CASE REPORT

Haemorrhagic cholecystitis in a newly anticoagulated patient

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Accepted 19 March 2017

SUMMARY

A 74-year-old man undergoing rehabilitation after pneumonia developed right upper quadrant abdominal pain. Five days earlier he had been commenced on apixaban for a new diagnosis of atrial fibrillation. Ultrasound and CT scans revealed an acalculous grossly thickened gallbladder, with high attenuation non-echogenic material both within and surrounding the structure. Active contrast extravasation was seen at the neck. On laparotomy, a perforated internally bleeding gallbladder containing a single calculus was found, with significant free blood within the abdomen. After cholecystectomy, the patient recovered slowly in hospital before nursing home placement.

BACKGROUND

Haemorrhagic cholecystitis is rare but carries significant morbidity and mortality. It encompasses both bleeding into the gallbladder lumen as the primary chemical irritant and as a secondary complication of acute cholecystitis. We present the case of a patient who developed this condition shortly after commencing anticoagulation.

CASE PRESENTATION

A 74-year-old man, previously living independently alone, was undergoing rehabilitation in a low acuity hospital following a seizure and subsequent bilateral hospital acquired pneumonia, when he became drowsy, complaining of right-sided abdominal pain. He was afebrile, saturating 95% on 2L/min supplemental oxygen, with blood pressure 135/90, and heart rate 130/min shown on ECG to be atrial fibrillation. On examination, he had a rigid abdomen, with diffuse tenderness worst in the right upper quadrant.

Figure 1 CT abdomen, non-contrast, coronal slice through gallbladder neck, showing high attenuation, suggestive of fresh clot.

The patient had a past history of a laparotomy two decades earlier for adhesional small bowel obstruction, hiatus hernia, temporal lobe epilepsy, hyperparathyroidism, hypertension, hypercholesterolaemia and lower limb spasticity.

Four days earlier, the patient had been commenced on apixaban 5 mg twice daily for a new diagnosis of atrial fibrillation. His other medications consisted of twice daily metoprolol 50 mg and sodium valproate 200 mg, and daily pantoprazole 40 mg, trandolapril 4 mg, amlodipine 5 mg, cholecalciferol 25 µg and rosuvastatin 5 mg.

Blood tests revealed a white cell count of $43.5 \times 10^9/L$ and haemoglobin falling from 165 g/L to 131 g/L over 18 hours. He was transferred to our tertiary referral hospital for further management.

INVESTIGATIONS

Ultrasound revealed a probe-tender grossly thickened 11 mm gallbladder wall, containing non-vascularised, heterogeneous material, thought to be biliary sludge and no calculi. There was neither intrahepatic nor extrahepatic duct dilatation.

A triple phase CT scan of the abdomen and pelvis confirmed the thick walled gallbladder and surrounding inflammatory change. Perihepatic high attenuation free fluid was perceived as inflammatory in nature. High attenuation material was seen in the gallbladder, thought to represent fresh blood and thrombus, and active contrast extravasation within the gallbladder neck on postcontrast images suggested ongoing bleeding (figures 1 and 2). No cholelithiasis was seen on plain or contrast imaging. Bilateral basal pulmonary atelectasis and pleural effusions were also present.

DIFFERENTIAL DIAGNOSIS

Preoperatively, the working diagnosis was haemorrhagic cholecystitis without perforation, with the surrounding free fluid thought inflammatory in nature. Calculous cholecystitis with secondary haemorrhage was considered less likely in the absence of radiological evidence of cholelithiasis.

TREATMENT

The patient was given 3000 units of prothrombinex, and proceeded to open cholecystectomy. He was found to have significant blood within the abdomen from a bleeding point within the gallbladder neck, where a single 6 mm calculus was also found. The gallbladder was densely adherent to the omentum, duodenum and stomach, although

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To cite: Kinnear N, Hennessey DB, Thomas R. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2016-214617

Figure 2 CT abdomen, venous phase post contrast, same coronal slice, showing new contrast trail inferiorly then laterally towards the gallbladder fundus, suggestive of active intra-luminal bleeding.

it had a largely unobstructed anterior surface. It had perforated from fundus to neck, with a large ovoid 300 mL thrombus protruding. No bile or pus were seen.

Evacuation of the thrombus revealed active bleeding from the gallbladder mucosa at multiple sites. Haemostasis was achieved with diathermy. Despite multiple attempts, a satisfactory cholangiogram could not be obtained, with contrast flow seen only into hepatic ducts and not distally into the common bile duct. The gallbladder was transected above the neck, and closed with absorbable suture. After lavage, two size 19 French Blake drains were placed. The procedure was an emergency performed after hours and no intraoperative photographs were taken.

Gallbladder specimen histology revealed transmural necrosis and haemorrhage, consistent with gangrenous cholecystitis. Most of the epithelium was ulcerated. The remnant epithelium

showed reactive changes, but there was no evidence of dysplasia or malignancy. Analysis of the single calculi revealed mixed composition.

OUTCOME AND FOLLOW-UP

After 24 hours in the intensive care unit, the patient recovered slowly, complicated by ongoing hospital acquired pneumonia with parapneumonic pleural effusions.

The failure of imaging to detect the calculus preoperatively was reviewed in departmental X-ray meeting with a consultant radiologist. It was concluded that the heterogenous intraluminal thrombi may have rendered ultrasound visualisation more difficult, and that the minimally radiolucent nature of the mixed composition stone may explain its non-detection on CT.

The patient received undergoing rehabilitation and physiotherapy on the ward. His successive hospital admissions had led to deconditioning and 8 weeks postprocedure the patient was transferred to a nursing home. On routine outpatient review, he remains alive and well 1 year later, with no complications.

DISCUSSION

Haemorrhagic cholecystitis is rare, with the literature limited to small series¹ and less than 30 English language case reports. It may be due to haemorrhage into an acalculous gallbladder as the primary cause of cholecystitis via chemical irritation. Alternatively, transmural infarction and erosion of the gallbladder wall in established acute cholecystitis, usually gangrenous, may cause bleeding secondarily.² Haemorrhagic cholecystitis has many possible causes, including trauma, neoplasms, aneurysmal rupture, portal hypertension, coagulopathy or anticoagulation therapy.³ It is possible that the documented proliferating prescription of these agents may increase the incidence of this entity in the future.⁴

Diagnosis remains difficult, as the typical presentation of right upper quadrant pain, fever, positive Murphy's sign and raised white cell count commonly leads to misdiagnosis as other biliary conditions calculous cholecystitis or cholangitis.

Imaging therefore is crucial to the diagnosis. Ultrasound may show thrombi as non-shadowing immobile intraluminal lesions, in addition to the usual wall thickening, pericholecystic fluids and sonographic Murphy's sign associated with cholecystitis. However, as this case illustrates, sonographic diagnosis remains challenging, with one retrospective study of confirmed haemorrhagic cholecystitis showing features suggestive of this diagnosis in only 74% of patients.¹ CT imaging may be enlightening, potentially revealing a fluid filled thickened gallbladder with internal active arterial bleeding.²

Initial management focuses on resuscitation of the patient, including reversal of any iatrogenic or pathological coagulopathy, with subsequent surgery the treatment of choice. If haemorrhage is contained within the gallbladder or the patient is not fit for theatre, they may benefit from cholecystostomy via interventional radiology. A single case report has documented the successful use in haemorrhagic cholecystitis of urokinase via cholecystostomy tube to lyse blood clots causing obstructive jaundice.⁵ Complications include hypovolaemic shock, perforation, recurrent haemorrhage or death.

Surgeons are increasingly faced with anticoagulated patients who require emergency procedures. Perioperative anticoagulation is becoming more complex with the advent of novel oral anticoagulant medications. Common antiplatelet and anticoagulant medications are summarised in table 1, along with details regarding preoperative cessation periods and antidotes.⁶

Table 1 A concise summary of perioperative anticoagulation

	Withhold pre-op	Antidote	Antidote reversal time
Antiplatelets			
GP IIb/ IIIa inhibitors <i>abciximab, tirofiban</i>	2 days	For all antiplatelets Desmopressin Platelet transfusion	<30 mins <30 mins
P2Y ₁₂ antagonists <i>clopidogrel, prasugrel, ticagrelor</i>	5 days		
Other <i>Aspirin, dipyridamole</i>	7–10 days		
Anticoagulation			
Heparin <i>heparin</i>	4 hours	Protamine	Immediate
<i>enoxaparin, dalteparin</i>	12–24 hours	Protamine*	Immediate
Direct thrombin inhibitors <i>dabigatran</i>	24 hours	Idarucizumab Tranexamic acid Factor VII Dialysis	Immediate Unknown Unknown Unknown
Factor Xa inhibitors <i>apixaban, rivaroxaban, fondaparinux</i>	2 days	Prothrombinex*	Unknown
Other <i>warfarin</i>	5 days	Vitamin K Prothrombinex Fresh frozen plasma	>12 hours Immediate <30 mins

*Reversal effect is partial or uncertain.

Pre-op, preoperatively; GP, glycoprotein.

Patient's perspective

(Taken 6 weeks postoperatively, while still an inpatient)

'The doctors had detected the abnormal heart rhythm a few days before, and started me on a blood thinning medication. I was alright for a few days, then I had lots of pain in my stomach on the right. I was sent here (Lyell McEwin Hospital) and they took my gallbladder out. The pain went away after that. I've still been coughing a lot, and I'm quite weak, too weak to go home. I hear I'm headed to a nice nursing home.'

Learning points

- ▶ Haemorrhagic cholecystitis is a rare but serious differential to uncomplicated calculous cholecystitis and cholangitis, particularly in the anticoagulated patient.
- ▶ Diagnostic imaging and prompt surgery are crucial to its correct diagnosis and management.
- ▶ Rising novel oral anticoagulant use may increase its incidence.

Contributors NK provided the initial concept and manuscript drafting. DBH and RT were responsible for manuscript review.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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