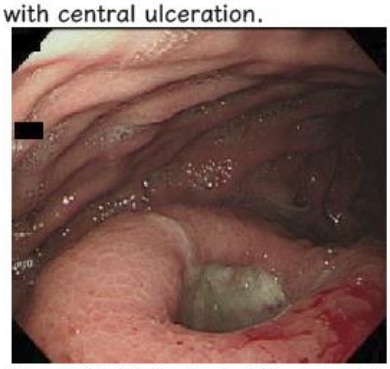


Figure 2 Colonoscopy revealed circumferential mucosal mass lesion at splenic flexure.

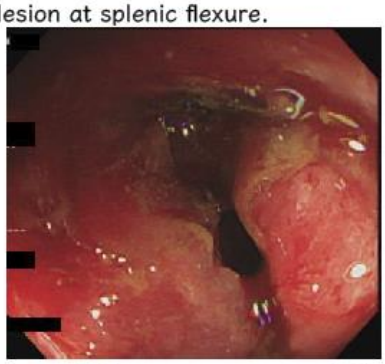


Figure 3 Abdominal CT revealed a large heterogeneous mass lesion (white arrows) with invasion to stomach. (A: axial view; B: coronal view)

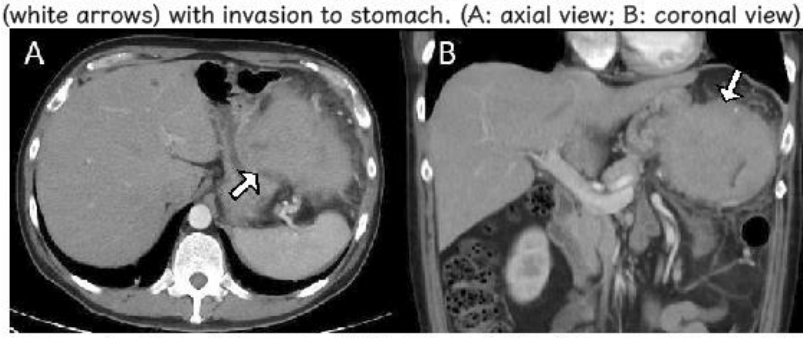


Figure 4 The follow-up EGD showed complete mucosal healing after 6 months of chemotherapy.

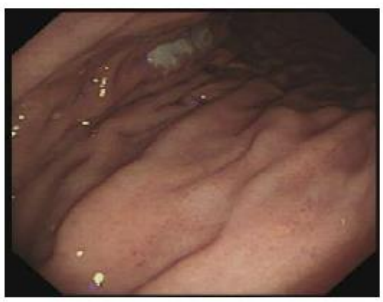
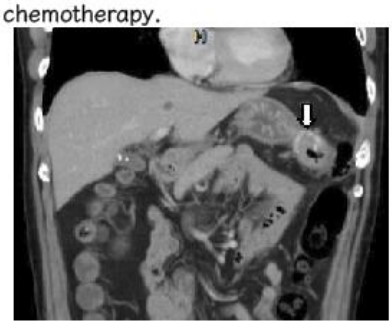


Figure 5 The follow-up abdominal CT showed apparent tumor shrinkage (white arrow) after 6 months of chemotherapy.



for the patient first. It revealed a huge subepithelial lesion at gastric greater curvature with wide and deep central ulceration (Figure 1 and Figure 2). Deep biopsy was performed from the ulcer edge to exclude malignancy. The abdominal CT (computed tomography) for tumor survey showed one large heterogeneous mass lesion (about 14cm) at the splenic flexure of colon with invasion to the stomach (Figure 3), and CT-guided biopsy was performed. Colonoscopy revealed circumferential mucosal mass lesion at splenic flexure with severe lumen stenosis, and biopsy was also performed. Tumor marker screen showed markedly elevated CEA (carcinoembryonic antigen) level (652.52 ng/mL).
Later the pathologic results from different biopsy sites (from EGD, colonoscopy, and CT-guided) all showed grade 2 adenocarcinoma. As a result, advanced colorectal cancer was diagnosed (clinical stage: cT4bN2bMb, stage IIIC, according to The American Joint Committee on Cancer staging 8th edition, 2016). The patient then received chemotherapy with FOLFOX6 regimen (oxaliplatin, leucovorin, 5-fluorouracil) plus palliative radiotherapy. The follow-up EGD and abdominal CT 6 months later showed complete resolution of the gastric mucosa and without obvious external compression (Figure 4 and 5).

Discussion

In locally advanced colon cancer patients, rectosigmoid colon is the most common area that may present as T4b disease initially, ranging from 66 to 89%. The most common invasion place is the abdominal wall, and may lead to malignant cutaneous fistula formation. Other adjacent organs being invaded depends on the primary colon cancer site. For example, cancers from cecum or sigmoid colon may invaded ovaries, fallopian tubes, uterus, or small bowel. On the other hand, cancers from hepatic flexure, transverse colon, or splenic flexure may invaded gallbladder, duodenum, stomach, pancreas, or spleen. Above all, stomach is not a very common adjacent organ being invaded by colorectal cancer. Because of the proximity of gastric greater curvature and the distal transverse colon, gastrocolic fistula was also reported in some cases.
In our case, the obtuse angle of the elevated mucosa with an ulceration in the central area pointed out the origination of the lesion may either from subepithelial area or external organs. Hence, we arranged abdominal CT scan and then colonoscopy for further detection of the primary tumor. Although CT scan is the most frequent tool used for clinical tumor staging of colorectal cancer. However, CT scan sometimes cannot differentiate peritumoral inflammation from direct tumor infiltration. As a result, using other evaluation tools (like EGD in our case) will also provide more accurate information.

Conclusion

To identify the invasion burden is crucial for surgical planning for locally advanced colorectal cancer. Careful pre-operative evaluation would be very important to avoid intraoperatively extended resection.

病例報告　112_C 174

擬似多處肺及骨頭轉移之肺部蘭格罕細胞組織球增生症

A case of pulmonary Langerhans cell histiocytosis mimicking multiple lung and bone metastases

黃宇勤[1] 莊政皓[2] 吳寬澧[2]
[1]高雄醫學大學附設醫院一般科 [2]高雄醫學大學附設醫院胸腔內科

Introduction

Langerhans cell histiocytosis (LCH) represents a neoplastic histiocytic disorder characterized by the aberrant proliferation of CD1a+/Langerin+ LCH cells within multiple organs such as the skeletal system, skin, and liver, among others. Infrequently, LCH may manifest with pulmonary involvement, making it challenging to discriminate it from other neoplastic lesions in the lung. Here, we demonstrate an LCH patient who was impressed with multiple lung and bone metastases initially.

Case presentation

A 43-year-old female presented with intermittent dull pain at the left chest wall for one month. This discomfort was notably exacerbated during deep breaths and radiated anteriorly across the chest. Her past medical history included left tinnitus and thyroid goiter. Notably, she had an extensive smoking history, consuming one pack of cigarettes daily for more than three decades.

On physical examination, she was afebrile with a normal chest wall appearance and symmetric expansions during inspiration. Auscultation of the bilateral lung fields did not reveal any abnormal breath sounds. Notably, tenderness was localized to the left lower lateral chest wall. The laboratory data disclosed within-range inflammatory parameters such as white blood cell count (WBC) and C-reactive protein (CRP) as well as a normal biochemistry profile. Chest plain film revealed multiple bilateral small lung nodules. Subsequent chest computed tomography identified multiple centrilobular nodules with cavitation in both lungs with a predilection for the upper lung zones. Additionally, an erosion was observed on the left posterior 8th rib. Further positron emission tomography (PET) was suggestive of the lung malignancy with multiple pulmonary metastases and a bony metastasis to the posterior aspect of the left 8th rib based on the evidence of high FDG uptakes on the aforementioned lesions. Tumor markers, including carcinoembryonic antigen (CEA) and squamous cell carcinoma antigen (SCC), as well as autoimmune markers, were assessed and found to be within normal limits. To collect the tissue for a conclusive diagnosis, the CT-guided biopsy for rib lesion and video-assisted thoracoscopy (VATS) wedge resection of the right lung nodule were performed, respectively. The pathological reports for both the rib and lung nodules revealed the presence of multiple clusters of histiocytic cell aggregations accompanied by infiltrations of eosinophils, lymphocytes, and neutrophils. Immunostaining further confirmed the diagnosis, with positive staining observed for CD1a, S100, and Langerin, collectively indicative of LCH.

Subsequently, the patient was commenced on corticosteroid therapy with a daily oral dose of 30mg of prednisolone. She also took the advice regarding the cessation of cigarette smoking. Following the initiation of treatment, the patient's left chest pain exhibited gradual

amelioration, and the serial pulmonary imaging assessments revealed a dramatic reduction in the size of bilateral lung nodules. The subsequent clinical course was uneventful, prompting a gradual tapering of the prednisolone dosage, which was ultimately maintained at 5mg per day.

Discussion

This report illustrates the diagnostic process of an adult patient with pulmonary LCH and subsequent treatment with steroid agents. LCH is one of the most common histiocytic disorders in pediatric patients, yet it is less prevalent in adults. Depending on the affected organs, LCH may be mistaken for various other conditions such as lymphomas, solid tumors, primary central nervous system tumors, vasculitis, cutaneous lymphoma, and other histiocytic disorders. The correct diagnosis relies on a combination of clinical, histopathological, immunophenotypic, and molecular findings. Besides, There is no standard staging system for Langerhans cell histiocytosis (LCH).

Smoking cessation is suggested universally to LCH patients. In asymptomatic patients, observation and follow-up may be enough. However, most patients may need corticosteroids or other immunosuppressants. Recently, targeted therapy such as BRAF inhibitors may be effective especially when the patient has BRAF V600E mutations. For individuals with end-stage pulmonary LCH, lung transplantation may be the last method.

In conclusion, LCH is a rare pulmonary disease representing a diagnostic challenge. A history of smoking in individuals of a relatively young age may raise suspicions regarding the condition. Nevertheless, the definitive diagnosis necessitates tissue confirmation. Treatment with corticosteroids often yields significant efficacy; however, the potential of disease relapse following the discontinuation of medication should not be overlooked.

病例報告　112_C 175

末期肺癌出現皮膚轉移擬似蜂窩性組織炎—案例報告及文獻回顧

Skin Metastasis Mimicking Cellulitis in An Advanced Lung Cancer Patients

顧天衡[1] 陳惇杰[2]
[1]高雄醫學大學附設醫院內科部 [2]高雄醫學大學附設醫院感染內科

Introduction

Among the symptoms and signs related to lung adenocarcinoma, chronic cough, sputum, chest pain and short breath were the most common. However, we should also be cautious of other rare manifestation, including signs of paraneoplastic syndrome or even skin presentation, especially when the patient was covered by history of COPD or a chronic cough was the only manifestation. We presented the rare and interesting case and make a literature review.

Case presentation

A 78-year-old female with hyperlipidemia, hyperthyroidism, suspect multinodular goiter related, benign brain tumor with unknown etiology, post tumor excision during 2007 to 2008, and L3 to L5 with 2 interbody fusion cage, who initially encountered due to acute fever with chronic left facial erythematous change and swelling. At first, facial cellulitis was suspected and Amoxicillin 1000mg + Clavulanic acid and Clindamycin were added, but the effect was limited. Therefore, other autoimmune disease or hematologic disease with skin manifestation were suspected, and later, the data showed borderline ANA level, anti-Mi2B and anti-Ro52 elevation, and significantly elevated CEA and CA-153 level. The rheumatologist was consulted who suggested Sjogren's syndrome, but the patient could not cooperate with the Schiremer' test. The dermatologist was consulted, and the pathology result of skin biopsy revealed lung origin metastasis. The bronchoscopy biopsy later confirmed grade 2 lung adenocarcinoma. Also, the breast surgeon performed mammography and core biopsy due to elevated CA-153, but the pathology results also indicated lung adenocarcinoma with breast metastasis. Therefore, the final diagnosis was made.

Discussion

In Taiwan, lung cancer is the second common malignancy, but accounts for the highest amount of mortality. Although lung cancer mostly metastasizes to the contralateral lung, liver, bones, brain, and adrenal glands, over 1-12% of patients with lung cancer can develop skin metastasis. The shape, form, color and lesion site vary in many studies. However, the prognosis of lung cancer with skin metastases usually is poor, and the survival ranging from 3 to 15 months.

Conclusion

In this case, the lung cancer developed a rare manifestation at an advanced stage. Fortunately, the treatment response is acceptable under Afatinib use.

病例報告　112_C 176

一個罕見上下肢同時發生急性肢體缺血的個案成功的藉由 Rotarex 機械血栓抽吸成功治療

A case of acute limb ischemia simultaneously over upper and lower limbs successfully treated by Rotarex mechanical thrombectomy

李柏瀚[1] 許栢超[1,2] 張景棠[1,2] 林子傑[1,2] 李孟光[1,2] 林宗翰[1,2] 蔡維中[1,2] 蘇河名[1,2] 林宗憲[1,2] 紀乃宇[1,2]
[1]高雄醫學大學附設中和紀念醫院內科部 [2]高雄醫學大學附設中和紀念醫院心臟內科

Introduction

Acute limb ischemia (ALI), characterized by a sudden decrease in limb perfusion within 14 days, constitutes a clinical emergency with the potential for limb loss and life-threatening consequences. Timely and precise diagnosis, as well as urgent intervention, are critical to preventing major complications such as limb loss and reperfusion syndrome. In addition, simultaneous ALI over upper limb and lower limb are rarely reported in the literature. Herin, we presented a 69-year-old patient who suffered from simultaneously ALI at right lower and left upper limb and successfully treated with Rotarex thrombectomy, angioplasty and catheter directed thromboylsis.

Case Presentation

We present a complex case of a 69-year-old male patient with multiple underlying medical conditions, including atrial fibrillation on long-term edoxaban therapy, concurrent right hypopharyngeal cancer with lung metastasis receiving chemotherapy, chronic kidney disease, and coronary artery disease. The patient presented to our emergency department with sudden-onset left arm and right lower limb pain, paresthesia, and persistent cold sensation. He had recently undergone right upper lobe lung wedge resection and had discontinued edoxaban therapy for 2 weeks.

Physical examination revealed a pale left upper limb and right lower limb with weak radial and dorsalis pedis pulsation. Laboratory tests indicated elevated levels of C-reactive protein (CRP) at 43 mg/L and D-dimer at 9.04 mg/L. Emergent left upper limb computed tomography angiography revealed thrombosis below the left brachial artery, confirming acute limb ischemia. Percutaneous angioplasty was immediately performed. Initial angiography revealed extensive thrombosis at the left axillary, ulnar, and radial arteries. A similar thrombotic picture was observed in the right common iliac artery, right external and internal iliac arteries, and right femoral artery. Fortunately, the bilateral renal arteries and superior mesenteric artery remained patent. We successfully treated the patient with Rotarex thrombectomy of the left axillary, brachial, ulnar, and radial arteries, followed by balloon angioplasty. Similar procedures were performed on the right common iliac, external iliac, and common femoral arteries. Foutain catheter were placed in the left axillary artery and right common iliac artery. Above mentioned intervention partially restored distal blood flow in the left upper limb and right lower limb. Subsequent angiography, conducted the following day, confirmed patent left axillary, brachial, ulnar arteries, and right external iliac and common femoral arteries. However, distal thrombosis persisted in the left radial artery and anterior tibial artery, which were successfully treated with angioplasty. Residual thrombosis was also identified in the right internal iliac artery, managed through angioplasty and bare metal stent placement. A follow-up brachial-ankle index assessment conducted two days later indicated normal results,

confirming the restoration of blood flow. The patient was discharged one week later, receiving long-term anticoagulation therapy with dabigatran without notable complications.

Discussion

ALI is a critical medical condition characterized by a sudden reduction in limb perfusion, carrying significant morbidity and mortality risks. With 30-day mortality rates ranging from 15% to 25% and a potential for 10% to 15% major amputation, urgent intervention is imperative to improve patient outcomes. Various treatment modalities have been employed, including anticoagulation, endovascular techniques such as aspiration, angioplasty, and stenting, catheter-directed thrombolysis, and surgical revascularization[1].

In recent years, the development of novel mechanical thrombectomy devices has revolutionized the field by enabling minimally invasive yet rapid removal of a substantial thrombotic burden within a short time frame. One such device, the Rotarex Device, operates on the principle of a spiral rotating at approximately 40,000 revolutions per minute, attached to the catheter's tip. This rotation induces thrombus fragmentation, facilitating subsequent aspiration-based thrombus extraction[2].

Notably, a study by Samuel Heller et al. in 2017 demonstrated the effectiveness of the Rotarex Device in reducing 30-day mortality rates, lowering amputation rates, and enhancing the success rate of revascularization in cases of ALI when compared to traditional thrombolysis[3].

Building upon this foundation, our case presents a unique application of the Rotarex Device in a patient suffering from simultaneous acute upper and lower limb ischemia due to cardiac emboli. This intervention resulted in rapid restoration of blood flow and patient recovery without any notable complications.

Conclusion

To the best of our knowledge, this is the first documented case showcasing the efficacy of the Rotarex Device not only in lower extremities but also in upper extremities, extending as distally as the radial artery. When considered alongside established treatment modalities, the combination of Rotarex thrombectomy with catheter-directed thrombolysis emerges as a promising therapeutic option for the management of ALI. Further research and clinical trials are warranted to validate its broader applicability and long-term outcomes in such cases.

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病例報告　112_C 177

以呼吸衰竭來表現的氣管內間變性淋巴瘤激酶(ALK)陽性的肺腺癌，成功使用 Brigatinib 治療而脫離呼吸器的案例報告 ： 來自原本的肺多形性肺癌還是另一個原發的肺腺癌?

A case report of ALK-positive lung adenocarcinoma manifested as respiratory failure, successfully treated with Brigatinib and weaned off the ventilator: Is it from the original polymorphic lung cancer or another primary lung adenocarcinoma?

蕭喻心[1] 張維安[2] 姜宏興[3] 賴薇安[4] 楊志仁[1,2]
高雄醫學大學附設醫院 [1]一般科 [2]內科部胸腔內科 [3]外科部胸腔外科 [4]病理部

Introduction

Pleomorphic carcinoma is distinguished by a combination of squamous, adenocarcinoma, or large cell carcinoma with over 10% composed of spindle cells and/or neoplastic giant cells. We detail a case diagnosed with ALK (anaplastic lymphoma kinase)-positive lung adenocarcinoma leading to respiratory failure. This report emphasizes the successful removal of a left main bronchus stent after one month of Brigatinib therapy and deliberates whether the endobronchial lung adenocarcinoma is primary or secondary.

Case Presentation

A 62-year-old female with a history of grade 3 left lower lung pleomorphic carcinoma, marked by spindle cell carcinoma and lung adenocarcinoma (pT2aN0M0, stage IB), previously underwent thoracoscopic left lower lobe lobectomy, mediastinal lymph node dissection and adjuvant platinum based chemotherapy. This time, she arrived at the Emergency Room displaying severe wheezing, hemoptysis, and dyspnea. Respiratory failure and a collapsed left lung necessitated intubation. A Chest CT identified a substantial lung mass in the subcarinal region, an obstructed left main bronchus, and some pleural effusion. Her condition was critical, and hospice care was considered. An urgent bronchoscopy depicted total occlusion of the left main bronchus due to a blood clot and an endobronchial tumor, with another clot in the right upper bronchus. Biopsy results confirmed grade 3 adenocarcinoma. Immediate genetic mutation testing was ordered. Given her fragile condition, tracheobronchial stenting was executed, followed by transbronchoscopic laser ablation of the tumor with stent implantation. Subsequent tests identified an ALK mutation. Treatment with Brigatinib, an ALK inhibitor, commenced at once. After successful weaning, the patient was extubated and discharged in stable condition without oxygen aid. One month post-discharge, her stent was removed, and Brigatinib treatment continued due to her ALK (+) lung adenocarcinoma.

Discussion

The World Health Organization classifies pleomorphic carcinoma as a subtype of sarcomatoid carcinoma in lung tumors. It carries a grim prognosis, showing resistance to traditional chemotherapy and a high relapse rate. Defined as a poorly differentiated non-small-cell lung cancer (NSCLC) comprising at least 10% spindle or giant cells, Brigatinib, an advanced ALK inhibitor, offers a prolonged progression-free survival in ALK-positive NSCLC patients compared to its first-generation counterpart, crizotinib. In this case, the onset of respiratory failure indicated potential pleomorphic carcinoma metastasis. The bronchoscopic biopsy

displayed an ALK-positive grade 3 adenocarcinoma. Whether this adenocarcinoma stems from the earlier pleomorphic carcinoma or is a distinct primary lung adenocarcinoma remains undetermined. Results from ALK staining for the previous pleomorphic carcinoma are awaited. In addition, genomic exam cannot be emphasized more in such a critical lung cancer patient, though her previous cancer is not treatable.

Conclusion

To conclude, the patient, previously diagnosed with pleomorphic carcinoma, presented with ALK-rearranged adenocarcinoma and suffered respiratory failure. Brigatinib treatment led to her successful recovery. However, the origin of the ALK (+) adenocarcinoma is yet to be ascertained.

病例報告　112_C 178

罕見的成年男性前縱膈腔卵黃囊腫瘤 ： 無精症是個前驅症狀?

A Rare Adult Mediastinal Yolk Sac Tumor：Is Azoospermia a Prodromal Sign?

郭偉儒[1] 楊志仁[2]
高雄醫學大學附設中和紀念醫院 [1]一般科 [2]內科部胸腔內科

Introduction

Primary mediastinal yolk sac tumors are rare tumors of the mediastinum. They typically present in the 2nd to 3rd decade of life, making them extremely rare in middle-aged individuals. Clinical manifestations can range from being asymptomatic to symptoms such as chest tightness, dyspnea, and superior vena cava syndrome. We present a unique case of a 54-year-old male with a significant mediastinal mass diagnosed as a yolk sac tumor, accompanied by an underlying condition of azoospermia-induced infertility.

Case Presentation

A 54-year-old male, with a history of hypertension, presented with intermittent chest tightness, dyspnea on exertion, and progressive shortness of breath for 2 months. Radiological examinations, including chest X-ray and computed tomography (CT), displayed a 15.5 cm mediastinal mass associated with lymphadenopathy, pericardial effusion, and pleural effusion. Laboratory findings indicated elevated alpha-fetoprotein (AFP) levels at 3550.6 ng/ml and raised lactate dehydrogenase (LDH) levels of 660.2 IU/L. Other markers such as β-hCG, CEA, β2-microglobulin, and liver function tests were within normal limits, leading to a provisional diagnosis of a mediastinal germ cell tumor. A CT-guided biopsy revealed immunoreactivity for SALL4, glypican-3, and CD117, with focal reactivity for PLAP. However, it was negative for CD30, OCT 3/4, and TTF-1. These findings were consistent with a yolk sac tumor. A testicular ultrasound was performed to rule out a testicular origin or potential metastasis, revealing bilateral testicular atrophy. The patient's medical history was also notable for infertility due to azoospermia.

Discussion

Extragonadal malignant germ cell tumors are rare, comprising about 10% of anterior mediastinal masses. Seminomas represent 4% of these, while yolk sac tumors, even rarer, account for around 7%. While these tumors predominantly occur in post-pubertal patients (averaging around 30 years of age), diagnosing a yolk sac tumor in patients over 40 is exceptional. Typical tumor markers include AFP, β-hCG, and LDH. Furthermore, chest CT can be instrumental in delineating adjacent structures and identifying associated abnormalities, like pericardial effusion, which can inform potential surgical interventions. Pathologically, these tumors might display a Schiller-Duval body, a characteristic glomeruloid perivascular arrangement. Immunohistochemistry often reveals positive staining for markers like CK AE1/AE3, CK7, EMA, Alpha Fetoprotein, and Glypican-3. The relationship between azoospermia and mediastinal yolk sac tumors remains enigmatic. It's observed that men with testicular cancers, including yolk sac tumors, frequently exhibit compromised semen quality. Infertile men presenting with semen abnormalities have an increased risk (almost 20-fold) of developing testicular cancer. Prior research also suggests that Klinefelter syndrome might

increase the risk of mediastinal germ cell tumors post-puberty, though the reasons are still ambiguous.

Conclusion

While primary mediastinal yolk sac tumors predominantly emerge in the 2nd to 3rd decade of life, they can also manifest in middle-aged individuals. The connection between azoospermia and these tumors remains speculative and warrants further investigation. However, given the malignant nature of mediastinal yolk sac tumors, clinicians should be vigilant and consider this diagnosis in young male patients presenting with infertility or azoospermia.

病例報告　112_C 179

以器質化肺炎表現的抗 MDA5 抗體陽性皮肌炎病例：個案報告

A Patient with anti-MDA-5 Positive Dermatomyositis Presents with Organizing Pneumonia: A Case Report

温家誠[1] 王麗雅[2] 顏瑜瑩[2] 蔡毓真[1,3,4]
[1]高雄醫學大學附設醫院內科部 [2]高雄市立大同醫院專科護理室 [3]高雄醫學大學附設醫院一般醫學內科 [4]高雄醫學大學附設醫院胸腔內科

Introduction

Among all DM (dermatomyositis), melanoma differentiation-associated gene (MDA-5) was known for rapid progression of interstitial lung disease. It's a rare autoimmune disease predominantly reported in East Asia. Herein, we reported a mortal case with MDA-5 pneumonitis and acute respiratory failure.

Case presentation

A 55-year-old male with hypertension presented to our clinic with non-productive cough, nasal congestion, chest tightness and dyspnea on exertion for 3-4 days. High fever for one day was also mentioned. He worked as a disinfection personnel for decades, and he denied recent travel/contact/cluster history. The initial physical examination showed no apparent skin rash, and the auscultation showed no obvious wheezing nor crackles. The chest radiography revealed bilateral, especially right lung middle/lower lobe consolidation. Under the impression of as community acquired pneumonia, he was hospitalized. Empirical antibiotic use with amoxicillin + clavulanate was administered. However, his fever persisted after 2 weeks of antibiotic treatment, and the chest radiograph showed limited improvement. He also mentioned about progressive dyspnea and weakness. Chest CT (computed tomography) was performed for survey and revealed bilateral lower lobe-predominant consolidations, compatible with the characteristic of organizing pneumonia.

His fever subsided after steroid use. Follow-up blood test showed elevated CPK (Creatine-phospho-kinase) 659 IU/L and LDH (lactate dehydrogenase) 471 IU/L. Autoimmune profiles was checked, and revealed ANA (antinuclear antibodies) titer <1:40. The anti-MDA-5 antibody revealed positive. A diagnosis of clinically amyopathic dermatomyositis was impressed. After discussion with the Rheumatologist, Methylprednisolone 40mg three times per day was prescribed, but the clinical improvement was limited. Gradually progressed malaise, along with poor appetite and decreased body weight were noticed. The treatment with Rituximab was proposed, but the patient hesitated due to the expense. Due to personal reason, he decided to discharge with oral prednisolone.

One week after discharge, he was sent to our emergency room due to progressive shortness of breath. Acute respiratory failure related to ARDS (acute respiratory distress syndrome) was impressed. He was intubated with mechanical ventilator support immediately. Unfortunately, profound shock, acute kidney injury, and impaired liver function developed despite under Methylprednisolone 40mg three times per day and antibiotics use. Two days after the admission, the patient expired under acute respiratory failure along with multi-organ failure.

Discussion

The prevalence of anti-MDA5 DM ranges from 7 to 60%, with higher prevalence in Asian (11-60%) than in Caucasian (7-16%). Among the patients, two-thirds are female at median age of 50. The presence of typical skin rash, such as Gottron's papules and heliotrope, rash was commonly described in anti-MDA5 DM. However, myositis related symptoms might not presented, and was referred to as CADM (clinically amyopathic dermatomyositis). An early lung involvement might present prior to skin lesions. Among the literature, the most common CT presentation was bilateral ground-glass pattern. In one study, Bilateral ground-glass attenuation, air-space consolidation, and reticular shadows were observed in 20 (100%), 15 (75%), and 3 (15%) patients, respectively. In another study, lower lung consolidation or ground-glass attenuation (GGA) pattern (50.0%) and random GGA pattern (33.3%) were the predominant patterns.

Combination therapy of high-dose glucocorticoids and other immunosuppressant should be considered. A multicenter prospective study form Japan showed combined immunosuppressive regimen of high-dose glucocorticoids, tacrolimus, and intravenous cyclophosphamide had significantly higher survival rate comparing to high-dose glucocorticoids followed by immune-suppressants. A case series reported that rituximab was applied in patients who failed to respond to high-dose systemic steroid and other intensive immunosuppressive therapies. Other agents had been reported, such as tofacitinib, basiliximab, daratumumab, IVIG (intravenous immunoglobulin) and plasma exchange, but the outcome was limited.

The prognosis was still poor even under the therapies mentioned above. The lack of presence of muscle weakness and skin presentation surely obscured the diagnosis. The six-month survival rate was 41% in a retrospective cohort study.

Conclusion

A prompt diagnosis was crucial for the concern of the rapid progression. The patient was certainly a reminder for the well-known disease, with little clinical clue at the first presence.

病例報告　112_C 180

胃鏡意外發現的頸段食道平滑肌瘤

A case of leiomyoma was accidentally found in the cervical esophagus during Esophagogastroduodenoscopy(EGD)

楊啓昇[1]　林志豪[1,2]
高雄醫學大學附設醫院 [1]內科部 [2]腸胃內科

Introduction

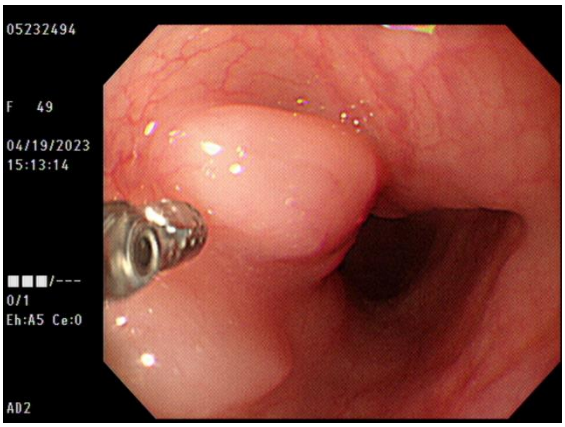
Leiomyomas of the gastrointestinal tract are relatively rare lesions. It was originated from any smooth muscle fiber in the gastrointestinal tract without malignant potential that may develop in any part of the gastrointestinal system. We report a case of a 49-year-old female with an underlying disease of teratoma post operation more than 10 years ago, who came to our hospital for a regular health examination. Ultimately diagnosed with leiomyoma in the cervical esophagus.

Case report

A 49-year-old female had a history of teratoma post operation for more than 10 years ago and gastroesophageal reflux disease (GERD).

The patient intermittently followed up at clinics with gastroesophageal reflux disease (GERD). Her activities of daily living are totally independent. One week before the examination, she complained of a heartburn sensation. She denied fever with chills, dyspnea, rhinorrhea, sore throat, abdominal pain, nausea, vomiting, and dysuria. Then, she went to our clinics for help. There was no allergy to NSAID (nonsteroidal anti-inflammatory drug). She lived at home with her family. She denied any alcohol, betel nut, cigarette use. She also denied cancer history in her family.

Figure 1. submucosal tumor by clearly visualizing a mass protruding into the lumen of the esophagus, with normal looking mucosa covering the swelling.



Initially, the patient was alert and fully oriented. The temperature was 36.1℃, no fever was noted. There was no wheezing in bilateral lungs. The heart sounds were normal. Blood specimens were obtained for laboratory analysis in this hospital. White blood cell count and platelet count were normal, as were urea nitrogen, glucose, total protein, globulin, direct and total bilirubin, aspartate aminotransferase, alanine aminotransferase, and lactic acid and the plasma anion gap. Posteroanterior chest radiograph showed no area of consolidation and no lobar collapse or pulmonary masses.

Esophagogastroduodenoscopy(EGD) was arranged, the report showed an erosive esophagitis, Los Angeles classification grade A and esophageal tumor was noted, the size was around 1.5cm over 16-17 cm from incisor. [figure 1]. Pathological specimens was sent, the report showed hyperplastic squamous epithelium, with focal nodular proliferation of bland-appearing CD34 negative / CD117 negative / Desmin-positivity in spindle cells arranged in interlacing fascicles, favored leiomyoma. After confirming the diagnosis, due to the size of

the tumor being around 1.5cm without obvious symptoms, the patient kept following up at our Clinics.

Discussion

Leiomyoma is thought to have a lower malignant potential, and the image under esophagogastroduodenoscopy showed submucosal tumor by clearly visualizing a mass protruding into the lumen of the esophagus, with normal looking mucosa covering the swelling. Further CT scan or endoscopic ultrasonography (EUS) are a valuable investigation in confirming the diagnosis[1]. An endoscopic ultrasound will delineate the intramural nature of the tumor with no associated mediastinal lymph node enlargement. Once diagnosed, all patients with symptomatic tumors are advised excision or enucleation of the tumor[2]. In some cases, esophageal leiomyoma larger than 5 cm is also a candidate for operation[3]. Surgical operation is the most effective method, and the prognosis is good. Endoscopic mucosal (EMR) and submucosal dissection (ESD) are also options, the procedure can be successfully applied with low complication rates in experienced hands instead of treatment methods with higher morbidity such as surgery[4].

Conclusion

We presented this case with an underlying disease of teratoma post operation more than 10 years ago and gastroesophageal reflux disease (GERD), who accidentally found leiomyoma during esophagogastroduodenoscopy examination. Due to the tumor size being about 1.5cm, below 5cm and the patient denied any discomfort, she was kept follow-up Esophagogastroduodenoscopy(EGD) at our clinics.

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病例報告　112_C 181

一個急性腸繫膜缺血的案例透過 Rotarex 機械性血栓抽吸和進一步的導管直接溶栓成功治療

A case of acute mesenteric ischemia successfully treated by Rotarex mechanical thrombectomy and further catheter-directed thrombolysis

張恩嘉[1] 紀乃宇[1,2] 張景棠[1,2] 林子傑[1,2] 李孟光[1,2] 林宗翰[1,2] 蔡維中[1,2] 蘇河名[1,2] 林宗憲[1,2] 許栢超[1,2]
高雄醫學大學附設中和紀念醫院 [1]內科部 [2]心臟內科

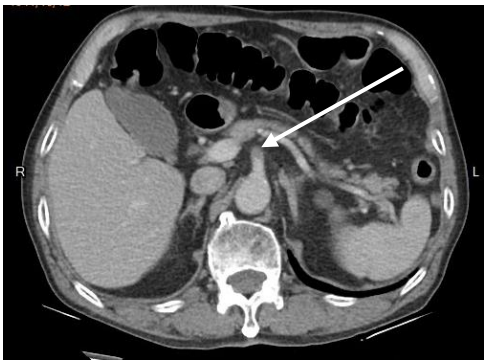
Introduction

Acute mesenteric ischemia (AMI) is typically defined as a group of diseases characterized by an interruption of blood supply to various portions of the small intestine, resulting in ischemia and secondary inflammatory changes. If left untreated, this process can lead to life-threatening intestinal necrosis[1]. Mortality rates for acute mesenteric ischemia remain high. Statistically, the overall mortality rate for cases requiring surgical intervention exceeds 50 percent[2]. Treatment options for acute mesenteric ischemia caused by acute mesenteric thrombosis include endovascular and surgical revascularization. For endovascular intervention, both of percutaneous mechanical thrombectomy (PMT) and catheter-directed thrombolysis (CDT) can be used for treatment of AMI, however, PMT might decrease the treatment duration and improved the sucess rate. Herein, we present a case of acute superior mesenteric artery (SMA) thrombosis in which the patient underwent percutaneous angioplasty with Rotarex PMT.

Case presentation

The patient is an 81-year-old man with a history of hypertension. He presented with acute onset diffuse abdominal pain that had been ongoing for four days, accompanied by complaints of abdominal fullness, nausea, and vomiting. Initially, he sought medical attention at another hospital's emergency room.

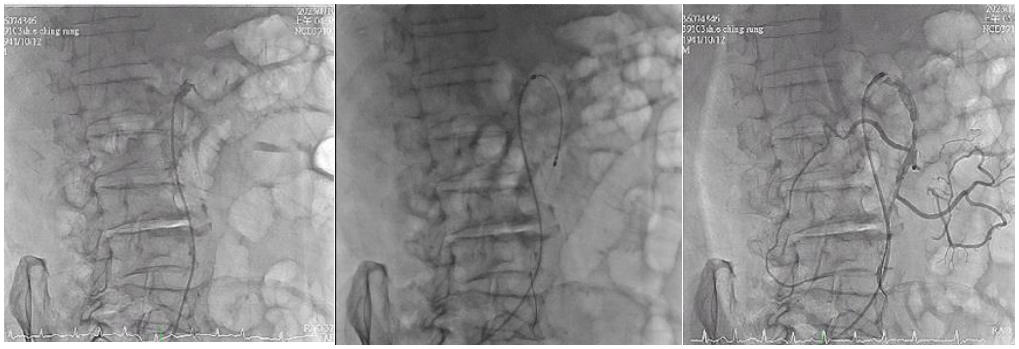
Figure1



An abdominal CT scan with contrast at the previous hospital revealed suspected thrombosis of the SMA (Figure 1), resulting in bowel ischemia. Subsequently, he was transferred to our hospital for further management. Upon arrival at the emergency room, his initial vital signs were as follows: blood Pressure (BP): 146/91 mmHg, heart rate (HR): 97 bpm, respiratory rate (RR): 15 cpm, body temperature (BT): 38.1℃, and oxygen saturation (SpO2): 100%. Laboratory tests indicated lactate acidosis and elevated C-reactive protein (CRP) levels [Lactate: 3.39 mmol/L, HCO3-: 18.5 mmol/L, CRP: 222 mg/L]. Due to the suspicion of acute SMA thrombosis, we promptly arranged angiography for him. The angiography revealed a 100% occlusion of the SMA from its orifice with a significant thrombus burden (Figure 2-1). We performed balloon angioplasty and Rotarex PMT to treat the SMA thrombosis (Figure 2-2) and inserted a Fountain catheter for further CDT. After several days treatment of CDT, follow-up angiography showed greatly improve blood flow of SMA(Figure 2-3). Afterward, we initiated treatment with rivaroxaban 15mg twice daily and patient was discharged uneventfully.

Discussion

Figure 2-1　　Figure 2-2　　Figure 2-3



Acute SMA thrombosis is a severe and potentially fatal condition as it provides the primary arterial supply to the small intestine and ascending colon[3]. Early detection and prompt treatment are crucial in managing mesenteric artery thrombosis. When there is clinical suspicion of AMI, performing computed tomography angiography (CTA) as soon as possible is essential. Delay in diagnosis is the predominant factor contributing to continued high mortality rates, which can range from 30% to 70%[4].

Treatment options for AMI resulting from acute mesenteric thrombosis include both endovascular and surgical revascularization. The use of percutaneous endovascular intervention in treating AMI remains a topic of debate, primarily because it does not involve direct inspection of the bowel. However, percutaneous intervention offers the advantage of being a less invasive procedure compared to laparotomy, making it particularly suitable for older and more frail patients.

The Rotarex system is a device of PMT that employs a catheter to remove detachable occlusion materials within the artery. The catheter generates a powerful vortex that breaks down the debris and creates suction to transport the materials into an external collection bag[5]. Following thrombectomy, additional management options include balloon angioplasty, CDT, or stent implantation. PMT helps restore blood flow to the mesenteric artery more rapidly and can prevent further bowel ischemia. Additionally, it may shorten the duration of CDT and parenteral anticoagulation.

Conclusion

AMI carries a high risk of mortality, emphasizing the importance of making an accurate diagnosis. PMT by Rotarex device is a rapid and convenient option for AMI, particularly for frail or elderly patients. In addition, PMT may also reduce the treatment duration and restore blood flow to the SMA sooner. This could potentially decrease the ischemic duration of the SMA and improve the outcome.

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病例報告　112_C 182

顱底念珠菌骨髓炎成功治癒案例

Successful treatment of a mixed candidal and bacterial skull base osteomyelitis with antibiotics and hyperbaric oxygen therapy – A rare case report

劉宇馨 林俊祐
高雄醫學大學附設中和紀念醫院內科部

Introduction

Candidal osteoarticular infections are most often seen in immunocompromised patients, resulting from hematogenous seeding to the bone or joint. The most common affected sites in adults are vertebral disc and knee joints. Here we reported a rare case presented with mixed pathogens of candida and bacteria osteomyelitis involved skull base.

Case presentation

A 57-year-old male with the underlying disease of diabetes mellitus poor control and psoriasis vulgaris. He suffered from severe headache for at least three months. Associated symptoms were ears pain, tinnitus, neck stiffness, slurred speech, dysphagia, unsteady gait, nausea, and vomiting. Brain CT scan at a local hospital revealed a mass over left Rosenmuller fossa. MRI revealed no CNS involvement. Biopsy of the nasopharynx was done, and pathology showed negative for malignancy. After the patient was discharged from this local hospital without definite diagnosis and specific management, fever, general malaise and drowsy consciousness were noted for one week. He then visited our hospital for help. Nasopharyngeal carcinoma and CNS infection were both suspected. Neurological examination revealed drowsy consciousness, slow response with dysphagia and slurred speech. CSF study was done and revealed pleocytosis with monocytes predominant. He was admitted to internal medicine ward for further management. Acyclovir 500 mg Q8H was given initially for suspect aseptic meningitis. Ceftazidime and Amikacin were both prescribed for suspected malignant external otitis. Operation approaching the mass lesion from nasopharynx was done. Resected tissue culture yielded *Pseudomonas aeruginosa*. Pathology examination reported invasive candidiasis. PAS stain demonstrated some entrapped yeast and pseudohyphae of candida. Based on the diagnosis of invasive fungal infection with osteomyelitis over skull base and meningitis, mixed with bacterial infection, Amphotericin B was given for two weeks and adjusted to Fluconazole due to hypokalemia and hypomagnesemia. Brain CT scan revealed bony erosion over the clivus bone in the left aspect and highly suspect infection / inflammation process, osteomyelitis with perilesional spreading in left aspect of skull base. Hyperbaric oxygen therapy was initiated. Ceftazidime was adjusted to Ciprofloxacin. After condition became stable, the patient was discharged with oral form Ciprofloxacin, Fluconazole and kept on hyperbaric oxygen therapy in OPD. ESR, skull base CT and bone scan were checked for following up. Skull base CT six months after discharge revealed retropharyngeal pre-vertebral soft tissue thickening along with mild demineralization of the clivus, which showed much improvement. Neurological symptoms, including slurred speech and unsteady gait, improved after treatment. The patient received Ciprofloxacin for six months and Fluconazole for totally one year. There was no neurological sequela of his daily life. No recurrence was seen in the following ten years.

Conclusion

Candidal skull base osteomyelitis is a rare site of invasive candidiasis and is difficult to diagnose. The patient had good response after antibiotics and hyperbaric oxygen therapy.

病例報告　112_C 183

轉移性大腸直腸癌患者經 Alpelisib 治療後引起的腸胃道毒性：病例報告

Alpelisib-induced gastrointestinal toxicity in a metastatic colorectal cancer patient: A Case Report

謝華蓁[1,3] 張哲墉[2,3] 陳立宗[2,3] 吳政毅[2,3] 范文傑[4] 吳宜珍[2,3]

[1]高雄醫學大學附設醫院內科部 [2]高雄醫學大學附設醫院胃腸內科 [3]高雄醫學大學醫學系 [4]高雄市立大同醫院一般及消化系外科

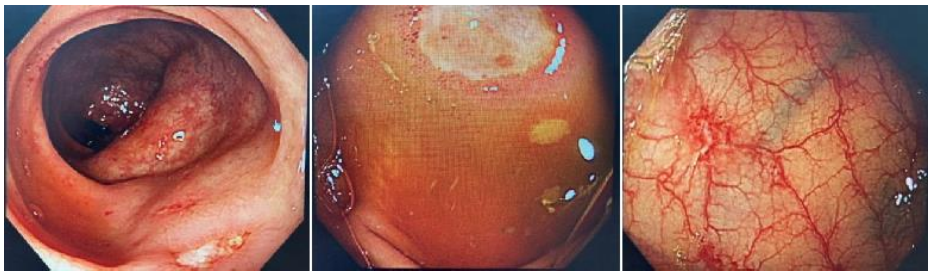
Introduction

The *PI3K* (Phosphatidylinositol 3-kinase)/*Akt*/*mTOR* signaling pathway is involved in regulation of cell proliferation, tumor angiogenesis, metastasis, apoptosis, and drug resistance. Activations of the pathway caused by *PIK3CA* gene mutation is related to the pathogenesis and progression of colorectal cancer, which also found in multiple human cancers, including breast, ovarian, brain, liver, stomach, head and neck, and lung. Alpelisib, *PI3Kα* inhibitor approved for hormone receptor positive, *HER2* (human epidermal growth factor receptor 2) negative, *PIK3CA*-mutated, advanced/metastatic breast cancer treatment, is now evaluated for colorectal cancer in clinical trials. The common drug-related toxicities of Alpelisib consist of hyperglycemia, gastrointestinal disorders (such as diarrhea, nausea and decreased appetite), skin rash, and fatigue. Herein, we presented the case of metastatic colorectal cancer who developed gastrointestinal toxicities under Alpelisib treatment.

Case presentation

A 65-year-old female was diagnosed with ascending colon adenocarcinoma, cT2N1M0, stage III in March 2021, with initial presentation of positive fecal occult blood test. She received laparoscopic right hemicolectomy, and pathological report disclosed ascending colon adenocarcinoma, pT3N2aM0, stage IIIA. She then underwent 12 courses of adjuvant chemotherapy with mFOLFOX6 (Leucovorin+ 5-Fluorouracil+ Oxaliplatin) from April 2021 to December 2021 followed by oral UFUR with disease free status. However, new liver tumors were found on abdominal CT in March 2023; biopsy confirmed metastases from colon adenocarcinoma. The gene study showed *KRAS* mutation, and she was treated with 3 courses of chemotherapy with FOLFIRI (Leucovorin + 5-Fluorouracil + Irinotecan) and Bevacizumab. But, abdominal CT in July 2023 showed tumor progression. Chemotherapy with 5-fluorouracil plus Leucovorin were prescribed every two weeks. Her liver tumor Next-generation sequencing showed mutation in *PIK3CA E545K, TP53, SMAD4, KRAS, and APC.* She received Alpelisib 150mg twice daily since August 2023 and the ALP (alkaline phosphatase) level decreased gradually. However, diarrhea, nausea, abdominal discomfort and hyperglycemia occurred days after Alpelisib

Figure 1. During colonoscopy, multiple cotton-like hyperemic mucosa lesions with erosions and ulcerations from sigmoid colon to anastomosis site and terminal ileum. Rectum was relatively sparing. Vasculitis-associated colitis and ulcers was impressed.



usage. Medications for symptoms relief and sugar control were given with limited response and only improved after tapering Alpelisib to 150mg once daily. Colonoscopy showed discrete ulcerations over sigmoid colon to anastomosis site and terminal ileum. Pathology revealed ulcers with inflammatory infiltrates in vascular walls simulating vasculitis, and degenerated crypts with microabscess or cryptitis (Figure A). There was no evidence of CMV or TB infection. Thus, Alpelisib-induced colitis was impressed, and we kept Alpelisib 150mg daily and gave sucralfate with diosmectite for symptom control.

Conclusion

About 15-20% of colorectal cancer has *PIK3CA* mutations, with hotspot mutations in exon 9 (*E545*, *E542*) and exon 20 (*H1407*), which is associated with tumor recurrence and prognostic for poor overall survival independently in stage III colon cancer. With the treatment of *PI3Kα* inhibitor with Alpelisib, over half have presented with adverse effects of hyperglycemia and diarrhea in breast cancer. Colitis also raised concerned in recent studies, leading to dose reduction or drug discontinuation. Our patient developed hyperglycemia and diarrhea in few days, and diffuse colon ulcers extending to terminal ileum was confirmed in 1 month after Alpelisib exposure. Such experience reminds physicians about the side effect of Alpelisib as well as the underestimation of colitis incidence. Therefore, colonoscopy should be considered for early recognition and intervention.

病例報告　112_C 184

對於泰格莎(Osimertinib)引起的嚴重間質性肺炎(interstitial lung disease)，是否一定要放棄泰格莎使用？ 一個成功以合併泰格莎及低劑量類固醇成功治療的案例

Should Osimertinib be discontinued in cases of previous grade 3 ILD induced by Osimertinib? A successful rechallenge with Osimertinib, combined with a low dose of steroids, might be a viable option.

謝秉儒 楊志仁
高雄醫學大學附設醫院胸腔內科

Introduction

EGFR inhibitors have become a standard first-line treatment for metastatic lung adenocarcinoma, especially among non-smoking Asian women. Adverse effects of EGFR inhibitors have been reported, including skin rashes, diarrhea, stomatitis, paronychia, and rare interstitial lung disease (ILD). According to prior studies, the occurrence rate of ILD induced by Osimertinib is approximately 2%-4%, with a mortality rate ranging from 10% to 25%. Consequently, rechallenge with Osimertinib is typically discouraged when grade 3 ILD is detected. However, given the superior efficacy of Osimertinib in treating lung cancer with T790M mutations compared to other drugs, reconsideration of its rechallenge becomes pertinent. This report presents a case where Osimertinib-induced Grade 3 ILD was successfully managed using a low-dose steroid.

Case Presentation

A 65-year-old non-smoking woman was diagnosed with lung adenocarcinoma (cT4N2M1b, stage IVA) along with brain metastasis, due to the positive EGFR Exon 21 mutation (L858R) was identified, treated with Afatinib 30 mg as the first line therapy commenced from 2022/03/02. Though her condition became much better with a regressed mass, progressive dyspnea with increased right pleural effusion was observed from April 2023. CT scans indicated disease progression. A subsequent pleuroscopy-aided biopsy of the right pleura detected metastatic adenocarcinoma with an Exon 20 (T790M) mutation. Osimertinib (80mg) treatment began on 2023/05/24. After three weeks, the patient exhibited progressive dyspnea. Chest X-rays revealed an increasing bilateral Ground-glass opacity pattern, accompanied by left side pleural effusion. During hospitalization, her condition rapidly deteriorated, leading to impending hypoxemic respiratory failure. CT scans displayed mixed Ground-Glass opacity across both lungs. Lab results didn't indicate any infections. A diagnosis of Osimertinib-induced grade 3 ILD was made. The treatment with Osimertinib was halted, and methylprednisolone 40 mg Q12H was initiated. The patient's health improved gradually. After a three-week halt in Osimertinib treatment, the drug was reintroduced at 80 mg alongside a protective daily dose of prednisolone (10 mg). The combination was well-tolerated over a two-month period, with prednisolone being tapered to 5 mg daily. No recurrence of ILD was noted during this period.

Discussion

Osimertinib remains the top therapeutic choice for lung adenocarcinoma patients with acquired Exon 20 (T790M) mutations. For mild to moderate ILD induced by Osimertinib,

rechallenge might be possible. Some case studies suggest that reintroducing Osimertinib, along with steroids, can effectively counteract pneumonitis. However, due to the potential life-threatening nature of grade 3 ILD, restarting Osimertinib is typically not recommended. Our case underscores the relatively short interval (3 weeks) between initial Osimertinib administration and the onset of ILD. After successful systemic steroid treatment, Osimertinib rechallenge appeared both safe and effective, especially given the lack of severe adverse events noted in prior studies. To date, no instances of patients with EGFR TKI-induced grade 3 pneumonitis undergoing a successful rechallenge have been published. Steroid dosage recommendations remain uncertain, although dosages equivalent to those for organizing pneumonia (0.5 mg/kg) are commonplace. This report offers the first documented case of a successful rechallenge using a full dose of Osimertinib combined with low-dose prednisolone following grade 3 Osimertinib-induced ILD.

Conclusion

Reintroducing Osimertinib in conjunction with low-dose prednisolone appears to be a viable and safe therapeutic option for patients previously diagnosed with Osimertinib-induced ILD in lung adenocarcinoma cases.

病例報告　112_C 185

BNT162b2 mRNA COVID-19 疫苗引發血栓性血小板低下性紫斑症

BNT162b2 mRNA COVID-19 vaccine -Induced Thrombotic Thrombocytopenic Purpura

何博彥 [1] 吳青芳 [2,3] 紀伯叡 [4,5,6] 裴松南 [7]

[1] 義大癌治療醫院內科部 [2] 義守大學醫學院 [3] 義大癌醫院內科部腎臟科 [4] 義大大昌醫院內科部腎臟科

[5] 義大醫院內科部腎臟科 [6] 義守大學醫學院中醫學系 [7] 義大癌醫院血液腫瘤科

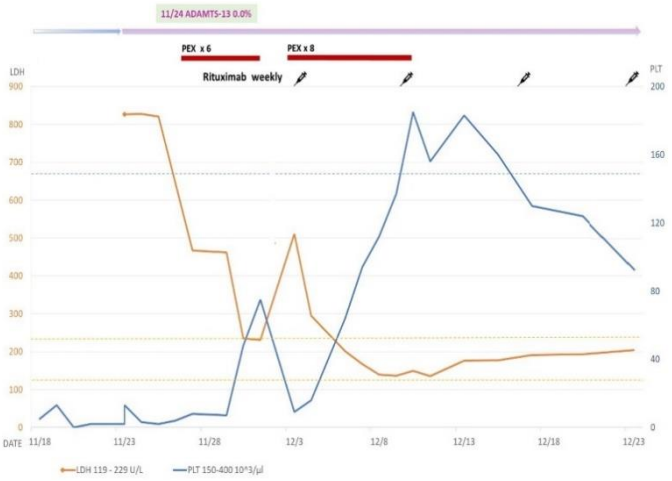
Introduction

In recent years, the outbreak of Coronavirus Disease 2019 (COVID-19) has spread worldwide. To mitigate the spread of the virus, many countries have implemented COVID-19 vaccination programs. While vaccination is an important health tool to suppress the pandemic, some unexpected adverse events have been reported following massive vaccination including cases of vaccine-induced thrombotic thrombocytopenic purpura (TTP). To alert clinicians the rare but treatable complications after vaccination, we reported a case of TTP induced by BNT vaccine.

Case presentation

This 37-year-old Taiwanese female developed fever, migratory limb numbness, thrombocytopenia and neurological symptoms following the first dose of the BNT162b2 mRNA COVID-19 vaccine (BNT vaccine). Initially, complex partial seizure was considered. However, after comprehensive evaluation, including hemogram, biochemistry, coagulation tests, blood smears and bone marrow examination, TTP was highly suspected. Immediate plasma exchange and steroid therapy were initiated. (Fig. 1), While the treatment response was inadequate, rituximab was added and her clinical symptoms improved, along with relevant blood tests improving Plasma ADAMTS13(A Disintegrin And Metalloproteinase with a Thrombospondin type 1 motif, member 13) activity prior to initiation of therapy was 0%, which was available one week later, and the diagnosis of TTP was confirmed. The patient was discharged uneventfully, and there is no evidence of relapse during the two-year follow-up.

Fig. 1 LDH: Lactate dehydrogenase, PEX: Plasma Exchanae PLT: Platelet.



Discussion

The presented case demonstrates typical TTP clinical manifestations and laboratory findings. Prompt diagnosis and intervention, including steroids, plasma exchange and subsequent rituximab therapy, prevented further deterioration of the patient's condition. Notably, without timely treatment, TTP typically follows a progressive course with common occurrences of neurologic deterioration, cardiac ischemia, irreversible renal failure, and death. Our case not only shares our experience in diagnosing and treating TTP but also emphasizes the importance for healthcare professionals to consider TTP as a potential

diagnosis when encountering patients with similar symptoms, such as unexplained neurological symptoms, thrombocytopenia, anemia, and fever after COVID-19 vaccination.

Conclusion

Due to the rarity and diverse clinical presentations of COVID-19 vaccine-induced thrombotic thrombocytopenia (TTP), clinicians often face challenges in promptly diagnosing the condition, leading to delays in appropriate treatment. Potential occurrence of TTP in cases of post vaccination thrombocytopenia and MAHA should always be kept in mind to initiate treatment early. Understanding the underlying mechanisms by which COVID-19 vaccines may trigger TTP is crucial for ensuring vaccine safety and optimizing patient care. Continued vigilance and research will contribute to our knowledge and aid in the development of strategies to minimize vaccine-related adverse events.

病例報告　112_C 186

肺泡蛋白質沉積症
Pulmonary Alveolar Proteinosis – A Case Report and Literature Review

蔡韙仲[1] 吳信宏[2,3] 魏裕峰[4,5]
[1]義大醫院內科部 [2]台東馬偕醫院內科部胸腔內科 [3]正修科技大學通識中心
[4]義守大學醫學院 [5]義大癌醫院內科部胸腔內科

Introduction

Pulmonary alveolar proteinosis (PAP) is a rare lung disease causing impaired gas exchange due to protein accumulation in alveoli. Autoimmune PAP is the most common form. Symptoms include dyspnea and infection susceptibility. Whole lung lavage is the primary treatment, and other options like GM-CSF therapy and transplantation are considered for refractory cases. This case presentation and review provide insights into PAP's etiology, diagnosis, and treatment.

Case Report

A 56-year-old Asian man presented with a six-month history of progressively worsening dyspnea on exertion and cough with sputum. He denied hemoptysis, chest pain, lower extremity swelling, fevers, chills, night sweats, weight loss, skin rashes, arthralgia or myalgia. His past medical history including hypertension and asthma with regular medication control. He was ever a 15 pack-year smoker and occasionally consumed alcohol, but both quitted over 10 years. He denied any illicit drug use. No exotic travel or sick contacts history. He worked in an electronics factory and rice mill for 2-3 years.

He visited Taitung MacKay Memorial Hospital where chest X ray (CXR) and computed Tomography (CT) of the chest showed diffused ground-glass opacities (GGO) with superimposed interstitial reticulation over bilateral lung field (Figure 1 and 2). He was transferred to E-Da Cancer Hospital for further evaluation and treatment. On physical examination, the patient's vital signs were as follows: temperature 36.1°C; blood pressure 164/93 mmHg; pulse rate 110 beats/min; respiratory rate 20 breaths/min; and oxygen saturation 90% on ambient air. Auscultation of bilateral lung demonstrated no significant rales, rhonchi or wheezes. Other examinations including the cardiac, vascular, abdominal, lymphatic and integument examinations were unremarkable.

Figure 1 Chest x-ray showed diffuse bilateral alveolar consolidations

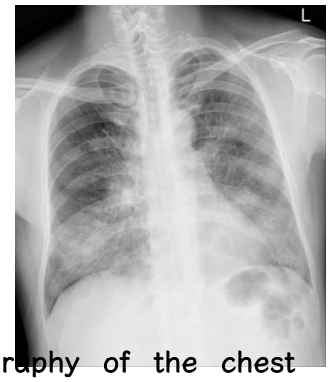
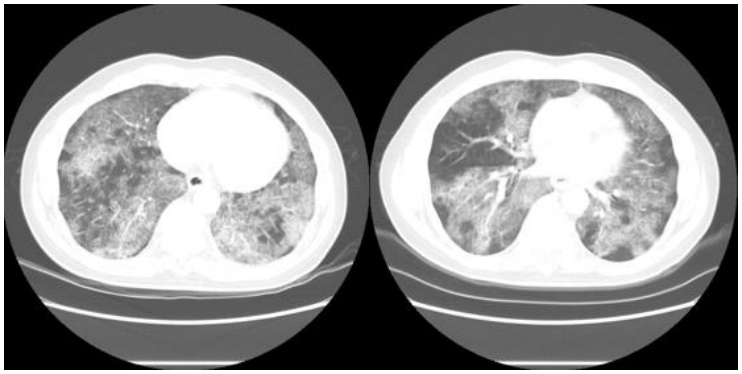


Figure 2. Computed tomography of the chest demonstrated diffuse ground-glass opacities with superimposed interstitial reticulation



On laboratory evaluation, the patient's complete blood counts and comprehensive biochemistry test disclosed leukocytosis with neutrophilia and higher hemoglobin (18.6 g/dL).

High carcinoembryonic antigen (CEA) was also found (18.72 ng/ml).

Figure 3A. Thoracoscopic wedge resection of left lower lobe revealed diffuse yellow plaque over both lobes of the lung

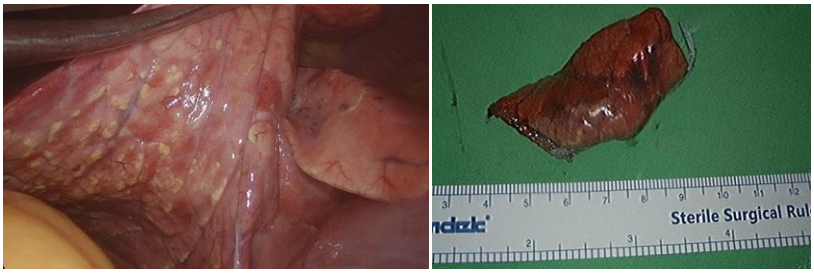


Figure 3B. Pathology of resected lung tissue showed accumulation of amorphous eosinophilic materials in the alveolar spaces, compatible with pulmonary alveolar proteinosis

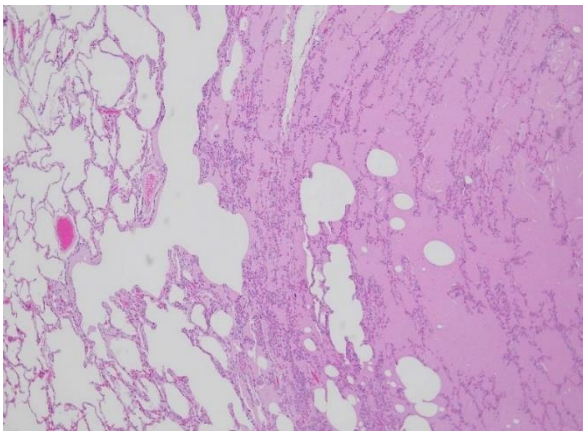
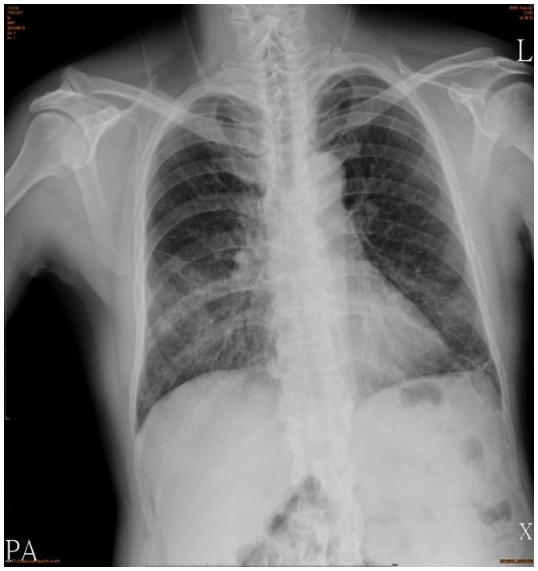


Figure 4. Whole lung lavage of each lung disclosed cloudy proteaceous material

Figure 5. Chest x-ray 1-month after whole lung lavage showed significant improved bilateral lung infiltration



Based on the clinical manifestations and image studies, the differential diagnosis including bacterial or viral pneumonia, pneumocystis jiroveci pneumonia infection, PAP, lymphoma, and adenocarcinoma in situ. The patient underwent a bronchoscopy but no endobronchial lesions was found. Bronchial washing was performed for culture and cytology studies. Due to desaturation during the procedure, biopsy was not performed. The microbiologic studies including fungus, aerobic and mycobacterial cultures were all negative. Cytology disclosed no malignant cells either. Pulmonary function test revealed mild restrictive ventilatory defect. Empiric antibiotic with intravenous levofloxacin and systemic steroid with methylprednisolone were administrated but no clinical improvement, including dyspnea and followed CXR. Thoracoscopic wedge resection of left lower lobe was arranged for definite diagnosis thereafter. On surgery, gross view revealed diffuse yellowish plaque over both lobes of the lung (Figure 3A). Pathology report showed accumulation of amorphous eosinophilic materials in the alveolar spaces (Figure 3B). Based on the clinical and pathological findings, consistent with a diagnosis of PAP.

Since the diagnosis of PAP was made, whole lung lavage (WLL) was performed under general anesthesia 1 week later (Figure 4). After the procedure, his clinical symptoms including dyspnea and cough improved. In the meanwhile, followed CXR 1 month later showed improved also (Figure 5). His condition remained stable at least 3 months after WLL.

Discussion

We presented a successfully treated PAP patient with whole lung lavage (WLL). WLL remains

the primary treatment for PAP despite its complexity. PAP has three types: autoimmune, secondary, and congenital. Autoimmune PAP is most common, caused by anti-GM-CSF antibodies, leading to GM-CSF deficiency. Smoking is a risk factor. Symptoms include dyspnea, cough, hypoxemia, and infection susceptibility. Diagnosis involves clinical symptoms, imaging, bronchoscopy, and biopsy. WLL is recommended for moderate-to-severe cases. GM-CSF supplementation via subcutaneous administration has shown efficacy. Corticosteroids and rituximab are options, while plasmapheresis and lung transplantation are limited. Prognosis varies, with WLL improving survival, although infections remain a concern. Pulmonary fibrosis may worsen prognosis.

Conclusions

PAP has advanced, revealing impaired alveolar macrophage maturation and disrupted surfactant clearance as key factors in autoimmune PAP. WLL remains the primary treatment, with GM-CSF-based therapies showing a promise outcome. Future research is warranted on elucidating disease mechanisms and identifying new therapeutic options to improve clinical outcomes for patients with PAP.

病例報告　112_C 187

Metastatic squamous cell carcinoma of the buccal mucosa to the heart- a case report

陳宗禮[1]　蘇裕傑[2]
[1]義大醫院內科部　[2]義大醫院血液腫瘤科

Introduction

The most common sites for metastasis from head and neck cancers are the lungs, bones, and liver. We present a rare case of squamous cell carcinoma of the buccal mucosa that suspect metastasized to myocardium of the left ventricle, left upper lung and right adrenal gland.

Case presentation

A 48-year-old man without personal history, but with family history of lung adenocarcinoma and a long history of smoking, alcohol and betel nuts, presented with mouth pain and an ulcerative mass over right buccal. He was diagnosed with squamous cell carcinoma in July, 2020 following tumor wide excision, segmental mandibulectomy, partial maxillectomy, right neck dissection and free flap. According to the eighth edition of the staging manual of the American Joint Committee on Cancer, the pathological stage was pT4aN0, stage IVA. However, recurrent tumor with distal metastasis to lung and left adrenal gland was noted in followed computed tomography (CT) and whole-body positron emission tomography (PET). Therefore, he recevied operation and concurrent chemoradiotherapy (CCRT) and then EXTREME regimens with cetuximab, cisplatin and 5-FU during 2021-2022. One year later, this patient complained of palpitation and mild dyspnea on exertion without chest pain or cold sweating. So, echocardiography was performed and the report disclsoed left ventricle lateral and apical wall mass, 4*4 cm, heterogeneous density, broad base with suspect central necrosis pattern. Normal left ventricle size with preserved left ventricle contractility, left ventricle ejection fraction was 66%. Electrocardiography (ECG) demonstrated new onset-ST-segment changes but cardiac enzymes were within normal limits. In addition, chest CT performed in July, 2023, demonstrated necrotic metastatic lesions including myocardium of the left ventricle. Following SCC revealed 4.6 (reference range: <1.5). Due to high risk of surgery to biopsy, subsequent thallium scan was performed and the report showed irreversible myocardial ischemia in apex, anterior-apical, inferior-apical and inferior segments of left ventricle and reversible myocardial ischemia in inferior-septal, anterior-lateral and posterior segments of left ventricle. He receved radiotherapy to the left ventricle. Moreover, we began immunotherapy with nivolumab plus cetuximab in August, 2023. Besides, we prescribed bisoprolol plus low dose digoxin with 0.125 mg daily for rate control. After the fourth cycle with immunotherapy plus cetuximab and radiotherapy, echocardiography showed left ventricle lateral and apical wall mass without progression. Markedly declined SCC level was presented in the following lab data. Now, the patient's heart rate was within 90 beats per min during sleep and 110 beats per min when awake. Both palpitation and dyspnea on exertion improved. Consequently, cancer status is stationary now.

Conclusion

Cardiac involvement is often not assessed because of its low prevalence. Cardiac metastasis should be considered in patients with malignancies presenting with nonspecific cardiac symptoms.

病例報告　112_C 188

一位 78 歲女性出現腹痛和腹瀉，隨後被診斷為急性胰臟炎、肝炎和急性心肌梗塞-報告一個少見的病例

A 78 year old woman with abdominal pain and diarrhea who was subsequently diagnosed as a case of acute pancreatitis, hepatitis and acute myocardial infarction -report of an unusual case

許桂華[1]　林少琳[1,2] 李其澧[1] 許智能[1] 何淵智[2] 張維興[3]
高雄阮綜合醫院 [1]加護病房 [2]心臟內科 [3]腸胃內科

Introduction

Acute pancreatitis and hepatitis associated with acute myocardial infarction (AMI) are rare on occurrences. Transient organ failure is seen in approximately 20% of all cases of acute pancreatitis[1]. In this report, we present our initial experience in successful managing a 78-year-old female patient diagnosed with these illnesses.

Case presentation

The patient has medical histories of hypertension and type 2 diabetes. She was sent to our Emergency Room on February 1st, 2023, with abdominal pain and diarrhea. Lab. data revealed elevated troponin I (8047.5 pg/ml). Electrocardiogram (ECG)showed ST elevation in leads II, III, and aVF, which indicating an inferior wall AMI. The patient received aspirin 300mg and brilinta 180mg upon arrival at the ER. Subsequently, she underwent cardiac catheterization and two drug-eluting stents were deployed in the right coronary artery (ostium to mid segment). During the procedure, the patient developed bradycardia and received a temporary pacemaker implantation. Afterward, she was admitted to the Intensive Care Unit (ICU) and received dual antiplatelet therapy, antihypertensive medication, and statins. Additionally, she was diagnosed with acute pancreatitis based on abdominal distention, elevated lipase (1217 U/L) and amylase (229 U/L) levels, and confirmed through abdominal CT scans. Since the patient had anorexia and nausea feeling, she was kept on nothing per oral (NPO) status but received IV glucose for nutritional support. Antibiotics with ceftriaxone was given since the ER for avoid infection.

In the second day of admission, impending hepatic failure was indicated by elevated SGOT (5000 U/L) and SGPT (1884 U/L) levels. To treat both conditions, the patient received IV hydration, Foy (gabexate mesilate) IV, Monoammonium glycyrhizinate (SNMC) IV, and silymarin orally. Smofkabiven IV was administered on the third day for nutritional support. By the fourth day, significant improvements were observed in lipase levels (from 5520 to 729 U/L), amylase levels (from 940 to 478 U/L), and SGPT levels (from 1884 to 1482 U/L). The patient's bradycardia improved and EKG monitor showed sinus rhythm, with heart rate of 60 bpm, which leading to temporary pacemaker removal. Oral feeding was initiated on the fifth day, and the patient was transferred to a regular ward on the seventh day. He was eventually discharged from our hospital after another 11 days treatment. Patient has followed up at our CV and GI OPD regularly thereafter.

Discussion

Severe pancreatitis associated with hepatitis may have a high rate of organ failure and

mortality. This case had a high levels of hepatic enzymes. Fulminant hepatitis and previous cholecystectomy were revealed by abdominal sonography and serial biochemical data. Hepatitis B antigen and hepatitis C antibody were negative. Thus, the hepatitis related to poor perfusion secondary to acute MI and pancreatitis was favored.

It is imperative that clinicians are aware that acute pancreatitis can mimic an acute myocardial infarction. Previous article has reported that 34 total cases with acute pancreatitis who presented with ECG changes consistent with AMI but without true coronary artery thrombosis[2].Coronary angiography is useful to make a differential diagnosis promptly. In this report, coronary angiography has confirmed that this case did have a coronary artery stenosis in the right coronary artery.

This patient improved considerably after our aggressive treatment, which including prompt hydration, antibiotic and other measures. Prompt hydration avoid fluid insufficiency, reperfusion injury and organ damage via perfusion. Adequate intervention (FOY, SNMC, resuscitation) also reduce cytokine and oxidative stress. Antibiotics given may decrease infectious risk secondary to necrotizing pancreatitis.

Conclusion

This report highlights our initial experience in managing a patient with inferior wall AMI associated with acute pancreatitis and hepatitis. Emergent cardiac catheterization study stratified underline risk factors and moderate fluid resuscitation avoid persistent organ failure. Aggressive investigation andearly moderate hydration are crucial for saving the patient's life.

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病例報告　112_C 189

經動脈導管栓塞治療急性胃竇潰瘍出血

Transarterial embolization for gastric antral ulcer bleeding

楊宗翰[1]　歐建麟[2]
[1]國軍左營總醫院心臟內科　[2]國軍左營總醫院腸胃內科

Introduction

Gastric antral ulcer bleeding is used to be treated with proton-pump inhibitor and endoscopic hemostasis. But if refractory or recurrent bleeding, surgical intervention would be considered afterwards. However, in some old-aged patients with multiple comorbidities, surgery may not be the choice of patients and the family. In this circumstance, transarterial embolization is a less invasive therapy alternatively.

Case presentation

A 80-year-old woman with medical history of diabetes with insulin control and uremia on maintenance hemodialysis suffered from hematemesis and tarry stool for two days before emergent department visit. Immediate endoscopic epinephrine local injection with hemoclips were performed under diagnosis of gastric antral large ulcer bleeding. (Figure 1) After three days of high dosed proton-pump inhibitor treatment and blood transfusion at intensive-care unit, the hematemesis and tarry stool persisted. Second endoscopy survey was done with persistent oozing ulcer confirmed. Surgical intervention was suggested but declined by patient and family. Alternatively, transarterial embolization was proposed and then accepted.
The procedure was performed via the femoral approach with celiac artery engaged with the guiding catheter (Cook Medical Beacon Tip Torcon NB Advantage Catheter RC1 5.0Fr). A microcatheter (Terumo Progreat™ 2.7 Fr microcatheter system) was advanced to proximal right gastroepiploic artery with following angiogram showing a small area contrast extravasation and stasis. (Figure 2) Gelatin sponge was injected and after that, the stasis and extravasation disappeared. (Figure 3) The tarry stool subsided, and the hemoglobin level was stabilized. The patient was transferred to general ward and discharged with no we complication.

Figure 1 An H1 ulcer, 1.5cm, low body with hemorrhage noted (Forrest Ib)

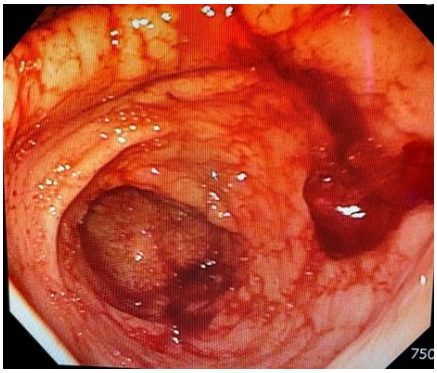


Figure 2 proximal right gastroepiploic angiogram showed contravasation and stasis(arrow)

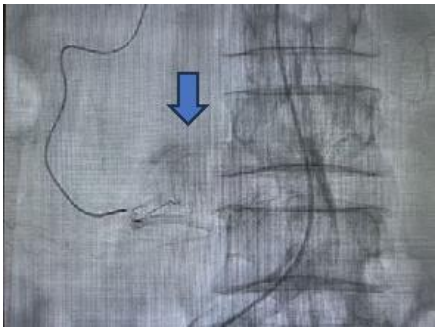
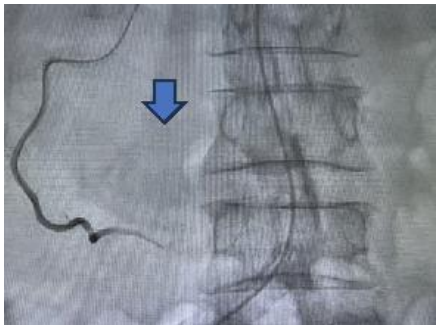


Figure 3: After the gelatin sponge hemostasis, the contrast extravasation disappeared.



Discussion

Patients suffered from melena or hematemesis should be evaluated with Glasgow-Blatchford score at emergent department and whom score greater than 6 should receive further intervention, including medication and endoscopic hemostasis. But if patients with recurrent bleeding, surgical intervention or transarterial embolization are the next two candidates of treatment. The re-bleeding rates is lower in surgery groups, but transarterial embolization is a less invasive method.

Conclusions

Transarterial embolization is a minimal invasive therapy for massive or recurrent gastric antral ulcer bleeding before surgical intervention.

病例報告　112_C 190

經皮穿腔中膈心肌血管線圈栓塞術治療阻塞性肥厚心肌症

Percutaneous Transluminal Septal Myocardial Ablation (PTSMA) with coils for Hypertrophy Obstructive Cardiomyopathy

楊宗翰
國軍左營總醫院心臟內科

Introduction

Hypertrophic obstructive cardiomyopathy (HOCM) is an idiopathic subaortic stenosis disease that would lead to multiple symptoms, including angina, dyspnea and life-threatening ventricular tachycardia. The indication of PTSMA include symptoms with left ventricular outflow tract pressure gradient ≥ 50mmHg and left ventricle septal thickness >15mm. The treatment success is pressure gradient drop ≥ 50% or < 30mmHg.

Case presentation

A 39-year-old woman was brought to emergent department by ambulance because of out-of-hospital cardiac arrest with cardiac defibrillation performed via Automated External Defibrillator. The coronary angiogram was done soon after the return of spontaneous circulation, but no stenosis or thrombus found. Transthoracic echocardiography (figure 1) approved the HOCM diagnosis (septal thickness: 27mm, left ventricular outflow tract pressure gradient: 141mmHg and anterior mitral leaflet systolic anterior motion). After complete recovery of consciousness with no morbidity, implantable cardioverter defibrillator pacemaker operation was performed and then the PTSMA. The procedure was performed via the right radial artery approach and left main coronary artery engaged with the Judkins Left (JL 3.5) guide catheter. A microcatheter (FineCross ™ MG microcatheter, 2.6 Fr) was advanced to first septal branch with 2 coils (Cook G52732 Nester ® Embolization Coil .018, 3cm x 3mm) deployed. (Figure 2) Post-procedure left ventricular outflow tract pressure gradient was 65mmHg. The patient was transferred to general ward and discharged with no complication. The left ventricular outflow tract pressure gradient after 1 month was 17.8 mmHg. (Figure 3)

Figure 1 Echocardiography - septal thickness: 27mm, left ventricular outflow tract pressure gradient: 141mmHg and anterior mitral leaflet systolic anterior motion.

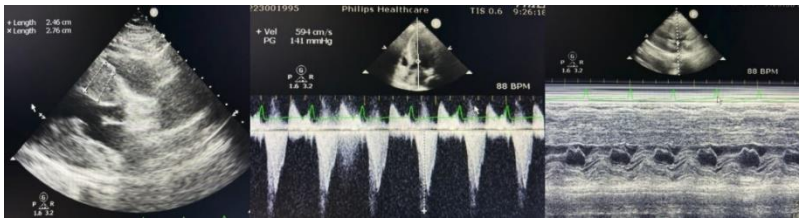


Figure 2 Coronary angiogram Left anterior descending artery-first septal branch embolized with coils (arrow)

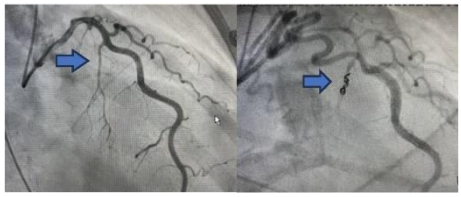
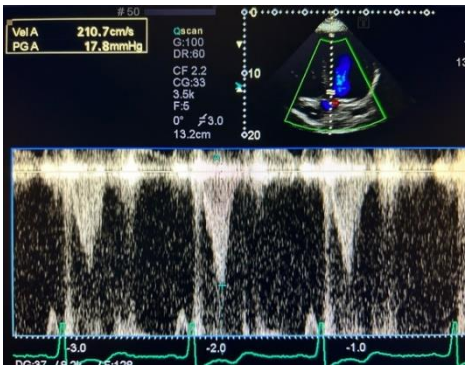


Figure 3: Echocardiography following echocardiography showed the pressure gradient drop to 17.8 mmHg.



Conclusions

In some selected patients, coils embolization is a simple and safe choice different from alcohol septal ablation.

病例報告　112_C 191

在解便時在肛門口發現一個突起的息肉

A protruding polyp during defecation at anus

蔡元榮 [1,2] 李永葉 [3] 林連豐 [1] 郭志榮 [1] 阮盛豪 [1] 詹益群 [1] 林群峰 [1] 張琳璲 [1]
[1] 屏東基督教醫院內科部胃腸肝膽科 [2] 美和科技大學護理系 [3] 馬來西亞理科大學醫學院

Introduction

Anal papillae that are hypertrophied are essentially skin tumors that protrude from the dentate line, or the junction between the skin and the anal epithelial lining. They are typically asymptomatic, but may occasionally become large enough to be felt by the patient or be prone to prolapse. We reported a case of hypertrophied papillae mimicking condyloma acuminatum.

Case presentation

A 63 years old man presented to outpatient clinic with the chief complaint of a polyp like lesion found at anus during defecation for weeks. He denied any bloody stool passage nor difficulty in stool passage. DRE showed a palpable mass lesion around anus. Colonoscopy was performed that showed a whitish elongated polyp with about 1.2cm in length. Biopsy was done that showed condyloma acuminatum. Patient was referred to colorectal surgeon. Surgery was performed with the result showed hypertrophied papillae.

Discussion

Hypertrophied papillae refer to a benign polypoid lesion characterized by the excessive growth of connective tissue in the area of the anal column. The reactive hyperplasia of the connective tissue might be due to irritation, injury or infection. The differential diagnosis includes hemorrhoids, condyloma acuminatum and anorectal tumors. Endoscopic polypectomy or surgical resection is recommended in symptomatic cases.

Conclusion

Hypertrophy papillae is a benign disease with no malignant potential with polypectomy or surgery recommended in symptomatic patient.

病例報告　112_C 192

出乎意外的葛雷－特那氏徵象：藥物引起溶血性貧血

The unexpected cause of Grey Turner sign: Drug induced hemolytic anemia

蔡元榮 [1,2] 李永葉 [3] 林連豐 [1] 郭志榮 [1] 阮盛豪 [1] 詹益群 [1] 林群峰 [1] 張琳璡 [1] 陳昶宏 [4]

[1]屏東基督教醫院內科部胃腸肝膽科 [2]美和科技大學護理系 [3]馬來西亞理科大學醫學院 [4]屏東基督教醫院內科部神經科;

Introduction

Grey Turner's sign is bruising of the flanks, which is the area of the body between the final rib and the top of the hip. The bruising shows as a blue discoloration and is an indication of retroperitoneal hemorrhage, or bleeding behind the peritoneum, the abdominal cavity's lining. We reported a peculiar cause of the Grey-Turner sign with levofloxacin as an offending agent that causes hemolytic anemia.

Case presentation

A 66-year-old man with the history of right upper lung pneumonia with brain metastasis and autoimmune hemolytic anemia, warm type, presented to our emergency department with the chief complaint of intermittent generalized seizures for one day. In addition, his CXR showed right lung pneumonia, and in the suspect's case of nosocomial infection, antibiotics with cefoperazone/sulbactam were administered. Due to intermittent fever and the progression of pneumonia, the antibiotic was shifted to levofloxacin on day eight of his hospitalization. Acute jaundice and anemia developed. A prominent ecchymosis over the right flank developed on the same day. The patient was negative for hepatitis B and C. A gastroenteroscopy was performed and showed a negative result for peptic ulcer disease. Sonography, abdomen, and CT further confirmed there was no retroperitoneal hemorrhage. Steroids and immunosuppressants were given. Gradually, his ecchymosis resolved with an improvement in jaundice and anemia. It was concluded that the Grey Turner sign in this patient was highly associated with hemolytic anemia related to the use of levofloxacin.

Discussion

Grey Turner's sign is named after British physician George Grey Turner, who discovered the link between severe pancreatitis and the symptom. Grey Turner's sign is non-specific and may be present with almost any condition causing intra-abdominal or retroperitoneal bleeding, such as ruptured abdominal aortic aneurysm, ruptured ectopic pregnancy, splenic rupture, ruptured hepatocellular carcinoma, perforated duodenal ulcer, bleeding intra-abdominal metastases, perirenal hemorrhage, and hemorrhagic ascites.

Conclusion

We reported an unusual cause of the Grey-Turner sign with levofloxacin as an offending agent, causing hemolytic anemia.