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CASE REPORT

Rare but fatal if missed – intraoperative Takotsubo syndrome in adult liver transplantation: lessons for anaesthesia and intensive care clinicians

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Takotsubo syndrome is an important and often overlooked cause of reversible non-ischaemic perioperative cardiac decompensation. We report a case of intraoperative Takotsubo syndrome in an adult liver transplant recipient that occurred approximately 45 minutes after reperfusion of the implanted liver graft. In addition to multi-organ dysfunction requiring intensive life support, the recipient required venoarterial extracorporeal membrane oxygenation. Despite a prolonged hospital stay, three-month follow-up confirmed complete recovery of cardiac function. This case highlights the need for increased awareness of this condition and the need to facilitate appropriate care and referral pathways should perioperative Takotsubo syndrome occur.

Keywords: Takotsubo syndrome, liver transplant, perioperative cardiac decompensation, extracorporeal membrane oxygenation

Case report

A 55-year-old recipient underwent a deceased donor ABO-compatible whole liver transplant. The patient was known to the Wits Transplant Unit having been waitlisted for end-stage liver disease (ESLD) from steatohepatitis with progression to cirrhosis, complicated by portal hypertension, hepatic encephalopathy, and ascites that required multiple in-hospital admissions. Chronically, portal hypertension was managed using carvedilol, ascites with furosemide and spironolactone, with rifaximin and lactulose used for the management of hepatic encephalopathy.

As part of the medical workup required for waitlisting (three months before transplantation), cardiac angiography showed no evidence of occlusive coronary artery disease or pulmonary hypertension (PHT), and systolic and diastolic functions were well preserved with normal left ventricular ejection fraction (LVEF). The respiratory assessment was also normal. A trans-jugular intrahepatic portosystemic shunt was placed for the management of refractory ascites, but the patient subsequently developed endotipsitis requiring hospital admission two months preceding the liver transplant (adequately controlled by the time of transplant).[1] A month prior to the surgery, the patient had an abdominal hernia repair which was uneventful.

On the day of the transplant, the patient was stable with evidence of ascites but no encephalopathy or bleeding oesophageal varices. Laboratory studies revealed hyponatraemia, kidney dysfunction likely secondary to diuretic usage, and a Model for End-Stage Liver Disease Score (MELD score) of 24. All other clinical and laboratory findings were consistent with cirrhosis and portal hypertension, and the patient had a fair-effort tolerance with no evidence of preclusive frailty or sarcopenia.

For the transplant procedure, anaesthesia induction was achieved by the intravenous (IV) administration of 120 mg of propofol and 100 mg of rocuronium. As per protocol, prophylactic antibiotics were administered by IV infusion of 4.5 g of piperacillin and tazobactam. Endotracheal intubation was performed with a size 8.0 endotracheal tube positioned at 21 cm at the teeth, and intermittent positive pressure ventilation was instituted. Bilateral radial arterial catheters were placed, and with ultrasound guidance, a 9 French multi-access catheter sheath was introduced into the right internal jugular vein (IJV) and a three-lumen central venous catheter was inserted. Noradrenaline as per protocol was used for the haemodynamic instability associated with the different phases of liver transplantation, calcium chloride, dextrose-insulin, and bicarbonate infusions were initiated as per protocol, and the transplant was commenced. Trans-oesophageal echocardiography (TEE) performed before incision revealed a similar cardiac profile as was detected preoperatively with normal heart valves, preserved LVEF, no evidence of diastolic dysfunction, and no PHT.

The patient was anhepatic two hours later, and 1 gram of IV methylprednisolone was administered. Reperfusion of the implant liver was uneventful: typical right ventricular (RV) dysfunction associated with the anhepatic phase returned to normal within 20 minutes, blood pressures were stable, and LVEF was maintained; the metabolic acidosis was resolving, and the noradrenaline infusion had been reduced from 0.6 µg/kg/min to 0.08 µg/kg/min. Biliary anastomoses were commenced, and a second dose of 4.5 g of IV prophylactic antibiotics was given.

After 45 minutes, following reperfusion of the transplanted graft, the patient developed hypotension, sinus tachycardia, and worsening metabolic acidosis requiring increased inotropic and fluid support. Haemodynamic instability worsened with a blood pressure of 90/50 mmHg on a noradrenaline infusion increased to 0.8 µg/kg/min. Repeat TEE revealed a diminished LVEF of 45% with positive regional wall motion abnormalities and RV dilatation, without any obvious ischaemia. This raised concerns about a possible pulmonary embolism (PE), however, there was no evidence of PHT. Left ventricular (LV) apical ballooning became apparent approximately 30 minutes later. At this point, the differential diagnosis included a major adverse cardiac event

– acute coronary syndrome (ACS), acute PE, and intraoperative Takotsubo syndrome (TS). The surgery was completed 12 minutes later, and a Quinton catheter was placed in the left IJV anticipating the need for continuous veno-venous haemodialysis (CVVHD) support in the face of refractory metabolic acidosis and ongoing haemodynamic instability. While still in theatre, the patient developed atrial fibrillation managed with 300 mg of IV amiodarone. Once stabilised, the patient was transferred from theatre to ICU where, upon arrival, they developed a polymorphic ventricular tachycardia treated with 4 g of IV magnesium sulphate, 300 mg of IV amiodarone, and 100 mg of IV lignocaine, with nine attempts at synchronised direct-current cardioversions. A cardiology consult confirmed the diagnosis of intraoperative TS evidenced by a dilated and ballooning LV apex; LVEF of 35%, and a mildly dilated right ventricle with normal cardiac valves. At this time, troponin I and Pro-BNP levels were 241 ng/l and 190 ng/l respectively, with the latter peaking five hours later at 972 ng/l – suggestive of acute cardiac failure and supporting the diagnosis of intraoperative TS.

Ongoing haemodynamic instability, metabolic acidosis, and ensuing multi-organ dysfunction despite CVVHD and life-support measures necessitated the initiation of venoarterial extracorporeal membrane oxygenation (ECMO) for 14 days followed by a prolonged hospital stay of 67 days. Post-discharge, three-month follow-up echocardiography showed full recovery of cardiac function, normal liver function from the newly transplanted graft, and residual renal dysfunction not requiring chronic dialysis.

Discussion

TS, first described in Japan in 1990 in the setting of severe emotional stressors, is now known to occur in numerous clinical settings, including the perioperative scenario. The condition, which results in acute LV apical ballooning and takes its name from the traditional Japanese octopus trap that resembles this shape, can present a diagnostic and therapeutic challenge for perioperative teams.[2,3] Perioperative TS is widely reported in the context of liver transplantation, with cases typically developing in the postoperative period, and demonstrating varying levels of cardiac dysfunction and requirements for support.[4] In our case, haemodynamic instability unresponsive to maximal inotropic support and subsequent echocardiographic features developed intraoperatively in the absence of an obvious aggravating cause, illustrating the need for anaesthesiologists to consider the diagnosis when faced with acute onset cardiac failure in the operating room. In the setting of liver transplantation, there is only one report in literature describing a case of postoperative TS requiring ECMO for rescue.[5] To our knowledge, this is the first case of intraoperative TS requiring ECMO to be reported in the international literature, and the first case from South Africa.

Epidemiology

TS is diagnosed in 1–2% of patients presenting with ACS. A strong predilection for female patients exists with over 85% of cases occurring in this population. The incidence of perioperative TS is unknown and likely underappreciated due to a lack of awareness as a cause of haemodynamic instability and the wide spectrum of severity of presentation.[2,6,7]

Clinical presentation and diagnosis

Presentation is similar to that of ACS with dyspnoea, chest pain, and haemodynamic compromise. Perioperatively, as described in this patient, features are non-specific. Therefore the diagnosis may be complicated by the plethora of distracting and mimicking pathophysiological states such as surgical site pain, hypotension, tachycardia, and the systemic inflammatory response.

Most centres, including Wits Donald Gordon Medical Centre, utilise the 2008 Revised Mayo Clinic criteria to establish the diagnosis of TS (Figure 1).[8]

Revised Mayo Clinic criteria:[9]

i. Transient LV midsegment hypokinesis, akinesis, or dyskinesis that extends beyond a single epicardial vascular distribution, with or without a stressful trigger and apical involvement.
ii. Absence of obstructive coronary artery disease or angiographic evidence of acute plaque rupture.
iii. New electrocardiographic changes, i.e. ST-segment elevation and/or T-wave inversion or elevated troponin level.
iv. Exclusion of pheochromocytoma and/or myocarditis.

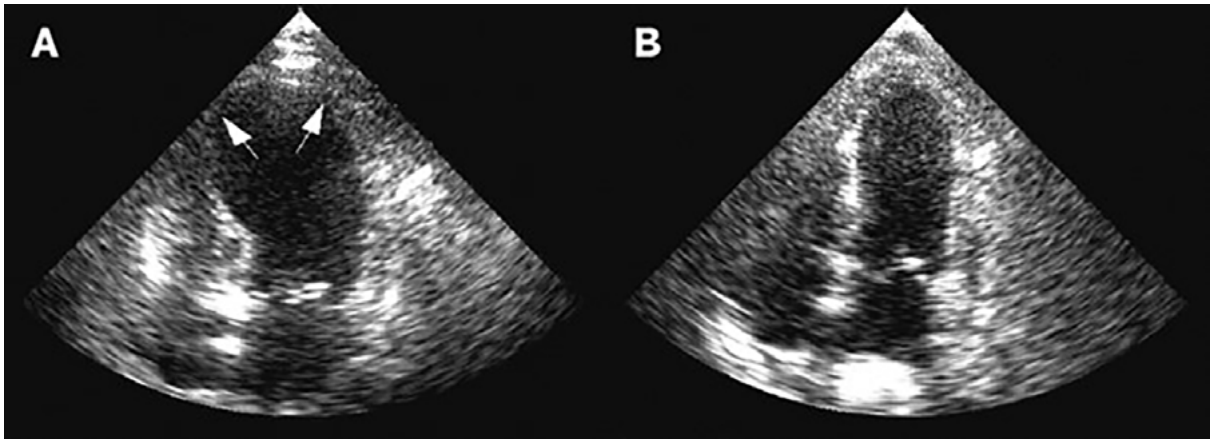

Figure 1: *A – Echocardiograph showing dilatation of the left ventricle in the acute phase (of TS); B – Resolution of left ventricular function on repeat echocardiograph six days later*[8]

Echocardiographic features associated with the commonest variant demonstrate a systolic mid- or apical LV hypokinesis or dyskinesis with preservation of the basal LV segment function. Other variant LV dyskinesias may occur and RV dysfunction can occur in up to 25% of patients.[2,3] Cardiac biomarkers such as troponins are elevated, but less so than in acute myocardial infarction. Electrocardiographic changes are non-specific and may mimic the ACS. As in our case, the patient may also develop associated dysrhythmias, which may be exacerbated by perioperative electrolyte abnormalities.[2,3,6]

Coronary angiography is often performed in these patients due to the similarity of the syndrome with acute myocardial infarction and although coronary arterial disease is not often associated, characteristic apical ballooning is obvious during left ventriculography.[2] Lastly, cardiac magnetic resonance imaging is often diagnostic and elucidates an important feature of the syndrome: marked myocardial oedema.

Pathogenesis

The pathogenesis of TS is yet to be elucidated and the mechanism of cardiac dysfunction remains unclear. It also remains unknown whether the echocardiographic pattern is attributable to the same underlying molecular process. Theories such as catecholamine excess, microvascular dysfunction, and coronary vasospasm have all been postulated. The former may explain the perioperative pathogenesis most accurately and there are numerous salient features which support this hypothesis, namely (i) the demonstration of both an excess of catecholamines and endomyocardial evidence of catecholamine toxicity in murine models; (ii) the observation that a similar reversible cardiomyopathy exists in some patients with poorly controlled phaeochromocytomas; (iii) high levels of catecholamines that may induce a negative inotropic effect via a switch from stimulatory to inhibitory G-protein coupled adrenoreceptor signalling.[10] In liver transplant patients specifically, pathogenesis is thought to be multifactorial with cirrhotic cardiomyopathy associated with ESLD hypothesised to be implicated in the pathogenesis.[4]

Management

The mainstay of care is support, especially in the perioperative setting. The treatment of heart failure, management of arrhythmias, prevention and treatment of thrombotic events, and pharmacological and mechanical support of cardiac function remain the crux of care both intra- and postoperatively.[2] In patients who develop severe complications, e.g. malignant arrhythmias, as noted in this patient, mechanical circulatory support such as ECMO may be required to relieve ventricular strain, as well as minimise inotropic requirements as these have been implicated in the pathogenesis.[5]

Although initially thought of as a non-fatal and fully reversible condition, the severity of TS, especially perioperatively, contributes to significant complication and mortality rates. Aside from increased awareness of this condition among perioperative anaesthesiologists and attending clinicians, additional appropriate support in the form of ECMO (from a certified centre) needs to be secured in the care pathway to enable access to this lifesaving treatment modality. Patients who survive initial haemodynamic compromise will have a full clinical and complete recovery of ventricular function.[2,3]

Conclusion

TS is a rare (and reversible) cause of perioperative haemodynamic instability and acute LV failure. The condition, which has a high complication rate and is associated with significant mortality, must be recognised early by treating perioperative clinicians so that appropriate and effective treatments may be timeously initiated.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

Written informed consent for the publication of the patient's clinical details was obtained from the patient. Any identifiable information about the patient is omitted.

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