Gallbladder hemorrhage–An uncommon surgical emergency: A case report

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BACKGROUND
Gallbladder hemorrhage is a life-threatening disorder. Trauma (accidental or iatrogenic such as a percutaneous biopsy or cholecystectomy surgery), cholecystolithiasis, biliary tract parasitosis, vasculitis, vascular malformations, autoimmune and neoplastic diseases and coagulopathies have been described as causes of hemorrhage within the lumen of the gallbladder. The use of non-steroidal anti-inflammatory drugs and anticoagulants may represent a risk factor.

CASE SUMMARY
We report the case of a 76-year-old male patient. An urgent contrast computed tomography scan demonstrated relevant distension of the gallbladder filled with hyperdense non-homogeneous content. The gallbladder walls were of regular thickness. Near the anterior wall a focus of suspected active bleeding was observed. Due to the progressive decrease in hemoglobin despite three blood transfusions, this was an indication for urgent surgery.

CONCLUSION
Early diagnosis of this potentially fatal pathology is essential in order to plan a strategy and eventually proceed with urgent surgical treatment.

Key Words: Gallbladder; Hemorrhage; Anticoagulants; Cholecystectomy; Surgery; Case report

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Core Tip: Gallbladder hemorrhage is an uncommon life-threatening disorder. There are many causes of this condition: trauma, cholelithiasis, biliary tract parasitosis, vasculitis, vascular malformations, autoimmune and neoplastic diseases and coagulopathies. We report the case of a 76-year-old male patient. An urgent contrast computed tomography scan demonstrated relevant distension of the gallbladder filled with hyperdense non-homogeneous content and a focus of suspected active bleeding. The patient underwent urgent surgery to stop the hemorrhage. Early diagnosis of this insidious and potentially fatal pathology is essential to plan the best treatment strategy for patients.

INTRODUCTION

Gallbladder hemorrhage is a rare condition, which can be difficult to diagnose. It manifests symptoms present in other more common pathologies, such as fever, nausea, abdominal pain, and Murphy’s sign. Trauma (accidental or iatrogenic such as a percutaneous biopsy or cholecystectomy surgery), cholelithiasis, biliary tract parasitosis (e.g., ascariasis), vasculitis, vascular malformations, neoplastic diseases, and coagulopathies have been described as causes of hemorrhage within the lumen of the gallbladder. The use of non-steroidal anti-inflammatory drugs (NSAIDs) and anticoagulants may represent a risk factor. During the evolution of flogosis, necrosis of the gallbladder mucosa may result in bleeding from the vessels located within the organ wall. The use of imaging methods such as ultrasound, computed tomography (CT) and angiography can be useful in diagnosing this uncommon condition. As a medical emergency with a reported mortality rate of 15%-20%, early diagnosis is mandatory and can result in a better outcome for the patient[1-4]. We describe the case of a patient treated with NSAIDs and anticoagulants, who developed severe anemia due to intracolecystic hemorrhage that required urgent surgery.

CASE PRESENTATION

Chief complaints
The patient complained of abdominal pain and constipation.

History of present illness
We report the case of a 76-year-old male patient who attended the emergency room due to abdominal pain and constipation.

History of past illness
In the anamnesis he presented osteoporosis, parkinsonism, vertebral stabilization (metal plates and screws) for L2-L3 arthrodesis (2016), L1-L2 spondylodiscitis, chronic pain in the lumbar region, stiffness in the upper limbs and lower limbs, small steps and impairment of the extensor muscles of the spinal column with bent spine syndrome. In July 2020, due to trauma, he attended the emergency room, where, lacking diagnostic evidence, he was discharged and transferred to a rehabilitation institution. He had been taking the following drugs for the last few years at home: Pantoprazole, CardioASA, Bromazepam, Durogesic, and Cardicor.

Personal and family history
No relevant personal and family history.

Physical examination
On physical examination, the patient appeared oriented, cooperative, eupnoic, malnourished, with muscle atrophy and widespread hypotonia. Abdominal examination demonstrated diffuse abdominal pain. His heart rate was 68 bpm, blood pressure was 120/70 mmHg, and temperature was 36°C.

Laboratory examinations
Blood chemistry showed the following: hemoglobin 11.2 g/dL; white blood cell count 10.790/μL; total bilirubin 0.50 mg/dL; aspartate aminotransferase 40 U/L; alanine aminotransferase 28 U/L; alkaline
phosphatase 115 U/L; amylase 406 U/L; C-reactive protein: 150 mg/L.

**Imaging examinations**

To assess the suspicion of chronic pancreatitis, the patient underwent abdominal ultrasound, and the pancreas showed multiple calcifications in the parenchyma. Moreover, the aorta demonstrated an irregular caliber with progressive stenosis. This finding required an in-depth study; therefore, CT angiography was performed and the common right artery demonstrated CT signs of dissection and ulcerated atheromatous plaque at the origin. Dilated gallbladder, slightly dilated extrahepatic biliary tract, increased volume in the pancreatic gland with small hypodense formations in the pancreas head (maximum diameter 3 mm) were also highlighted. Due to the finding of ulcerated atheromatous plaque, Fondaparinux 2.5 mg/d was administered as suggested by the vascular surgeon consultant.

However, the persistence of continuous lumbar pain led the patient to NSAIDs and morphine-like analgesic self-administration, the dosage of which was increased and reduced according to the patient's symptoms relief. Approximately 10 d after Fondaparinux administration, the patient suddenly experienced severe anemia, hyperbilirubinemia, increased cholestasis and transaminase. On physical examination the abdomen was painless. No blood was found in the stool. An urgent abdominal ultrasound, with the patient still in bed, was performed. Evidence of distended gallbladder filled with non-homogeneous hyperechoic material and a slightly dilated intrahepatic biliary tract were observed (Figure 1). The common bile duct was not visible due to intestinal gas.

Therefore, the patient underwent an urgent CT scan, which demonstrated relevant distension of the gallbladder filled with hyperdense non-homogeneous content. The gallbladder walls were of regular thickness. Near the anterior wall, a focus of suspected active bleeding was noted. Intra- and extra-hepatic biliary ducts demonstrated wider dilatation when compared to the previous CT scan (Figure 2).

**FINAL DIAGNOSIS**

Gallbladder hemorrhage.

**TREATMENT**

Our hospital is an emergency referring center, with multidisciplinary expertise readily available. An interventional radiological consultation was sought with the aim of evaluating the risk-benefit ratio of cystic artery embolization and/or cholecystostomy. The risk of gallbladder necrosis due to cystic artery occlusion and the risk of hemoperitoneum due to percutaneous drainage led the surgical team to select upfront surgery. The decrease in hemoglobin despite three blood transfusions, coagulation disorders and worsening of his general condition required an effective and timely solution. Therefore, the patient underwent urgent surgery. Open cholecystectomy was performed. Choledocotomy with Kehr tube apposition completed the surgery due to the presence of dilated hepatocoledocus (approximately 25 mm) (Figure 3A). When the gallbladder was inspected at the backtable, it appeared entirely occupied by clots (Figure 3B).

**OUTCOME AND FOLLOW-UP**

A further blood transfusion, plasma and supportive medical therapy were administered during the perioperative period. The patient had a regular post-operative course until discharge. The T tube was removed 50 d after surgery. Histological examination demonstrated acute lithiasic cholecystitis without any relevant finding.

**DISCUSSION**

Gallbladder hemorrhage is a rare complication of cholelithiasis, and is difficult to diagnose due to the non-specificity of the symptoms, which may easily lead to possible thoracic aortic dissection for back pain or acute cholecystitis for right hypochondrium pain. It can also manifest with fever, nausea, jaundice, melena and increased indices of inflammation and markers of liver damage in blood tests (neutrophilic leukocytosis, hypertransaminasemia, hyperbilirubinemia)[1-4].

Among the causes of gallbladder hemorrhage, trauma, neoplasms of the biliary tract, lithiasic cholecystitis, parasitosis, vasculitis, autoimmune diseases, and primary or secondary coagulopathies (e.g. liver cirrhosis, renal failure) have been reported[5-10]. Most patients diagnosed with gallbladder hemorrhage have comorbidities and most take anticoagulants and NSAIDs. To date, approximately 51
case reports have been reported in the literature since 1980[5]. We performed a brief revision of the cases reported in the literature, and their treatment strategies (Table 1). Among the reports, over 80% of patients underwent surgery with cholecystectomy. Of these, 6/45 patients underwent elective laparoscopic cholecystectomy after conservative treatment. Open surgery was dominant in the urgent setting (24 vs 15 patients), and we could hypothesize that this surgical technique was chosen with the aim of better evaluation and control of extra-gallbladder sources of hemorrhage.

The elevated prevalence (47%) of patients treated with antiplatelet agents and/or anticoagulants clearly underlines these drugs as risk factors. However, the role of other causes of hemorrhage (accidental or iatrogenic trauma, cholelithiasis, neoplasm, vascular anomalies and coagulopathies) in patients who did not take the aforementioned drugs is not insignificant.

Finally, we can assume that the incidence of this rare pathology is somehow underestimated, given the small number of cases in the literature. In the case described in this report, the patient had been taking cardioaspirin at home.

Moreover, the finding of dissection of the right iliac artery and ulcerated atheromatous plaque, and the thromboembolic risk derived from the patient's bed rest due to chronic lumbar pain suggested the administration of low molecular weight heparin. The self-administration and potential abuse of NSAIDs may have represented an additional risk factor.

Cholelithiasis and the intake of antithrombotic drugs may have played a primary role in the etiology of gallbladder hemorrhage. The damage caused by gallbladder mucosal stones usually heals spontaneously, but this may not occur in patients taking anticoagulants, creating blood oozing that can result in
Table 1 Case reports in the literature since 1980

| Ref. | Journal | Patient age/gender | Anti-coagulation | Treatment choice |
|------|---------|-------------------|------------------|-----------------|
| Nguyen D et al [16], 2021 | Journal of Radiology Case Reports | N | Cystic artery embolization, cholecystectomy |
| Chen X et al [17], 2021 | Hepatobiliary Surgery and Nutrition | 63 F | Not mentioned | ERCP and ENBD, cholecystectomy |
| Leaning [18], 2021 | Journal of Surgical Case Reports | 73 M | Y-Apixaban | Laparoscopic Cholecystectomy |
| Azam et al [19], 2021 | Journal of the National Medical Association | 55 M | Y-Apixaban | Cholecystectomy |
| Yam et al [20], 2020 | Radiology Case Reports | 51 F | N | Cystic artery embolization, cholecystostomy, open cholecystectomy |
| Gomes et al [21], 2020 | BMJ Case Reports | 87 M | Y-Aspirin | Open cholecystectomy |
| Kishimoto et al [22], 2020 | Gan To Kagaku Ryoho. Cancer and Chemotherapy | 96 F | N | Laparoscopic cholecystectomy |
| Tarazi et al [23], 2019 | Journal of Surgical Case Reports | 87 M | Y-Warfarin | Cholecystostomy |
| Reens et al [24], 2019 | The Journal of Emergency Medicine | 76 M | Y-Warfarin | Cholecystostomy |
| Itagaki et al [25], 2019 | Journal of Medical Case Reports | 86 F | Y-Edoxaban | Conservative with IV antibiotics, elective laparoscopic cholecystectomy |
| Honda et al [26], 2019 | Journal of Clinical Rheumatology: practical reports on rheumatic & musculoskeletal diseases. | 71 M | N | Laparoscopic cholecystectomy |
| San Juan López C et al [27], 2019 | Revista espanola de enfermedades digestivas: organo oficial de la Sociedad Espanola de Patología Digestiva. | 55 M | N | Laparoscopic cholecystectomy |
| Ng et al [28], 2018 | BMJ Case Reports | 68 F | N | Open cholecystectomy |
| Liefman et al [29], 2018 | International Annals of Medicine | 73 F | Y-Rivaroxaban | Conservative with IV antibiotics, elective laparoscopic cholecystectomy |
| López et al [30], 2018 | Radiology | 84 M | Not mentioned | Laparoscopic cholecystectomy |
| Berndtson et al [31], 2017 | Surgical Infections Case Reports | 75 F | N | Open cholecystectomy |
| Choi et al [32], 2017 | Trauma Image and Procedure | 65 M | N | Laparotomy + open cholecystectomy |
| Kinney et al [33], 2017 | BMJ Case Reports | 74 M | Y- Apixaban | Laparotomy + open cholecystectomy |
| Sishida et al [34], 2017 | Case Reports in Gastroenterology | 79 M | Y-Heparin for dialysis | ERCP and ENBD |
| Oshiro et al [35], 2017 | International Surgery | 61 F | Y – Warfarin | Conservative with IV antibiotics, elective laparoscopic cholecystectomy |
| Yoshida et al [36], 2017 | J-Stage | 73 M | Y | Laparoscopic cholecystectomy |
| Tsai et al [37], 2016 | Medicine | 80 M | N | Cholecystostomy, elective laparoscopic cholecystectomy |
| Calvo Espino et al [38], 2016 | Cirugía Española | 59 M | N | Laparotomy + Open cholecystectomy |
| Cho et al [39], 2015 | Korean Journal of Thoracic and Cardiovascular Surgery | 61 M | Y-Warfarin | Cholecystostomy drainage |
| Aljiffry et al [40], 2014 | Journal of Surgical Case Reports | 57 M | N | Cystic artery embolization + open cholecystectomy |
| Orozawa et al | International Surgery | 58 F | N | Laparoscopic cholecystectomy |
Acute bleeding. The patient's medical history, physical examination, laboratory tests and radiological imaging are relevant to the diagnosis, to exclude other pathologies[11,12], in order to promptly plan a strategy, as gallbladder hemorrhage represents a potentially fatal surgical emergency. An initial evaluation with ultrasound can be carried out. Most cases of gallbladder hemorrhage demonstrate ultrasound features not common in acute cholecystitis.

The sonographic findings in hemorrhagic cholecystitis include focal wall thickening, intraluminal membranes and non-shadowing, non-mobile intraluminal echogenic material. There may be some echogenic layering material for which the differential diagnosis includes sludge[13]. The suspicion can be further confirmed by CT examination, which may demonstrate high attenuation within the gallbladder lumen with layering high attenuation fluid-fluid level representing blood or sludge. An early phase contrast-enhanced CT helps to detect active extravasation of contrast and blush within the lumen of the gallbladder[5,6].
The most suitable treatment for gallbladder bleeding is urgent laparoscopic or laparotomic cholecystectomy. In some selected cases, it is possible to plan a non-interventional strategy with antibiotic therapy and supportive medical therapy, postponing subsequent cholecystectomy surgery\cite{5,10}.

Rarely, in the case of patients ineligible for surgery, a percutaneous cholecystostomy may be indicated\cite{14,15}. In our case, given the patient’s sudden anemia, despite blood transfusions and supportive medical therapy, due to the persistence of hemodynamic instability we proceeded with urgent surgery.

**CONCLUSION**

Gallbladder hemorrhage is a life-threatening complication of cholelithiasis. Early diagnosis of this potentially fatal pathology is essential in order to plan a treatment strategy and eventually proceed with urgent surgical treatment, to ensure timely life-saving decisions and the best results for the patient.

**FOOTNOTES**

**Author contributions:** All authors discussed the results and contributed to the final manuscript.

**Informed consent statement:** Written informed consent was obtained from the patient for publication of this case report.

**Conflict-of-interest statement:** All authors report no relevant conflict of interest for this article.

**CARE Checklist (2016) statement:** The authors have read the Care Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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**S-Editor:** Wu YXJ

**L-Editor:** Webster JR

**P-Editor:** Wu YXJ
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