CASE REPORT

Spontaneous acalculous gallbladder perforation post-cardiac transplantation

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SUMMARY
Spontaneous acalculous gallbladder perforation is a rare radiological and clinical phenomenon with life-threatening consequences. In the setting of recent cardiac transplantation, the condition is increasingly uncommon and difficult to diagnose preoperatively. We describe a case of spontaneous acalculous gallbladder perforation in an intensive care unit (ICU) patient, most likely due to a combination of cardiac transplantation and immunosuppression. There are no such documented cases in the literature with an established preoperative diagnosis, to the best of our knowledge. Abdominal CT and targeted ultrasound proved complimentary in establishing the diagnosis, facilitating successful and timely treatment with urgent cholecystectomy.

BACKGROUND
Spontaneous acalculous gallbladder perforation is a rare but catastrophic phenomenon in critically ill and immunosuppressed patients. Mortality associated with gallbladder perforation is often confounded by delayed diagnosis. Radiology plays a key role in identifying this condition and facilitates timely surgical intervention.

CASE PRESENTATION
A 45-year-old man underwent cardiac transplantation in 2016 for ischaemic cardiomyopathy at a tertiary hospital specialising in cardiothoracic medicine in Brisbane, Australia. Relevant medical history included atrial fibrillation/flutter, hypertension, dyslipidaemia and depression.

A routine cardiac biopsy on day 14 after transplantation had revealed mild rejection while on a standard immunosuppression regimen of tacrolimus, mycophenolate mofetil and prednisolone. Immunosuppressive doses were accordingly adjusted. On day 35, worsening rejection was clinically suspected due to the development of first-degree and second-degree heart block, necessitating treatment with isoprenaline. An empirical pulse treatment with methylprednisolone 1000 mg daily for three doses was also given, and the daily prednisolone dose was increased from 30 mg to 80 mg daily. Tacrolimus was continued at 3 mg twice a day and mycophenolate mofetil at 1500 mg twice a day.

The patient’s postoperative ICU course was timely surgical intervention.

At day 40 post-transplant, while on the aforementioned immunosuppressive regimen, the patient was investigated for severe upper abdominal pain while weaning from mechanical ventilation in ICU.

INVESTIGATIONS
The patient’s haemoglobin had reduced from 101 g/L to 88 g/L. White cell count was elevated to $31 \times 10^9$/L, and platelets reduced to $95 \times 10^9$/L. Bilirubin was elevated to 41 µmol/L, with a markedly raised gamma-GT of 1090 U/L, alkaline phosphatase of 512 U/L and moderately raised transaminases.

Non-contrast CT abdomen (in light of AKI) demonstrated hypertensive haemobilia (~75 HU) within the gallbladder lumen and haemoperitoneum within the right paracolic gutter and pelvis. The fundal gallbladder wall could not be discerned (figure 1A–D). Subsequently, abdominal ultrasound confirmed the presence of contiguous haematoma within the gallbladder lumen into the peritoneum, across a defect within the gallbladder fundus (figure 2A–D).

TREATMENT
Within hours of the investigations, the patient underwent emergency laparoscopic cholecystectomy and abdominal washout. At surgery, the gallbladder was found to be necrotic and perforated, with moderate-volume haemoperitoneum (figure 3A, B).

OUTCOME AND FOLLOW-UP
Towards completion of the surgery, the patient became bradycardic with eventual loss of cardiac output. Resuscitation was successful with chest compressions and an epinephrine infusion. Follow-up ultrasound after 9 days demonstrated no collection or biliary obstruction.

A protracted recovery in intensive care ensued, complicated by an episode of cardiac arrest requiring automated implantable cardioverter-defibrillator (AICD) insertion, fungal infective endocarditis, post-transplant lymphoproliferative disorder and pulmonary embolism. The patient was discharged from ICU after 75 days to inpatient rehabilitation, but required readmission to ICU and the cardiology ward for episodes of sepsis and hypotension. AKI had resolved during admission.

He returned home following physical rehabilitation at 8 months post-transplant, and at the time of this report, the patient continues to live in the community with an ongoing antirejection regimen of...
everolimus, tacrolimus and prednisolone. The patient is receiving ongoing physiotherapy and occupational therapy in the community, for consideration of lower limb prostheses. No long-term sequelae of gallbladder perforation have been encountered.

**DISCUSSION**

In critically ill patients with ICU admissions over 2 days, the documented incidence of acalculous cholecystitis (ACC) is 0.2%–0.4%. Immunosuppression and prolonged ICU treatment have been associated with the development of ACC. The patient’s clinical course, imaging and laboratory data are consistent with this diagnosis.

**Figure 1** (A–D) Non-contrast helical CT abdomen in a 45-year-old male patient with abdominal pain, day 40 post-cardiac transplantation.

**Figure 2** (A–D) Targeted upper abdominal ultrasound demonstrating contiguous haemobilia and haemoperitoneum, across a defect within the gallbladder fundus (arrows).
stay further increases the risk and, if untreated, may lead to perforation and fatal outcomes. The mortality rate of ACC is commonly documented at 30%, with a range of 10% with early diagnosis, to 90% with delayed diagnosis. Furthermore, the risk of morbidity and mortality in cardiac transplant patients with acute cholecystitis (calculous and acalculous) has been shown to be elevated, predominantly in the immediate postoperative period.

Likewise, gallbladder perforation is associated with significant morbidity and mortality, with a median mortality rate of 10% from a previous systematic review. Its incidence ranges from 0.8% to 11%. More commonly, gallbladder perforation is seen in the setting of complicated calculous cholecystitis. Spontaneous acalculous perforation, on the other hand, is rare.

Cases of gallbladder perforation have been previously documented in the context of steroid therapy, peritoneal dialysis and diabetic or elderly patients. We report a case of spontaneous Niemeier type perforation in a patient 40 days post-cardiac transplantation. Pancreaticobiliary disease has been reported to occur 17.4 times more frequently in cardiac transplant recipients than the general population. Factors likely contributing to perforation in this patient were (1) surgical vagotomy at the time of transplantation, leading to gallbladder dysmotility and stasis; (2) gallbladder ischaemia due to ischaemic cardiomyopathy, during transplantation, and in the post-transplant period during episodes of rejection; (3) immunosuppression during steroid administration; and (4) prolonged ICU stay complicated by sepsis, AKI and peripheral limb ischaemia requiring below-knee amputation.

In the context of immunosuppression, mechanical ventilation and sedation, the classical signs of ACC—fever, positive Murphy’s sign, right hypochondriac tenderness and guarding—were masked in this patient. The non-specific pattern of hepatic enzyme derangement was likely attributed to the combination of cholestatic disease and polypharmacy, reducing their value in the diagnostic process. Submitting a cardiac transplant patient with multiple comorbidities to abdominal surgery without prior radiology work-up to exclude non-surgical causes was not considered as an option by the surgical team. For this reason, non-contrast CT was implemented as the first-line modality to identify a likely source of sepsis and exclude non-surgical causes of abdominal pain prior to further targeted investigation and exploratory surgery.

Abdominal CT demonstrated hyperdense haemobilia (75HU) within the gallbladder lumen, and contiguous hyperdense haematoma in the right paracolic gutter, with low-density fluid within the pelvis. This sentinel clot sign within and adjacent to the gallbladder raised suspicion of gallbladder perforation. Other diagnostic considerations were synchronous haemobilia and haemoperitoneum, secondary to coagulopathy or underlying vascular rupture. No radiodense calcified gallstone was demonstrated.

Targeted upper abdominal ultrasound was organised immediately following the CT scan. This proved pivotal in confirming the diagnosis of acalculous gallbladder perforation, with demonstration of the gallbladder wall defect and traversing haematoma on high-resolution cine view, and longitudinal and transverse images.

Diagnostic imaging provided a roadmap for aiding the surgical team in the decision to pursue operative management in an immunosuppressed, post-cardiac transplant patient, despite the inconclusive clinical picture. Surgical findings concurred with the radiological diagnosis, and the patient was managed successfully with emergency cholecystectomy.

ACC remains a condition commonly dealt with by abdominal surgeons. Where the clinical diagnosis of ACC is clear-cut, ultrasound may be sufficient for confirmation in haemodynamically stable patients. However, cardiac transplantation and its mandated immunosuppression made the diagnosis of this easily identifiable condition difficult due to the absence of characteristic clinical signs and inconclusive biochemical tests. Radiology provided a crucial role in identifying the development of gallbladder perforation, thus avoiding a fatal outcome in this patient.

**Learning points**

- Spontaneous acalculous gallbladder perforation is a rare but catastrophic complication of acalculous cholecystitis (ACC) in critically ill and immunosuppressed post-transplant patients. Mortality associated with gallbladder perforation is often confounded by delayed diagnosis, as characteristic clinical features of ACC may be masked.
- Abdominal CT and ultrasound are complimentary in identifying spontaneous perforation, resolving diagnostic dilemma and facilitating timely life-saving intervention.
- On abdominal CT, the presence of hyperdense clotted haemorrhage on either side of the gallbladder (sentinel clot sign) is highly suspicious for gallbladder perforation in the acute abdomen.
- Targeted abdominal ultrasound may be used for detailed visualisation of the gallbladder wall defect, as well as confirming the presence of haemobilia or haemoperitoneum.
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