Hemorrhagic Acalculous Cholecystitis: An Unusual Location of Uremic Bleeding

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Hemorrhagic acalculous cholecystitis is a rare but potentially fatal disease. An increased bleeding tendency is present in both acute and chronic renal failure with impaired platelet function. We herein present a case of hemorrhagic acalculous cholecystitis in a hemodialysis patient who suffered from acute abdomen and upper gastrointestinal bleeding. The pathogenesis may have been associated with ischemia and reperfusion injury, eventually leading to necrosis of the gallbladder wall. Abdominal ultrasound can aid in diagnosis. Biliary colic, jaundice, and melena are the typical symptoms of hemorrhagic cholecystitis, particularly in a patient with unexplained gastrointestinal bleeding. [J Chin Med Assoc 2009;72(9):484–487]

Key Words: hemodialysis, hemorrhagic cholecystitis, uremic bleeding

Introduction

Hemorrhagic complications in patients on hemodialysis have been described in many anatomic locations. Uremic bleeding is associated with uremic toxins, anemia, platelet dysfunction, use of antiplatelet or anticoagulant agents, comorbid conditions and aging. Hemorrhagic cholecystitis is uncommon but can be fatal. In addition, hepatobiliary pathology is common in hemodialysis patients, including acute or chronic hepatitis, gall stones, and gallbladder carcinoma.1,2 Hemorrhagic cholecystitis is easily overlooked since its symptoms mimic those of common hepatobiliary diseases with right upper quadrant abdominal pain, liver function impairment, leukocytosis and positive Murphy’s sign. Abdominal ultrasound (US) and computed tomography (CT) can help diagnose and demonstrate the characteristic findings of wall thickening of the distended gallbladder and heterogeneous materials inside. Here, we report a hemodialysis patient who suffered from spontaneous gallbladder hemorrhage and discuss the possible mechanisms of the disease.

Case Report

An 81-year-old Chinese male presented in 2007 with end-stage renal failure as a consequence of diabetic nephropathy and started regular hemodialysis thrice weekly at an outpatient hemodialysis facility in Taipei County. He was admitted to our nephrology section for chronic obstructive pulmonary disease with acute exacerbation and secondary bacterial lung infection. On admission, he was treated with bronchodilator inhalation, intravenous steroid and empirical antibiotic (cefuroxime).

Unfortunately, repeated frequent attacks of right upper quadrant abdominal pain developed during hemodialysis sessions 1 week later. The abdominal pain resolved soon after the immediate cessation of dialysis. Physical examination revealed right upper quadrant pain with positive Murphy’s sign, and icteric sclerae. Vital signs showed a body temperature of 36.5°C, heart rate of 115/min, respiratory rate of 16/min, and blood pressure of 160/86 mmHg. Laboratory data showed white blood cell count of 15,700/mm³ and...
Uremia-associated hemorrhagic cholecystitis

segments/lymphocytes 82.5%/7.1%, hemoglobin of 10.7 g/dL, platelet count of 312,000/mm³, blood glucose of 196 mg/dL, alanine aminotransferase of 605 U/L, aspartate aminotransferase of 701 U/L, total bilirubin of 2.2 mg/dL, direct bilirubin of 1.3 mg/dL, lactic dehydrogenase of 429 U/L, alkaline phosphatase of 205 U/L, γ-glutamyltransferase of 254 U/L, amylase of 134 mg/dL, lipase of 129 mmol/L, and C-reactive protein of 1.69 mg/dL. Abdominal US showed positive sonographic Murphy’s sign and a distended gallbladder with echogenic materials in the dependent portion of the gallbladder (Figure 1). Acalculous cholecystitis was impressed initially, and the antibiotic amoxicillin/clavulanate was administered for 2 weeks.

The patient was placed on a regimen of nothing per os and partial parenteral nutrition. However, tarry stools developed 3 days later. Nasogastric tube insertion with irrigation was negative for blood, and upper gastrointestinal endoscopy only showed gastric ulcer and duodenal erosion without active bleeding. Prothrombin time, partial thromboplastin time, and platelet counts were within normal ranges. The bleeding time was 6 minutes and 30 seconds. Since the patient’s abdominal pain had worsened, percutaneous transhepatic gallbladder drainage (PTGBD) was performed, and dark-colored blood was drained. Cholangiography (Figure 2A) was performed for check-up; PTGBD showed normal drainage without contrast extravasation, and multiple filling defects within the gallbladder. Non-contrast CT of the abdomen (Figure 2B) revealed some heterogeneous materials with near blood density in the gallbladder.

The patient felt dizzy due to hypotension (30% reduction in his baseline blood pressure) and low level of hemoglobin. On the premise of hemorrhaging from the gallbladder, hemoglobin level was maintained at 10–11 g/dL by blood transfusion of packed red blood cells. Desmopressin was intravenously administered. The amount of dark-colored blood drained by PTGBD was about 50 mL/day. The abdominal pain resolved and the patient’s liver function returned to normal. The patient began oral intake smoothly 1 week later. He underwent elective exploratory cholecystectomy 3 weeks after PTGBD, during which dark blood clots that filled the distended gallbladder were found (Figure 3). Pathology (Figure 4) revealed fibrosis and chronic inflammatory cell infiltration in the lamina propria and muscular layer of the gallbladder wall. The patient recovered without any surgical complications.

Discussion

Uremic patients have a high risk of bleeding due to uremic toxins, anemia, platelet dysfunction, use of antiplatelet or anticoagulant agents, comorbidity and aging. However, the pathogenesis of uremic bleeding remains unclear. Platelet dysfunction in uremic patients includes defects in adhesion, secretion and aggregation of platelets.3 In addition, uremic substances like urea, guanidine-succinate, parathyroid hormone, phenol and tryptophan products can interfere with platelet function in uremic patients.4

In hemodialysis patients, gastrointestinal bleeding includes peptic ulcer disease (20–30%), gastritis (20%), telangiectasia in the stomach, duodenum, jejunum and colon (20–30%), and duodenitis and esophagitis.5 Gallbladder bleeding is uncommon in normal subjects. The underlying causes of hemorrhage from the gallbladder have been reported to be associated with trauma, neoplasms, rupture of aneurysms, arteriosclerosis, varicose veins with portal hypertension, and coagulopathy.2,6 Gallbladder bleeding is rare even in hemodialysis patients.

Hemorrhagic cholecystitis is an unusual disease. Our patient had biliary colic,7 leukocytosis, abnormal liver function, obstructive jaundice, and melena. Abdominal US showed gallbladder distension with wall thickening, and heterogeneous echogenic materials in the dependent part. Acute acalculous cholecystitis was diagnosed. Although CT, radioisotope imaging, and endoscopy may help with diagnosis, US is the initial imaging choice for intracholecystic hemorrhage. On US, such hemorrhage manifests as intensely echogenic mass-like lesions without acoustic shadows within the gallbladder. Color and duplex Doppler US help to confirm the absence of blood flow within the mass,
making the diagnosis of gallbladder tumor highly unlikely.8

The pathogenesis of acute acalculous cholecystitis is an acute necroinflammatory process, and its underlying causes include long-term absence of oral feeding, major surgery, sepsis, and burn and other critical conditions. In critically ill patients, dehydration due to prolonged absence of oral feeding results in calcium salt concentration and increased viscosity in the gallbladder.

In addition, low blood flow supply, ischemic injury of the gallbladder and bile stasis eventually lead to the concentration of calcium salts and necrosis of gallbladder tissue.9 Gremmels et al2 described their pathological findings of acute cholecystitis, showing that intramural inflammation damaged the mucosa with infarction and erosion. This led to microabscesses of the gallbladder wall, mural necrosis with ulceration, fibrinous exudates, and purulent debris within the gallbladder lumen. The mucosal breakdown may cause hemorrhage into the gallbladder lumen,2 and the intraluminal exudates and debris may mix with blood.

In the present case, bile culture was negative for bacteria, tuberculous bacilli and fungi. Bile cytology also revealed no malignant cells. We therefore inferred that the acute hemorrhagic acalculous cholecystitis in our patient was secondary to ischemic change of the gallbladder. Although hypotension or bleeding did not occur during hemodialysis, low perfusion of the gallbladder associated with the hemodynamic changes

Figure 2. (A) Cholangiography reveals several filling defects (arrows) in the gallbladder and proximal bile duct. (B) Non-contrast computed tomography of the abdomen reveals some heterogeneous, highly attenuated materials with near blood density (arrow) in the gallbladder. The catheter for percutaneous transhepatic gallbladder drainage (arrowhead) passes through the gallbladder.

Figure 3. (A) Distended gallbladder (about 10.2 × 7 cm) with mild wall thickening is noted. (B) The gallbladder is filled with dark blood clot-like material. (C) No gallstones were found within the gallbladder.

Figure 4. This section shows gallbladder tissue with fibrosis and chronic inflammatory cell infiltration (arrows) in the lamina propria and muscular layer. Congestion is also noted.

Uremia-associated hemorrhagic cholecystitis during dialysis cannot be excluded. In addition, a combination of heparin use in hemodialysis, uremic coagulopathy and concomitant vascular disease may lead to bleeding tendency and gallbladder hemorrhage.

Treatment for hemorrhagic acalculous cholecystitis was previously exploratory cholecystectomy, but laparoscopic cholecystectomy is now the key therapy. However, the mortality rates (30%) for laparoscopic cholecystectomy and open cholecystectomy are the same. Poor prognosis and numerous complications have been reported, such as postoperative hemorrhage and hypovolemic shock. The difficulty of surgical treatment for such a disease in hemodialysis patients is mainly due to bleeding. Our patient was initially treated with nothing per os and partial parenteral nutrition supplementation. The bleeding propensity was corrected by blood transfusion of packed red blood cells, desmopressin infusion and non-heparinized hemodialysis. PTGBD further improved the clinical symptoms of jaundice and liver dysfunction. PTGBD in our patient was indicated for diverting bile from the biliary tract obstruction caused by the blood clots and a time lag of 2 weeks for elective cholecystectomy.

In summary, hemorrhagic acalculous cholecystitis is a rare but often fatal disease. Its risk factors include critical illness, diabetes, malignant disease, and uremia. In patients with a high risk for bleeding diathesis who present with biliary colic, hematemesis, jaundice and melena, the possibility of hemorrhagic acalculous cholecystitis should be considered. Early diagnosis of this potentially fatal condition is important to facilitate urgent surgical treatment.

References