Gallbladder bleeding-related severe gastrointestinal bleeding and shock in a case with end-stage renal disease

A case report

Jun-Li Tsai (MD)\textsuperscript{a}, Shang-Feng Tsai (MD)\textsuperscript{b,c,d,e,*}

Abstract
Gallbladder (GB) bleeding is very rare and is caused by cystic artery aneurysm and rupture, or GB wall rupture. For GB rupture, the typical findings are positive Murphy’s sign and jaundice. GB bleeding mostly presented as hemobilia. This is the first case presented with severe GI bleeding because of GB rupture-related GB bleeding. After comparing computed tomography, one gallstone spillage was noticed. In addition to gallstones, uremic coagulopathy also worsens the bleeding condition. This is also the first case that patients with GB spillage-related rupture and bleeding were successfully treated by nonsurgical management. Clinicians should bear in mind the rare causes of GI bleeding. Embolization of the bleeding artery should be attempted as soon as possible.

Abbreviations: CKD = chronic kidney disease, CT = computed tomography, DM = diabetes mellitus, GB = gallbladder, GIB = gastrointestinal bleeding, PPI = proton pump inhibitor, TAE = transcatheter arterial embolization.

Keywords: end-stage renal disease, gallbladder bleeding, gastrointestinal bleeding

1. Introduction
Gastrointestinal bleeding (GIB) is mostly because of enteric bleeding. Gallbladder (GB)-related bleeding is seldom reported. The GB-related bleedings mostly manifested as hemobilia (bleeding into biliary tract), but rarely as GIB (bleeding in to gastrointestinal tract). Some cases are because of cystic artery aneurysm and rupture, and others are because of GB rupture. Typically, the manifestations of GB rupture are abdominal pain and jaundice. Herein, we report the first case of GB stone spillage-related GB rupture, presented uniquely with severe GB bleeding as GIB rather than hemobilia, and present a literature review.

2. Case report
This 80-year-old man has been a patient of type 2 diabetes mellitus (DM) for 15 years, while also presenting with chronic kidney disease (CKD) (8.87 mg/dL of serum creatinine, and 6.16 mL/min/1.732 m\textsuperscript{2} of glomerular filtration rate), cirrhosis, 2 GB stones, and hypertension. The routine medications were as follows: sodium bicarbonate, erythropoietin, amiodipine, furosemide, and calium acetate. This time, he was admitted for dyspnea and fever. Septic workup revealed pneumonia (22,000 cells/cm\textsuperscript{3} of white blood cells and 20 mg/dL of C-reactive protein), and acute pulmonary edema. Ampicillin-sulbactam was prescribed soon after admission. Two days after admission, we initiated hemodialysis for persistent oliguria and progression of dyspnea. Following this, he received regular hemodialysis and antibiotics. Unfortunately, 7 days after admission, shock (systolic blood pressure dropped from 160 to 70 mmHg) and severe tarry stool occurred. He also complained right upper abdominal and right lower back pain along with intermittent constipation recently. The hemoglobin declined from 10 to 6.3 g/dL. Blood transfusion with a 4-unit packed red blood cell, desmopressin, and proton pump inhibitor (PPI) were all prescribed after this event. The duodenoscopy showed superficial gastritis and reflux esophagitis without a definite bleeding source. Within 2 days of bleeding, there was less tarry stool with decreasing hemoglobin (8.0 g/dL), along with stable blood pressure. However, he suffered from hypovolemic shock again (70 mmHg of systolic blood pressure) with massive tarry and bloody stool. Fluid resuscitation, blood transfusion, and PPI were all given again to stabilize his vital signs. Hemoglobin dropped to 5 g/dL. The colonoscopy did not reveal any active bleeding. Because of recurrent GIB without definite source, abdominal computed tomography (CT) was ordered, to locate any source of bleeding. The abdominal CT showed, in addition to 1 GB stone, high-density lesions and blood clots in the GB with contrast extravasations (Fig. 1B), which was compatible with right upper abdominal pain. There were no hemobilia. After meticulous tracing with the CT, there was 1 stone over the right retroperitoneum (Fig. 1C), which may cause right lower back pain and constipation. Compared with the previous abdominal CT (undertaken 9 months previously) (Fig. 1A), there were 2 GB...
stones without contrast-enhancement in the GB, and no right retroperitoneal stone, indicating GB stone spillage. The GIB was in favor of GB rupture-related, and the angiography disclosed active bleeding over the GB from the medial anterior branch of the cystic artery (Fig. 1D). Transcatheter arterial embolization (TAE) was carried out to stop vascular bleeding. Two days later, the patient had fever, jaundice, and right upper abdominal distention with Murphy’s sign. The total bilirubin increased from 0.1 to 6.4mg/dL. Post-TAE-related cholecystitis was impressed. Therefore, a 10-French percutaneous transhepatic GB pigtail tube was inserted along the guide wire into the GB. The bile culture yielded Klebsiella pneumoniae, and Cefoperazon was infused. Three days later, the fever subsided and total bilirubin was 1.3mg/dL. Two weeks later, the patient was discharged without fever, jaundice, and no presence of tarry stool. A cholecystectomy was performed later electively. During the whole course of admission, the hemodialysis was performed without heparinization, and he never took any antiplatelet or anticoagulation medication. This study had been approved by patient himself and he signed the informed consent.

3. Discussion

Incidences of GB bleeding are rare. Until now, 23 cases towing to cystic artery aneurysm with rupture bleeding have been reported.[1] The cause for cystic artery aneurysm may be GB stone-related GB ulcers eroding into the cystic artery. Other cases of GB bleeding are hemorrhagic perforation because of serious complication of acute cholecystitis with very high mortality (60%) if gangrenous necrosis.[2] This is extremely rare, and there have only been 17 reported cases.[2] The incidence of hemorrhagic perforation of the GB occurs in 2% to 11% of acute cholecystitis.[3] This case is very unique because the GB bleeding was not caused by cystic artery aneurysm, as proved by angiography, and it was not due to acute cholecystitis because of normal bilirubin and no Murphy’s sign. It was mostly because this patient already had two GB stones, as shown in a previous abdominal CT scan, and in the fact he suffered from chronic cholecystitis. The manifestation and course of cholecystitis are less serious and relatively chronic. For a long time, GB stones caused transmural inflammation leading to necrosis, and a GB wall ulcer. That GB stones can lead to the formation of a decubitus ulcer of the GB, which has also been reported before.[4] During this admission, the GB stone eroded into the branch of the cystic artery, and led to GB wall rupture. The eroded branch of the cystic artery led to bleeding into the biliary tree as hemobilia, which is a rare cause of GIB. This unique presentation of GB owing to GB bleeding was first reported by Francis Glison in 1993.[4] More than 20 years later, these cases are still extremely rare. Furthermore, in this case, the GB-related bleeding entered gastrointestinal tract as GIB, instead of hemobilia. This presentation is further rare. Most presentations of GB spillage-related GB rupture are abdominal pain, Murphy’s sign, and jaundice. In this case, the patient did not have any of these typical presentations. The rarity of this cause of GIB can easily cause clinicians to miss this diagnosis, and delay treatment. Bleeding

Figure 1. (A) Two gallbladder stones (black arrows). (B) One gallbladder stone (black arrow head), with contrast extravasations (white arrows). (C) One stone over right retroperitoneum (black arrow). 1. Active bleeding over gallbladder from medial anterior branch of cystic artery (black arrow).
because of branching of the cystic artery, and improvement of condition due to embolization, both supported the severe GB was due to this extremely rare diagnosis. Besides, spillage of 1 GB stone can also support that the GB stone eroded the GB wall, and caused GB bleeding. To the best of our knowledge, most spilled GB stones occur during laparoscopic cholecystectomy and the incidence has been reported to be between 6% and 40%.\[5,6\] Until now, there was only 1 similar case owing to spontaneous spillage.\[7\] However, most manifestations of spillage of GB stones are gallstone ileus, and abdominal pain, which were different from our case. Our case only had severe GB. In summary, this is the first case with chronic GB-related chronic cholecystitis, followed by GB stone spillage presented with severe GB without jaundice or abdominal pain. In such a condition, it is very easy for clinicians to miss the diagnosis because of focusing on the enteric bleeding.

There are still other reasons for this severe GB. First, uremic bleeding is a well-recognized complication in patients with renal dysfunction, affecting platelet aggregation and/or the coagulation cascade. Second, Gençoğlu et al.\[9\] mentioned that the prevalence of GB stones in hemodialytic patients, increased when compared with healthy controls which, may be because of more blood transfusions and autonomic neuropathy. Moreover, the increased GB stones led to more GB stone-related GB. Finally, we can infer GB rupture secondary to ischemic change of the GB owing to pneumonia-related sepsis and fluctuations in blood pressure while hemodialysis. Although hypotension did not occur during hemodialysis, low perfusion of the GB is associated with the hemodynamic changes. Nevertheless, GB bleeding is still rare even in hemodialytic patients. Until now, only 3 cases have been reported with GB bleeding in hemodialytic patients.\[8–11\] Unlike this case, all 3 cases received heparin during hemodialysis.

Theoretically, the treatment of choice in this situation maybe urgent surgical intervention to stop bleeding and GB perforation-related sepsis. However, this is the first case to receive embolization to stop bleeding without surgical intervention. The reason is the very poor general health of the patient, which dissuaded the family from agreeing to the operation being carried out. Besides, in diabetic patients, less invasive procedure to reduce multiple comorbidities, we can try embolization to stop bleeding first rather than giving up.

4. Conclusion

We present a unique and extreme case of chronic GB stone-related chronic cholecystitis and GB stone spillage-related severe GB. We have demonstrated the success of nonsurgical management alone in its treatment. Clinicians should bear in mind the rare causes of GB. Embolization of the bleeding artery should be attempted as soon as possible.

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