Rare disease

Spontaneous haemorrhagic perforation of gallbladder in acute cholecystitis as a complication of antiplatelet, immunosuppressant and corticosteroid therapy

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Summary

An older lady presented 1 week after being discharged from hospital with acute cholecystitis. She suffered a sudden onset lower abdominal pain and was in hypovolaemic shock upon arrival. It was noted that she had been on antiplatelet therapy after suffering a recent myocardial infarction, an immunosuppressor and steroids for rheumatoid arthritis. Her admission bloods revealed a platelet count of 83 with normal clotting factors. After resuscitation, a CT scan confirmed fluid in the abdomen possibly arising from the right subhepatic space. During laparotomy, bleeding was noted from a perforated and ischaemic-looking gallbladder, with an intact cystic artery and duct and no biliary calculi evident. The gallbladder was removed and the patient was transferred to intensive therapy unit. She recovered well within the subsequent 8 days and was discharged. Her histology described 'haemorrhage within the gallbladder wall along with oedema, fibrosis and patchy inflammation and no signs of malignancy or gangrene'.

BACKGROUND

Haemorrhagic perforation of the gallbladder is an extremely rare but serious complication of acute cholecystitis.¹ There are roughly 16 reported cases of these in the literature and its incidence is reported to be higher with concomitant anticoagulation therapy.² In this article, we describe a case of a spontaneous haemorrhagic perforation of the gallbladder in a patient with acute cholecystitis most likely related to a combination of antiplatelet, methotrexate and prednisolone therapy, which to the best of our knowledge, has not been reported.

CASE PRESENTATION

A 74-year-old lady presented to the emergency department 6 h after the onset of sudden lower abdominal pain that woke her from sleep. This was associated with four episodes of brown, frothy vomiting and non-haemorrhagic diarrhoea. She had been to hospital a week previously under the surgical team with acute cholecystitis where an ultrasound demonstrated five calculi within a thin-walled gallbladder. She was discharged home after 2 days of intravenous antibiotic therapy to complete the remaining 5 days of the course orally. Her other relevant medical history included a recent myocardial infarction 2 months before, for which she underwent a triple coronary artery bypass and was started on a daily dose of 75 mg aspirin. In addition, she has been suffering from rheumatoid arthritis over the last 19 years for which she was placed on a maintenance dose of 5 mg prednisolone daily (increased to 20 mg during periods of active synovitis). Subsequently, a once weekly dose of 15 mg methotrexate was added 9 years ago.

At the time of admission, she was noted to be in hypovolaemic shock with a blood pressure of 68/40, heart rate of 92 and respiratory rate of 22. She appeared pale with cool

peripheries and a slightly prolonged capillary refill time of 2.5 s. Abdominal examination revealed a mildly distended and tender abdomen particularly on the right side with guarding and positive rebound tenderness. Bowel sounds were absent and digital rectal examination was unremarkable.

INVESTIGATIONS

Baseline investigations revealed a haemoglobin of 8.9 g/dl, white cell count of 15.8×10^9 , platelet count of 83×10^9 , C reactive protein of 7.9 and deranged liver function tests (bilirubin 38 $\mu\text{mol/l}$, total protein 37 g/l, alkaline phosphatase 132 IU/l, alanine transaminase 124 IU/l). Clotting profile and renal function tests were normal. Her blood gases showed a picture of respiratory alkalosis with a metabolic component while her urinalysis, erect chest and supine abdominal plain radiographs were normal.

Figure 1 CT abdomen/pelvis showing fluid in the right paracolic gutter (blue arrow) and subhepatic space (green arrow).

Figure 2 Gallbladder of the patient after removal. Perforation demonstrated by arrow.

DIFFERENTIAL DIAGNOSIS

After her initial fluid resuscitation, an urgent CT scan of her abdomen and pelvis was performed which demonstrated moderate free fluid in the abdomen and a large haematoma in the right paracolic gutter measuring 20×5×6 cm probably arising from the right subhepatic space (figure 1). The point of bleeding was postulated to be either from the hepatic arteries, portal vein or cystic arteries. She failed to respond to further resuscitation, showing evidence of ongoing bleeding and hence underwent an emergency surgery.

TREATMENT

A midline laparotomy was performed and 2 litres of fresh blood and clots were evacuated from the right paracolic and subhepatic space. The point of bleeding was noted from the mucosa of a perforated ischaemic-looking gallbladder (figure 2). The cystic artery, cystic duct and hepatic vessels were intact. A cholecystectomy was performed and she was subsequently transferred to the intensive therapy unit (ITU). She had received six units of packed red cells, three units of fresh frozen plasma and 2 L of colloids.

OUTCOME AND FOLLOW-UP

The patient was extubated on the 1st postoperative day and transferred to high dependency unit on day 2. She was switched from nasogastric feeds to soft diet by day 5 and continued to recover well. Her liver function tests were noted to be persistently elevated (table 1), however, an inpatient magnetic resonance cholangiopancreatography showed a normal biliary tree and the blood picture normalised over the next few days. She was discharged 8 days after her surgery with an outpatient appointment in 6 weeks. Histology described 'haemorrhage within the gallbladder wall along with oedema, fibrosis and patchy inflammation and no signs of malignancy or gangrene'.

DISCUSSION

Haemorrhagic perforation of the gallbladder occurs in 2%–11% of cases of acute cholecystitis.³ It has a reported mortality of 60% or higher if gangrenous and is postulated

Table 1 Progression of liver function tests postoperatively

Liver function tests	Day 3 (Postop)	Day 4 (Postop)	Day 5 (Postop)
Bilirubin (μmol/l)	18	16	23
Total protein (g/l)	45	52	59
Alkaline phosphatase (IU/L)	161	157	150
Alanine transaminase (IU/L)	80	65	62

to be the result of transmural inflammation leading to necrosis and eventually perforation. This is classified into three types; Type 1 – an acute event with free spillage of gallbladder content into abdominal cavity, Type 2 – a subacute process where the contents of the perforation is contained within an adjacent abscess and Type 3 – a chronic process involving the formation of a cholecystoenteric fistula.¹

Diagnosis is dependent on a combination of clinical picture, high index of suspicion and imaging. Detection on imaging such as CT scans or MRI can be difficult in small perforations and the findings are usually non-specific that is, pericholecystic fluid/abscess and collapse of the gallbladder lumen. A more suggestive sign would be the presence of extraluminal gallstones, which was not seen in our case.¹

In the event of a perforation, the treatment of choice is urgent surgical intervention (either laparotomy or laparoscopy) in combination with intravenous antibiotics. Patients who are unlikely to survive this may be more amenable to percutaneous catheter drainage.^{1 3}

Aspirin exerts its antiplatelet effects by inhibiting the synthesis of the prostaglandin thromboxane whose function includes the activation of new platelets as well an increase in platelet aggregation.⁴ Its use with the antifolate agent methotrexate is cautioned due to the latter's ability to cause bone marrow suppression and gastrointestinal bleeding.⁵ The concurrent use of these drugs in the patient may have resulted in her low platelet count which is known to predispose an individual to bleeding.

Long-term use of prednisolone as in the patient's case may have impaired her healing process that would have contributed to her unresolving and progressing acute cholecystitis.⁵ Steroids are also known to result in mucosal damage⁵ and could have contributed to small vessel fragility and thinning of the gallbladder wall. The combination of these factors along with her age certainly increased the likelihood of a haemorrhagic perforation. Her remarkably rapid recovery in view of her co-morbidities is probably attributed to prompt surgical intervention and ITU-led postsurgical care.

Cases of spontaneous haemorrhagic perforation of the gallbladder have been reported in the literature since 1960. Raycroft *et al* mentions a series of cases where the presentations were similar to a ruptured spleen or aneurysm and advocated early surgery similar to appendicitis.⁶ More recently, Pandya *et al*² and Mikou *et al*⁷ reported cases in patients who were on anticoagulant therapy. Additionally, Kim *et al* describes a haemorrhagic perforated gallbladder in 2007 where the presence of extraluminal gallstones was used to make a radiological diagnosis.⁸

Learning points

- ▶ Regular use of antiplatelet agents along with immunosuppressors and steroids may increase the possibility of haemorrhagic perforation in acute cholecystitis, a life-threatening complication.
- ▶ Surgeons should be mindful of this fact and consider early cholecystectomy.
- ▶ If it occurs, the treatment of choice is an emergency surgery and cholecystectomy along with ITU-led postsurgical care.

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Competing interests None.

Patient consent Obtained.

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