

Postoperative hemorrhage caused by portal hypertension associated with autoimmune pancreatitis

A case report

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Abstract

Rationale: Autoimmune pancreatitis is a form of chronic pancreatitis, characterized by diffused enlargement of the pancreas and irregular narrowing of the main pancreatic duct. The theory that portal hypertension is associated with autoimmune pancreatitis has not been emphasized. In addition, only a few studies report that the gastrointestinal tract hemorrhage caused by portal hypertension is associated with autoimmune pancreatitis.

Patient concerns: The patient was a 61-year-old male with pancreas occupying lesion detected in a physical examination. Preoperative CT showed portal vein diameter increased significantly (1.6 cm) and the junction of splenic and portal vein was capsuled by lesions and the splenic vein became thin. The Whippie procedure was performed for the correction of the lesion. The pancreatic tissue showed chronic inflammation and lymphocytic infiltration and fibrosis, and abundant IgG4⁺ cells. After the surgery, the patient suffered twice from postoperative hemorrhage (9 and 16 mos).

Diagnoses: Postoperative hemorrhage, autoimmune pancreatitis.

Intervention: Electronic gastroscopy, exploratory laparotomy, and titanium clips were used simultaneously to stop the bleeding. **Outcomes:** The patient recovered well after the surgery.

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Lessons: In this study, we present the case of repeated postoperative hemorrhage (9 and 16 mos). We discussed the correlation between postoperative hemorrhage and autoimmune pancreatitis, and the cause of postoperative hemorrhage.

Abbreviations: AIP = autoimmune pancreatitis, CT = computed tomography, CTA = computed tomography angiography, FDP = fibrin degradation product, MRI = magnetic resonance image, OOI = organ involvement, PH = portal hypertension, RBCs = red blood cells.

Keywords: autoimmune pancreatitis, case report, pancreatitis, portal hypertension, postoperative hemorrhage

1. Introduction

The concept of "autoimmune pancreatitis (AIP)" was proposed by Yoshida et al^[1] in 1995, which gradually became an independent clinical entity. AIP is a form of chronic pancreatitis, characterized by diffused enlargement of the pancreas and

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irregular narrowing of the main pancreatic duct. Patients commonly develop varying degrees of upper abdominal pain, along with obstructive jaundice and lymphocytic infiltration and pancreatic fibrosis. With histopathologically confirmed, the pancreatic tissues from patients show inflammation, fibrosis, and abundant IgG4⁺ cells.^{12–51} Moreover, AIP exhibits a dramatic steroid response.^[6]

AIP has been associated with lesions in various organs other than the pancreatico-biliary system,^[7–10] such as retroperitoneal fibrosis, sclerosing sialadenitis, renal tubulointerstitial nephritis, and chronic thyroiditis. However, the theory that portal hypertension (PH) is associated with autoimmune pancreatitis has not been emphasized. In addition, only a few studies report that the gastrointestinal tract hemorrhage caused by PH is associated with AIP. Herein, we report a patient treated with Whippie procedure who suffered twice from postoperative hemorrhage (9 and 16 months), discussing the correlation of PH with AIP, and the cause of postoperative hemorrhage.

2. Case report

A 61-year-old male was admitted to our hospital when pancreas occupying lesion was detected in a physical examination on February 19, 2014. The patient had suffered from upper abdominal pain with no other typical clinical symptoms after strenuous exercise, 3 months before hospital admission. The

Table 1		
Result of examinations of the patient.		
Examination	CT/CTA	Gastroscope
Preoperation (February, 2014)	The junction of splenic and portal vein was capsuled by lesions and the splenic vein became thin.	
Postoperative hemorrhage-I (December, 2014)	Abundant seroperitoneum. Remnant stomach at anastomosis and the colon showed edema and thickening. A wide gap at the operation area on the pancreas hook was fuzzy. The size of liver became smaller, and main portal vein was dilated. The low density of multiple cysts in the liver and calcification on the right liver lobe.	A varicose vein was found on the esophagus 30 cm to the incisor.
Postoperative hemorrhage-II (July, 2015)	Abundant seroperitoneum. Remnant stomachat anastomosis and some parts of colon showed edema and thickening. A wide gap at the operation area on the pancreas hook was fuzzy. Increased density of mesentery with evidence of multiple enlarged lymph nodes. The size of liver became smaller, and partial structure of porta hepatic was vague. The low density of multiple cysts in the liver and calcification on the right liver lobe.	A varicose vein was found on the esophagus 30 cm to the incisor, and varicose veins were noticeable in proximity to the Z-line. Four varicose veins were found in the inferior segment of esophagus.

CT = computed tomography, CTA = computed tomography angiography.

patient did not present any history of alcohol consumption or pancreatic disease. An upper-abdomen enhanced magnetic resonance image (MRI) revealed low-density occupation (3.2 \times 2.4 cm) on the pancreas hook. Preoperative CT showed portal vein diameter increased significantly (1.6 cm) and laboratory examination showed HBV (–). Other abnormalities included slight enhancement of pancreatico-biliary duct, stenosis of the inferior segment of the common bile duct, and enlargement of the superior one.

The results of enhanced computed tomography (CT) and computed tomography angiography (CTA) were shown in Table 1 and Figure 1A. A Whippie procedure was performed



Figure 1. A, February 21, 2014: preoperative CT, pancreas occupation. B, December 14, 2014: postoperative CT, the first postoperative hemorrhage. C, July 20, 2015: postoperative CT, the second postoperative hemorrhage. D, Titanium clip to deal with the suspicious bleeding spot on the gastroenteric stoma. E, December 15, 2014: electronic gastroscope, the suspicious bleeding spot on the anastomotic stoma.

for the correction of the lesion. During the surgery, we found 2 cysts in the liver and cirrhosis was mild but no space-occupying lesion and the pancreas head was swollen than normal. In addition, a 4 cm-diameter firm mass was found on the pancreas hook. The pancreatic tissue showed chronic inflammation and lymphocytic infiltration and fibrosis, and abundant IgG4⁺ cells (>50/HPF), along with 5 peripancreatic lymph nodes showing reactive hyperplasia. The hemorrhage during the operation was 1000 mL. An anti-inflammatory and inhibitory drug for gastric acid and pancreas secretion was administered as a postoperative treatment. In conclusion, the diagnosis of the current patient was autoimmune pancreatitis.

However, the patient showed hematochezia (500 mL, 2-3 times/d) on November 25, 2014, along with hematemesis (200 mL) on December 2, 2014. On December 4, 2014, the patient was admitted to our hospital again due to hematochezia for 9 days. Routine laboratory tests showed that hemoglobin was decreased to 56 g/L, whereas the fibrin degradation product (FDP) and D-Dimer were 8.2 and 2.76 mg/L, respectively. After active bleeding was stabilized, the patient was subjected to superior mesenteric angiography-DSA; however, any active bleeding spot on the celiac trunk and its branch was not detected. The electronic gastroscopy discovered esophageal varix in the patient, and we used a titanium clip on the suspicious bleeding spot in the gastroenteric stoma (Fig. 1D, E). As hematochezia and anemia were not distinctly alleviated, another electronic gastroscopy was performed, following which, the patient was stabilized and the routine laboratory tests demonstrated normal results.

Surprisingly, the patient had suffered from repeated hematochezia 8 times since July 14, 2015 to July 15, 2015 (Fig. 1C). Routine laboratory tests showed that hemoglobin, red blood cells (RBCs), and platelets decreased to 62 g/L, 1.98×10^{12} /L, and 57 \times 10⁹/L, respectively, and serum amylase was 30 IU/L. CT and electronic gastroscopy results were shown in Table 1. Colonoscopy showed severe sigmoid mucous edema. Because of the highly twisted structure of sigmoid colon and constant hematochezia, an exploratory laparotomy was performed to search for the bleeding area. Intraoperative colonoscopy found a protruding lesion on the splenic flexure of the colon with varicose veins as the basilar part and blood oozing on the surface. Titanium clips were used simultaneously to stop the bleeding. A liver biopsy showed no sign of cirrhosis and IgG4-related lesions. The patient recovered well after the surgery. All the procedures were implemented based on the principles of the Declaration of Helsinki. As this is a retrospective case report, patient consent was waived by our institutional ethic committee.

3. Discussion

AIP was firstly described as "primary inflammatory sclerosis" by Sarles et al,^[11] followed by some reports associating the pancreatitis patients with autoimmune factors. In 1995, the concept of AIP was proposed by Yoshida et al.^[11] The study postulated that AIP was often misdiagnosed as pancreatic cancer because of its similar clinical manifestation and imaging findings.^[11] The primary symptom may either be slight/medium upper abdominal pain or no visible symptom. AIP is often characterized by obstructive jaundice, upper abdominal pain, and weight loss.^[12–14] CT and MRI showed a diffused enlargement or local swelling, sausage-like, with irregular narrowing of the main pancreatic duct and enlargement of the proximal pancreatic. Patients with AIP can also develop stenosis of the common bile duct, sclerosing cholangitis, Sjögren syndrome, and cholestatic cirrhosis.^[13] The universal guidelines issued in 2011 suggested that the diagnosis of AIP was based on 5 features: characteristic imaging findings, elevated serum IgG4, other organ involvement (OOI), histopathology, and response to steroids. The pancreatic biopsy is dispensable and not specific. As the level of serum IgG4 is not elevated in some AIP patients, the specificity and sensitivity of serum IgG4 are yet controversial.^[7,14,15] Consequently, the imaging findings (CT and MRI) are considered as critical factors in various diagnostic criteria. A diffused enlargement of the pancreas is one of the main histopathological features of AIP, together with fibrosis of pancreatic tissue, lymphocytic infiltration, and fibrosis and acinus atrophy. The immunohistochemistry of AIP shows infiltration of IgG4⁺ cells and CD8⁺ T lymphocytes.^[14]

The first postoperative hemorrhage (at 9 months) in the patient occurred in the gastroenteric stoma. Several possible explanations for the hemorrhage are listed as follows: the removed area of stomach is considered small; the anastomotic stoma of stomach and the middle section of jejunum, which has poor acid resistance may show hemorrhage due to gastric acid corrosion; massive hemorrhage during operation (1000 mL); bile or pancreatic juice reflux destroyed gastric mucosa.

A majority of the cases of early postoperative gastrointestinal hemorrhage occur in gastroenterostomy and pancreaticojejunostomy. On the other hand, late postoperative hemorrhage occurs on various anastomotic stomas of the digestive tract, pancreatic section, and stress ulcer section, among which gastroenterostomy and pancreaticojejunostomy face the highest possibility of hemorrhage. Notably, the late postoperative hemorrhage may arise not only from the digestive tract but also intraabdominal hemorrhage through anastomotic stoma. The anastomotic hemorrhage may be caused by a marginal ulcer, necrosis, and exfoliation of the surface of pancreatic stump or loosening of threads and imprecision of saturation. Thus, hemorrhage may be caused by problems in manual sutures.^[12]

The second postoperative hemorrhage in the patient (at 16 months) is considered to be correlated to portal hypertension associated with AIP. The diagnosis may be based on increased portal vein diameter (before the Whippie procedure); mild cirrhosis (naked-eye observing); abundant seroperitoneum and hypoproteinemia; esophageal varices and splenomegaly; a protruding lesion was found on the splenic flexure of the colon with varicose veins as the basilar part. Combining hepatitis (-) and absence of cirrhosis in the liver biopsy of the patient, we can conclude that portal hypertension in the patient was not caused by HBV-related hepatic cirrhosis or decompensate cirrhosis, but more likely associated with AIP. Cheng et al^[14] reported a case of regional portal hypertension related to AIP, proposing an underlying mechanism of portal hypertension. The mechanism described that the tumescent pancreas was compressing the splenic vein, impeding the venous return, and increasing the venous pressure of gastrolienal veins. However, the pressures of the portal vein and superior mesenteric vein were normal. Therefore, splenomegaly and collateral circulation had gradually formed, and finally, all these factors led to regional portal hypertension. The pancreas is predisposed towards contraction because of inflammation and fibrosis, which will compress and narrow the splenic vein on the back.^[14,16] The patient in the current study exhibits the anatomic factor of regional portal hypertension. (Preoperative CTA: the junction of splenic vein and portal vein was capsuled by lesions and the splenic vein became thin).

IgG4-related diseases can develop lesions in various organs other than the pancreatico-biliary system as mentioned above.

Herein, we speculate that apart from the pancreas (abundant IgG4positive cells and lymphocytes infiltration), the spleen may also be involved. Obliterating phlebitis may encroach on the splenic vein, which causes rough vascular wall, and will alter the hemodynamic stability.^[14] These series of changes contribute to the form of regional portal hypertension and ending in variceal hemorrhage. As a spleen biopsy was not performed on the patient, the above theory is only an inference. Moreover, Amedei et al^[17] has proved the connection immune response and bacterial infections in gastric cancer patients. AIP is characterized by clinic-pathological feature of increased IgG4⁺ cell and CD8⁺ T lymphocyte. Hence, immunologic machinery should not be excluded until a conclusion has been reached on the etiology of AIP.

The treatment for AIP patients can be divided into 3 methods: drugs, endoscopic therapy, and surgery. Steroids can be used for the diagnosis and treatment. The surgery is a requisite when steroid therapy is ineffective or when it is difficult to distinguish AIP from pancreatic cancer or carcinoma of the bile duct. Occasionally, some patients are misdiagnosed and undergo surgery because of the similar imaging as in cancer. Nevertheless, if a patient indeed develops cancer, then the usage of steroids for diagnosis may potentially delay the surgery and facilitate tumor progression.^[18] In this case, the patient administered propranolol to decrease the portal vein pressure and any other syndromes were not found after treatment. Hence, the patient was discharged in July 2015.

In summary, AIP is a rare type of chronic pancreatitis, characterized by diffused pancreatic enlargement and irregular narrowing of the main pancreatic duct. Upper abdominal pain is the first common symptom. The diagnosis of AIP is based on 5 features: characteristic imaging findings, elevated serum IgG4, OOI, histopathology, and response to steroids.^[19] Here, we reported a rare case of delayed postoperative hemorrhage caused by portal hypertension associated with AIP. The alimentary tract hemorrhage in this patient is attributed to anastomotic hemorrhage and portal hypertension caused by the tumescent pancreas compressing the splenic vein. Thus, the spleen may be involved, and the alternation of hemodynamic stability is correlated to chronic inflammation.

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