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Case Report

Perforated Acalculous Hemorrhagic Cholecystitis without Hemoperitoneum in a Dialysis Patient: A Case Report and Literature Review

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Abstract

Hemorrhagic cholecystitis is a rare and fatal diagnosis with an incidence of 3.5% that requires immediate intervention. It is commonly underdiagnosed as it mimics other more common diseases. We describe a case of an older woman on hemodialysis diagnosed with perforated acalculous hemorrhagic cholecystitis without hemoperitoneum. The patient presented with non-specific gastrointestinal symptoms associated with increased inflammatory markers and liver transaminases. MRI showed a heterogeneous collection in the right infra hepatic region with central hyperdensity suggestive of hemorrhagic cholecystitis. Her past medical history was pertinent for atrial fibrillation and adrenal insufficiency, with the use of anticoagulation and steroids, respectively. The patient was started on intravenous antibiotics and underwent urgent cholecystectomy with findings of micro perforation in the gallbladder. Pathology samples revealed evidence of acalculous cholecystitis and necrosis. Unfortunately, the disease's course was complicated by multiorgan failure, and the patient passed away.

CASE PRESENTATION

A 69-year-old woman presented to our emergency department for altered mental status that started three weeks prior and was accompanied by acute onset of generalized abdominal pain. Associated symptoms were significant for nausea, vomiting, somnolence, and decreased PO intake.

Upon arrival at the emergency department, the patient was hemodynamically unstable with subsequent fever, hypotension, and somnolence. Abdominal examination revealed diffuse tenderness to palpation without evidence of rigidity.

Her past medical history was pertinent for end-stage renal disease (ESRD) on hemodialysis, paroxysmal atrial fibrillation, chronic demyelinating polyradiculoneuropathy (CIDP) in remission, adrenal insufficiency, hypertension, and coccygeal ulcer. Past surgical history includes a laminectomy two months ago and an open appendectomy.

Her medications are significant for sintrom 3mg daily and hydrocortisone 10 mg daily.

Laboratory tests revealed an elevated white blood cell count of 16.7x 103/ul (Neutrophil 96%), hemoglobin 13 g/dl, and platelets 249 000 /µL. The chemistry studies showed a marked increase in transaminases, namely gamma-glutamyl transferase (198 IU/L) and alkaline phosphatase (523 IU/L). Otherwise, chemistries showed INR 2.14, CRP 340 mg/l, LDH 544 U/L, and bicarbonate 18 meq/L. The rest of the aminotransferases, bilirubin, and PTT were within range.

An urgent abdomen CT scan without contrast was performed (Figure 1), and showed a 6 x 7 x 13 cm heterogeneous collection in the right infrahepatic region with central hyperdensity (blood density approximately 40 Hounsfield Unit). Findings correlated with hematoma versus the possibility of hemorrhagic cholecystitis.

A diagnosis of septic shock was made. The patient was subsequently started on stress dose steroids, pressors, and broad-spectrum intravenous antibiotics and then transferred to the intensive care unit

Once stable, the patient underwent an MRI and MRCP of the abdomen. Results (Figure 2-5), showed a distended gallbladder 12 x 7 x 6.8 cm with heterogeneous density and high T1 and

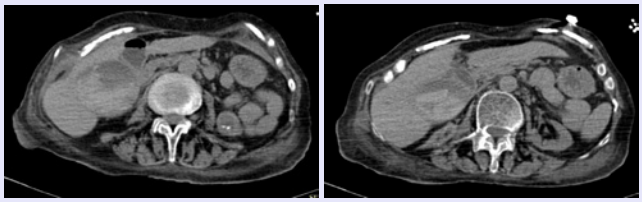

Figure 1 Abdominal CT scan. 6 x 7 x 13 cm heterogeneous collection of the right infra hepatic region with central hyperdensity suggestive of hematoma versus the high possibility of hemorrhagic cholecystitis.

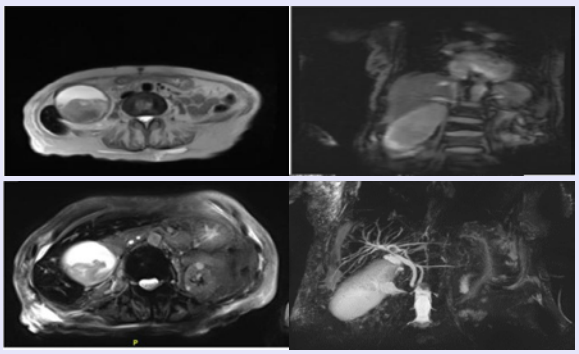

Figure 2,3,4,5 Abdomen MRI showing a distended gallbladder 12 x 7 x 6.8 cm with heterogeneous density with high T1 and low T2 signal intensity seen in its lumen suggestive of hemorrhagic cholecystitis. The intra and extrahepatic ducts are normal in caliber. No visible calculi.

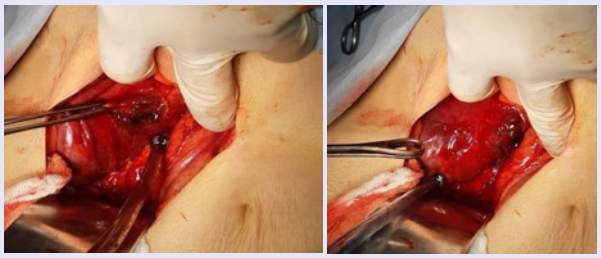

Figure 6 Gallbladder adherent to the stomach and omentum with micro-perforation.

low T2 signal intensity in its lumen, suggestive of hemorrhagic cholecystitis.

Based on these findings, the patient was rushed for urgent surgical laparotomy and cholecystectomy. The procedure unmasked an ischemic and friable gallbladder mucosa identified as adherent to the stomach and omentum with micro-perforation of the gallbladder (Figure 6). A large volume of hematoma was evacuated without evidence of stones (Figure 7).

Histological examination of the gallbladder showed acute cholecystitis with full-thickness necrosis and no cholelithiasis. Intra abdominal cultures and gallbladder cultures taken during the operation were negative.

Postoperatively, the patient became unstable. She was intubated and transferred to the intensive care unit for

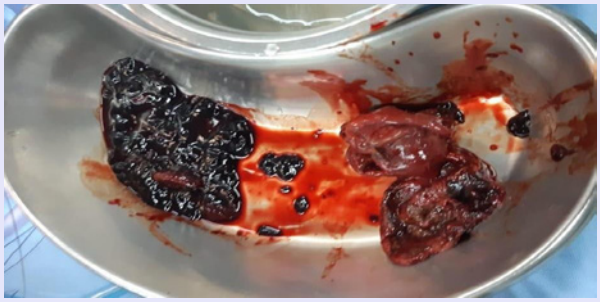

Figure 7 Acalculous gallbladder filled with dark blood clots.

stabilization. Antibiotics were escalated, and fluconazole was added for fungal coverage. Unfortunately, due to the patient's multiple comorbidities, multiorgan failure ensued, and the patient was deceased.

DISCUSSION

Background

Hemodialysis patients exhibit gastrointestinal tract hemorrhage secondary to multiple causes. We cite the most common in decreasing order of frequency as gastritis (20%), peptic ulcer disease (20%), telangiectasias (20%), esophagitis, and duodenitis. Rarely does bleeding occur in the gallbladder, leading to hemorrhagic cholecystitis [1].

In concurrence, hemorrhagic cholecystitis is a rare subtype of acute cholecystitis with an incidence of 3.5% [2], morbidity of 32 to 58 %, and a mortality rate of 15-20% [3].

Consequently, a high index of suspicion is required for timely diagnosis.

Pathophysiology

The pathophysiology of rupture and bleeding of the gallbladder incorporates several mechanisms. This can include necrosis with an erosion of the cystic artery and its smaller branches [4], wall irritation by a stone, mucosal inflammation, and gangrene [5].

Subsequently, transmural wall inflammation causes infarction and mucosa erosion, leading to bleeding into the gallbladder lumen. Bleeding and obstruction of the cystic duct results in distension and ischemic necrosis of its wall. If untreated, perforation and massive intraperitoneal hemorrhage occur [6,7].

The most frequent perforation site is the gallbladder's fundus due to its poor vascular irrigation [5, 8]. Perforation of the gallbladder can be categorized into three types: [8]

1. Type I is an acute process with leakage of bile into the peritoneal cavity

2. Type II involves subacute symptoms that cause a gallbladder abscess

3. Type III: Chronic process with the formation of a cholecystoenteric or cholecystocutaneous fistula [8].

On that account, early diagnosis and treatment are crucial.

Etiology

The causes of hemorrhagic cholecystitis are numerous, the most common of which are lithiasis (50% of cases) and anticoagulation [9].

In concurrence, Tarazi et al., performed an extensive literature review between 1985 and 2018, throughout which they identified only 30 case reports of hemorrhagic cholecystitis. Of those 30 patients, 45% were on anticoagulation [10]. In comparison, Jessie et al., underwent another retrospective review over six years, from 2012 to 2018. They noted that lithiasis and anticoagulation/antiplatelet therapy were the most common etiologies in 82% of cases [9].

Other causes include obstructive cholecystitis, gallbladder or bile duct malignancy, abdominal trauma, iatrogenic injury such as liver biopsies, aneurysmal rupture into the gallbladder, ectopic gastric or pancreatic mucosa, biliary parasites, vasculitis, bleeding disorders such as hemophilia, and to a lesser extent portal hypertension [1,3,4,7,8,10].

Risk factors

In comparison, risk factors for hemorrhagic cholecystitis include anticoagulation or antiplatelet use, steroid use, anti-inflammatory use, old age, cirrhosis and renal failure (by platelet dysfunction), atherosclerosis (which makes the blood vessels more friable and prone to erosions), alcohol, gallbladder malpositioning and thin gallbladder wall [1,4,5,10].

Notably, in patients with end-stage renal disease, uremic platelet dysfunction increases the risk of gallbladder bleeding whether they exhibit cholecystitis or not [5]. Such is the case of our patient who had cholecystitis along with multiple risk factors, including renal failure, old age, and use of anticoagulants and steroids.

Complications

Complications encompass gallbladder rupture, hemoperitoneum, and even subcapsular and perihepatic hematomas [9].

Gallbladder perforation is most often a complication of acute gangrenous cholecystitis, with a prevalence of approximately 8-12% and associated mortality of 24.1%. Notably, predisposing factors that increase the risk of gallbladder perforation are old age, male gender, systemic disease, and the long-term use of steroids [9].

DIAGNOSIS

A diagnosis of hemorrhagic cholecystitis is difficult to make as it is rare, and the presentation can mimic other more common disorders such as cholecystitis [3]. Rarely a diagnosis of hemorrhagic cholecystitis is made before surgery because the blood may pass through the cystic duct and escape the gallbladder [4].

Patients may present with abdominal pain, nausea, and vomiting, manifestations of bile duct obstruction, hematemesis, anemia, and hemophilia. All of these may compromise the patient hemodynamically and become fatal. Some patients might even present with simple back pain. The latter is easily confused with other etiologies [3,4,7]. So vigilance is warranted.

Consequently, signs of hemorrhagic cholecystitis can be uncovered as right upper quadrant pain, a positive murphy's sign, fever, leukocytosis, hydrops of the gallbladder, and hemoperitoneum [3,7,10]. A case review of 11 cases done by Calvo Espino et al., in 2016 indicated that 82% presented with abdominal pain, 5% with nausea and vomiting, 27% with anemia and/or hypotension, 27% with intestinal bleeding, and 27% with fever [9]. Jaundice may even occur in case of biliary system obstruction by blood clots.

Further, the classical presentation of hemobilia is named Quincke's triad. This syndrome encompasses jaundice, right upper quadrant pain, and upper gastrointestinal bleeding and is only found in about 30% of patients [4].

Subsequently, upper gastrointestinal bleeding transpires whenever a significant quantity of blood courses through the ampulla of Vater. In consequence, this can lead to hematemesis or melena [4,9]. Multiple diagnostic techniques may be used in this setting.

Gastroduodenoscopy can be used as a means of diagnosis. Hemobilia can be seen in 50 % of the cases unless the cystic duct is obstructed. The source cannot be identified by endoscopy and might be mistaken if a concomitant gastroduodenal ulcer is present [4].

Endoscopic retrograde cholangiopancreatography (ERCP) may also identify blood clots (seen as filling defects) and bleeding from the ampulla of Vater. However, this is only seen in 30% of the cases [4,7].

Lastly, arteriography should also be considered whenever the diagnosis of hemorrhagic cholecystitis is suspected. It can detect the source of hemobilia at a rate of more than 0.5mL/min with an associated sensitivity of 90%. Further, it can be used simultaneously as a treatment option [4].

Differential diagnosis

The differential diagnosis of hemorrhagic cholecystitis consists of acute cholecystitis, intraluminal gallbladder mass, biliary sludge, or even thoracic aortic dissection [4]. This is further explained by the following.

Blood clots in hemorrhagic cholecystitis may obstruct the cystic duct and mimic acute calculous cholecystitis. Both syndromes have similar presentations and radiological findings. Hemobilia alone cannot differentiate between both diagnoses since it can also occur in acute calculous cholecystitis in 9% of the cases (gallstone-caused micro-bleeding). In contrast, the presence of Quincke's triad raises the possibility of hemorrhagic cholecystitis [4].

In comparison, the blood clots may agglomerate and form a mass. Doppler ultrasound identifies a solid lesion when present, which can be mistaken as an intraluminal gallbladder mass [4].

On the other hand, blood products can be mistaken for dense gallbladder content and therefore lead to a diagnosis of biliary sludge. In this case, MRI serves to differentiate between blood

and sludge [4].

And finally, hemorrhagic cholecystitis might present as back pain and be mistaken for thoracic aortic dissection [3].

Imaging

Radiological evidence of bleeding in the gallbladder on top of the typical findings of cholecystitis guides us towards diagnosing hemorrhagic cholecystitis [1].

The CT scan is the best radiological test to identify hemorrhagic cholecystitis, with a sensitivity of 69.2% versus 38.4% for the ultrasound [8,9]. In comparison, MRI is an option in patients with severe symptoms or serious complications-when US and CT findings are inconclusive or contraindicated as in pregnancy-for suspected choledocholithiasis [9].

Findings vary according to the modality and are described as follows.

In ultrasonography, the appearance of blood in the gallbladder has been described as similar to that of bile seen with pus or thick sludge. Blood clots within the gallbladder will appear as clumps of echogenic material. These can undergo rapid metamorphosis, progressing from an initial solid appearance to a mixed, and finally, cystic appearance as the clots lyse and liquefy [8,11].

Consequently, patients with hemorrhagic cholecystitis may demonstrate the following unusual sonographic features: focal gallbladder wall irregularity, intraluminal membranes or coarse, non-shadowing, nonmobile intraluminal echoes. These mentioned irregularities are the main distinguishing factors between acute and Hemorrhagic cholecystitis [12]. Of note, ultrasonography can reveal perivascular or hepatic subcapsular hematomas as signs of complications [9].

A CT scan may show perivesicular inflammatory changes with surrounding fat stranding and a distended gallbladder as typical signs of acute cholecystitis [9]. Notably, blood is usually seen with greater intensity than bile and gallstones [8]. Hematomas are seen as high-density fluid with active extravasation in the gallbladder lumen on the arterial phase of a contrast-enhanced CT scan [7]. This has been referred to as an angiographic "pseudo vein sign" or "pseudo-artery appearance" as the contrast material extravasates from a blood vessel into the cavity of an organ that contains clotted blood [6]. Furthermore, hemoperitoneum is free hyperattenuating fluid in the abdominal cavity and constitutes a sign of perforation [9].

To illustrate, as per the case series done by Calvo Espino et al., in 2016 on 11 patients, CT scan done on all patients revealed the most common findings to be in decreasing order of prevalence: perivesicular inflammatory changes in all patients (100%), dense gallbladder content due to hemobilia in 91%, hemoperitoneum in 55%, perihepatic hematoma in 27%, dense content in the bile duct or bowel in 27%, and active bleeding in 18% of the patients [9].

Finally, MRI is the best imaging test for differentiating between hemorrhage at the wall versus that at the lumen of the gallbladder. This is observed as a high signal intensity of methemoglobin on T1-weighted imaging (WI) [9]. MRI is also more sensitive for differentiating between blood and ascitic liquid [8].

For instance, blood clots and hemorrhage may be shown as defects or low-signal-intensity lesions on T2-WI, causing the lack of visualization of the gallbladder or bile ducts on MRCP or a low-signal-intensity area in the lower dependent layer of a fluid-fluid level. Note that this finding must be considered with caution because choledocholithiasis and locules of gas can appear as low-signal filling defects surrounded by high-signal bile at MRCP [9].

TREATMENT

Regardless of the cause, hemorrhagic cholecystitis is a medical emergency with a high morbidity and mortality rate, especially when complicated by gallbladder perforation and bleeding. The treatment of choice is urgent surgical intervention by either open or laparoscopic cholecystectomy and intravenous antibiotics [2,3,6,8,10].

In patients who are poor surgical candidates and without active bleeding, radiological decompression of the gallbladder by cholecystostomy and conservative treatment with intravenous antibiotics may be considered [2,3,6,9,10]. Arteriography might also be an alternative for bleeding control [4].

In case of obstruction in the biliary ducts, ductal decompression can be done by ERCP [4,9].

In our patient, we identified multiple risk factors for developing acute hemorrhagic cholecystitis. This includes the use of anticoagulation and steroids as well as old age, renal failure, and subsequent platelet dysfunction.

A high index of suspicion was maintained, and proper imaging was done. As the patient was stable at the time of definitive diagnosis, we elected to perform surgical excision of the gallbladder while giving IV antibiotics. However, she regrettably passed away due to the patient's multiple comorbidities and the fatality of this condition.

CONCLUSION

In summary, hemorrhagic cholecystitis is a rare disease with high morbidity and mortality. Physicians should maintain a high index of suspicion, especially in patients with predisposing risk factors. This is critical for prompt management and circumvention of fatal complications.

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