Case Report

COVID-19 associated spontaneous hemorrhagic cholecystitis✩✩

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ABSTRACT

Hemorrhagic cholecystitis is a rare disorder associated with considerable morbidity and mortality. The clinical presentation of hemorrhagic cholecystitis is non-specific and imaging findings can be difficult to accurately interpret without a high level of suspicion. Most recent reports of hemorrhagic cholecystitis have been associated with concurrent therapeutic anticoagulation. Here, we report imaging findings of a case of acute, spontaneous hemorrhagic cholecystitis in a 67-year-old male patient admitted for hypoxic respiratory failure secondary to COVID-19 pneumonia.

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Introduction

Hemorrhagic cholecystitis (HC) is a rare condition associated with considerable morbidity and mortality [1]. Most reports describe HC as a complication of acute calculus cholecystitis often in the setting of therapeutic anticoagulation [2–5]. The purported mechanism is prolonged transmural gallbladder wall inflammation causing mucosal ischemia leading to an increased risk of intraluminal hemorrhage [4]. Establishing the diagnosis can be challenging as patients often present with non-specific symptoms that overlap with acute calculous and acalculous cholecystitis. Although laboratory findings can help narrow the list of differential considerations, imaging plays an important role in establishing the diagnosis [6]. According to the American College of Radiology Appropriateness Criteria, an abdominal ultrasound is considered usually appropriate as the best first imaging approach to right upper quadrant pain for suspected biliary pathology [7]. However, ultrasound findings of HC are non-specific. Given the widespread availability of computed tomography (CT) and its rapid image acquisition time, some authors argue CT represents the best modality for cases of suspected HC [5]. CT findings of HC include a distended gallbladder, wall thickening, and hyperattenuating bile with or without contrast extravasation on enhanced multiphase acquisitions [5].

The coronavirus disease-19 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)
2) continues to be a global public health threat [8]. In addition to potentially life threatening pneumonia, severe COVID-19 infection is associated with an increased risk of venous thromboembolism secondary to a hypercoagulable state [9]. Although the mechanisms underlying the increased risk of thrombosis are complex and incompletely understood, disruption of the vascular endothelium is believed to be a driving factor in the pathogenesis [10]. Here, we describe a case of spontaneous HC in a patient with COVID-19 infection on prophylactic anticoagulation.

Case report

A 67 year-old, former tobacco-smoking male with a history of hepatitis C virus, moderate emphysema, hypertension, coronary artery disease and ischemic cardiomyopathy 3 years status post orthotopic heart transplant presented to the hospital with progressive shortness of breath found to be nucleic acid test positive for SARS-CoV-2. Review of his vaccination records revealed he was fully vaccinated (Pfizer-BioNTech) but not boosted. The patient was admitted to the intensive care unit (ICU) for management of hypoxic respiratory failure secondary to COVID-19 pneumonia (Figs. 1A and B) and initially treated with high flow nasal canula before requiring intubation on hospital day 6. Not long after extubation on hospital day 15, the patient developed acute onset right upper quadrant pain, tachycardia, and hypotension. Laboratory workup revealed an acute rise in liver function tests (aspartate aminotransferase 2144 U/L [10-40 U/L], alanine aminotransferase 1705 U/L [110-55 U/L], alkaline phosphatase 351 U/L [45-115 U/L], and total bilirubin 4.4 mg/dL [0-1.0 mg/dL]) and a new leukocytosis (white blood cell count 20.3 K/µL [4.5-11.0 K/µL]) without a significant change in hematocrit. Prothrombin time and partial thromboplastin time were normal.

A right upper quadrant ultrasound revealed new gallbladder distention with layering luminal debris (Fig. 2). A CT of the chest, abdomen, and pelvis subsequently redemonstrated a distended gallbladder as well as hyperattenuating layering material with active contrast extravasation on portal venous images (Fig. 3). Coincident, on the patient’s chest images were new left upper lobe subsegmental pulmonary emboli (Figs. 1C and D). Given the patient’s critically ill state, the decision was made to manage the patient’s HC with a percutaneous cholecystostomy tube and antibiotics. At the time of cholecystostomy catheter placement, sanguineous fluid was aspirated. Chart review of the medication administration record for antplatelet/anticoagulant agents revealed the patient was treated with prophylactic level subcutaneous heparin (5000 units every 12 hours) and oral aspirin (81 mg daily). Following cholecystostomy catheter placement the patient clinically improved; the catheter was removed approximately 5 weeks post-placement.

Discussion

Hemorrhagic cholecystitis (HC) is the term used to describe the disorder of intraluminal hemorrhage into an inflamed gallbladder and is considered a rare complication of acute cholecystitis, most often associated with therapeutic anticoagulation [2-5]. Prior authors have proposed a mechanism whereby prolonged transmural gallbladder wall inflammation causes mucosal ischemia leading to the observed intraluminal hemorrhage [4]. Other less common causes, some of which may precede acute cholecystitis and not ascribe to the aforementioned pathophysiology, have been reported including cystic artery pseudoaneurysm rupture [11], hemorrhage associated with inherited and acquired coagulation disorders [12], blunt trauma [6], iatrogenic injury [13], malignancy related [14], and idiopathic [6]. Here we describe a case of HC in a patient with COVID-19 not on therapeutic anticoagulation.

To our knowledge, one other report has described a similar clinical scenario in a COVID-19 patient with HC suggesting a common underlying pathophysiology [15]. Given the increased risk of thromboembolic phenomena in severe COVID-19 patients, it stands to reason the predisposing event may be gallbladder wall ischemia secondary to thromboemboli. This is supported by the coincident diagnosis of subsegmental pulmonary emboli in our patient.

Early and accurate diagnosis of HC is critical to improving patient outcomes. The clinical diagnosis of HC can be challenging as patients present with non-specific symptoms including abdominal pain, fever, nausea, vomiting, hematemesis, and melena. Laboratory findings can be helpful in narrowing the differential, as patients may demonstrate elevated transaminase levels, hyperbilirubinemia, leukocytosis, and an acute anemia [6]. Although abnormal liver function testing and leukocytosis may be seen with acute cholecystitis with or without choledocholithiasis. Unfortunately, there are no specific laboratory tests for HC, underscoring the importance of incorporating imaging to identify the diagnosis. Imaging findings of HC are variable. Grayscale ultrasound findings may show a distended gallbladder with thickened walls with hyperechoic intraluminal material, mimicking sludge. We agree that multiphasic contrast enhanced CT of the abdomen is more useful given its widespread availability and fast acquisition. CT findings include a distended gallbladder, wall thickening, and hyperattenuating bile. Arterial and/or delayed images may show contrast in the gallbladder lumen if there is extravasation, as was shown here. It should be noted hyperattenuating bile is not specific for HC and can represent sludge, milk of calcium, or viscerous excretion of contrast material. Should blood products in the gallbladder lumen extend into the cystic and common bile ducts (hemobilia), biliary ductal dilatation may be observed. Hyperattenuating material (blood products) may also be seen in the gastrointestinal tract explaining episodes of hematemesis and melena in select patients [1,5,16]. Optimal first line management in clinically stable patients is cholecystectomy [6]. However, in critically ill patients or in cases deemed non-surgical, percutaneous cholecystostomy may be performed [17,18].

In summary, HC is a rare disorder with various causes and a high level of suspicion is necessary to arrive at the diagnosis in a timely manner. Vascular disruption associated with severe COVID-19 may represent another predisposing factor for HC, expanding the diversity of pathologies observed with this pervasive societal malady.
Fig. 1 – Contrast enhanced computed tomography images of the chest. (A and B) Axial and coronal projection images in lung windows demonstrating bilateral mosaic attenuation with peripheral predominant ground-glass opacities in the background of upper lobe predominant centrilobular and paraseptal emphysema. (C and D) Axial images in pulmonary angiogram windows demonstrating hypoattenuating filling defects in the subsegmental pulmonary arteries of the left upper lobe (arrows).

Fig. 2 – Right upper quadrant ultrasound. (A) Grayscale image demonstrating a distended gallbladder with layering echogenic intraluminal material (arrow). (B) Color Doppler image without evidence of abnormal flow within the gallbladder lumen.
Fig. 3 – Contrast enhanced axial projection computed tomography images of the upper abdomen. (A) Distended gallbladder with layering hyperattenuating luminal debris (white arrow). (B) Portal venous image demonstrating contrast material extravasation (black arrow) into the gallbladder lumen. (C) Inflammatory fat stranding near the gallbladder fundus (dashed white arrow). (D) Appearance of the gallbladder (GB) 1 year prior.

**Patient consent**

Informed consent for publication of the described clinical history was obtained.

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