
Unexpected case of gallbladder hemorrhage.

Maria Rosaria Valenti, Andrea Cavallaro, Maria Di Vita, Antonio Zanghi, Giovanni Longo Trischitta, Alessandro Cappellani
Abstract

BACKGROUND
Gallbladder bleeding is a life threatening complication. Trauma (accidental or iatrogenic such as a percutaneous biopsy or cholecystectomy surgery), cholelithiasis, 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 NSAIDs (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. Urgent contrast CT scan demonstrated relevant distension of the gallbladder filled by hyperdense non-homogeneous content. Gallbladder walls were of regular thickness. Near the anterior wall a focus of suspected active bleeding has been described. Due to the progressive decrease in hemoglobin despite three blood transfusion, indication for urgent surgery was given.

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

Key Words: gallbladder; hemorrhage; anticoagulants; FANS; cholecystectomy; surgery


Core Tip: Gallbladder bleeding is an uncommon life threatening complication. 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. Urgent contrast CT scan demonstrated relevant distension of the gallbladder filled by hyperdense non-homogeneous content with a focus of suspected active bleeding. It was given indication for urgent surgery to stop hemorrhage. The early diagnosis of this insidious and potentially fatal pathology is essential to plan the better strategy for the patient.

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, 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, coagulopathies have been described as causes of hemorrhage within the lumen of the gallbladder. The use of 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, CT and angiography can be useful in diagnosing this uncommon condition.

As a medical emergency with a reported mortality rate of 15-20%, an early diagnosis is mandatory and preludes to a better outcome for the patient [1-4].

We describe the case of a patient treated with NSAIDs and anticoagulants, who developed a severe anemia due to intracolecystic hemorrhage that imposed urgent surgery.

CASE PRESENTATION

Chief complaints

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History of present illness
We report the case of a 76-year-old male patient who accessed the emergency room for 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, because of a trauma, he entered in the emergency room, where, lacking diagnostic evidence, he was discharged and addressed to a rehabilitation institution. He has been assuming some drugs in the last years: Pantoprazole, CardioASA, Bromazepam, Durogesic, Cardicor at home.

Personal and family history
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Physical examination
On physical examination, the patient appeared oriented, cooperative, eupnoic, malnourished, with muscle atrophy and widespread hypotonia. Abdominal examination demonstrated diffuse abdominal pain. HR 68 bpm, BP 120/70 mmHg, TC 36 °C.

Laboratory examinations
Blood chemistry showed: Hb 11.2 g/dL; WBC 10.790/µL; total bilirubin 0.50 mg/dL; AST 40 U/L; ALT 28 U/L; alkaline phosphatase 115 U/L; amylase 406 U/L; CRP: 150 mg/L.

Imaging examinations
To assess the suspicion of chronic pancreatitis, the patient underwent abdominal ultrasound: pancreas appeared with multiple calcifications in the parenchyma. Moreover, aorta demonstrated irregular caliber with progressive stenosis. This finding required an in-depth study, therefore CT angiography was performed: 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 pancreatic gland with small hypodense formations in correspondence of the head (maximum diameter 3 mm) were also highlighted. Due to the ulcerated atheromatous plaque finding, Fondaparinux 2.5 mg/day was administered as per vascular surgeon consultant suggestion.

However, the persistence of continuous lumbar pain led the patient to NSAIDs and morphine-like analgesic self-administration, the dosage of which is increased and reduced according to the patient's symptoms relief.

Approximately 10 days after Fondaparinux administration, the patient suddenly experienced severe anemia, hyperbilirubinemia, increased cholestasis and transaminase. On physical examination the abdomen was painless. No blood in the stool.

An urgent abdominal ultrasound, with patient still in the bed, was performed. It demonstrated evidence of distended gallbladder filled with not-homogeneous hyperechoic material and slightly dilated intrahepatic biliary tract (Fig 1). Common bile duct was not viewable due to intestinal gas.

Therefore, the patient underwent urgent CT scan: it demonstrated relevant distension of the gallbladder filled by hyperdense non-homogeneous content. Gallbladders walls were of regular thickness. Near the anterior wall, a focus of suspected active bleeding has been described.

Intra and extra hepatic biliary ducts demonstrated wider dilatation when compared to the previous CT scan exam. (Fig 2)

**FINAL DIAGNOSIS**
Gallbladder hemorrhage

TREATMENT
Our hospital is an emergency referring centre, with several multidisciplinary expertise readily available. A radiological interventional consultation was promptly asked with the aim to evaluate the risk-benefit ratio of cystic artery embolisation and/or cholecystostomy. The risk of gallbladder necrosis because of cystic artery occlusion and the risk of hemoperitoneum due to percutaneous drainage led the surgical team to the choice of upfront surgery. The decrease of hemoglobin despite three blood transfusion, the coagulation disorders and the worsening of general condition required an effective and timely solution. Therefore indication for urgent surgery was given.
Open cholecystectomy was performed. Choledocotomy with Kehr tube apposition completed the surgery because of dilated hepatocoledocus finding (approximately 25 mm). (Figure 3)
Once the gallbladder was inspected at the backtable, it appeared entirely occupied by clots. (Fig 4)

OUTCOME AND FOLLOW-UP
One more blood transfusion, plasma and supportive medical therapy were administered in the perioperative period. The patient had a regular post-operative course until discharge in an institution.
The T tube was removed 50 days after surgery. Histological examination demonstrated acute lithiastic cholecystitis without any relevant finding.

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

Among the causes, we can find trauma, neoplasms of the biliary tract, lithiasic cholecystitis, parasitosis, vasculitis, autoimmune diseases, primary or secondary coagulopathies (eg liver cirrhosis, renal failure).\textsuperscript{5-10}

Most patients diagnosed with gallbladder hemorrhage have comorbidities and most of them take anticoagulant and non-steroidal anti-inflammatory drugs.

To date, about 51 case reports have been reported in literature since 1980.\textsuperscript{5}

We have made a brief revision of the cases reported in the literature, with relative strategies of treatment. [Tab. 1]

Among the reports, over 80\% of patients underwent surgery with cholecystectomy.

Of these, 6/45 patients underwent elective laparoscopic cholecystectomy after conservative treatment. The open surgery was dominant in urgent setting (24 vs 15 patients): we could hypothesize this surgical choice with the aim to better evaluate and control eventual extra-gallbladder sources of hemorrhage.

The elevated prevalence (47\%) of patients treated with antiplatelet agents and/or anticoagulants clearly underlines the weight of these drugs as risk factor. However, still not negligible the role of other hemorrhage causes (accidental or iatrogenic trauma, cholelithiasis, neoplasm, vascular anomalies and coagulopathies) in patients who do not uptake the aforementioned drugs.

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 paper, the patient has been already assuming cardioaspirin at home.

Moreover, the finding of dissection of the right iliac artery and contextual ulcerated atheromatous plaque, the thromboembolic risk derived from the patient’s bedding because of chronic lumbar pain suggested the administration of low molecular weight
heparin. The self-administration and potential abuse of non-steroidal anti-inflammatory drugs may have represented an additional risk factor. Cholelithiasis and the intake of antithrombotic drugs may have played a primary role in the etiology. The damage caused by gallbladder mucosal stones usually heals spontaneously, but this may not happen in patients taking anticoagulants, creating blood oozing that can result in acute bleeding.

The patient's medical history, physical examination, laboratory tests and radiological imaging are relevant to assess the diagnosis, to exclude other pathologies\(^{11,12}\), in order to promptly plan a strategy: the gallbladder hemorrhage represent a potentially fatal surgical emergency.

An initial evaluation can be done with ultrasound. Most cases of gallbladder hemorrhage do demonstrate ultrasound features not common to acute cholecystitis.

The sonographic findings for 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 includes sludge\(^{13}\).

The suspicion can be further confirmed by CT examination. Computed tomography 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 in detecting the active extravasation of contrast and blush within the lumen of the gallbladder\(^{5,6}\).

The most suitable treatment for gallbladder bleeding is laparoscopic or laparotomic urgent 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 in election\(^{5,10}\).

Rarely, in the case of patients not eligible for surgery, a percutaneous cholecystostomy may be indicated\(^{14,15}\). In our case, given the sudden anemia of the patient, despite the
administration of blood unit and supportive medical therapy, due to the persistence of hemodynamic instability we proceed with urgent surgery.

CONCLUSION

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