Hind sight is 20/20: A Case of Occult Constrictive Pericarditis Leading to Early Graft Failure

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Herein, we present an unusual case of a liver transplant (LT) recipient who developed severe, unexplained right ventricular (RV) heart failure following liver reperfusion because of previously unrecognized constrictive pericarditis (CP). Transthoracic echocardiogram is the first-line test to diagnose CP with an estimated sensitivity of 87% and specificity of 91% in patients with heart failure.1 However, occult CP is notoriously difficult to diagnose, wherein baseline hemodynamics and systolic ventricular function are normal, until there is a sudden infusion of volume that causes significantly elevated filling pressures as encountered during liver reperfusion in LT.2

CASE DESCRIPTION

A 68-y-old Caucasian man with biopsy-proven cryptogenic cirrhosis and a sodium-model for end stage liver disease score of 13 with a serum creatinine of 1.3 underwent LT with a deceased brain-dead donor from a 42-y-old individual notable only for 30% hepatic steatosis on biopsy. While awaiting LT, he had unremarkable annual dobutamine stress echocardiograms with normal bilateral ventricular function and chamber size (left ventricular ejection fraction 65%, left atrial volume 56 mL, moderately dilated right atrial [RA] area 22 cm², RA pressure 10 mm Hg) as well as unremarkable chest x-rays and electrocardiograms. He denied any chest discomfort, dyspnea with exertion, history of lupus, or prior heart disease. On a myocardial perfusion scan 2 y before the LT, he was noted to have septal straightening and increased tracer uptake in the RV, suggestive of RV pressure overload. The interpretation of the patient’s preoperative studies indicated possible pulmonary hypertension but normal RV and LV function.

Following induction of anesthesia for LT, blood pressure was 147/83, pulse 84 bpm, and ventilator settings of pressure control ventilation-volume guaranteed, tidal volume 360 mL, 65% fraction of inspired oxygen, peak inspiratory pressure of 19 cm H₂O, and positive end-expiratory pressure 8 cm H₂O. However, the central venous pressure (CVP) was markedly elevated to 19 mm Hg, and there was no Swan-Ganz catheter placed. There was no significant ascites or pleural effusion. His initial intraoperative transesophageal echocardiography (TEE) demonstrated RA dilation and a conical-looking heart with preserved biventricular function. There was no significant tricuspid regurgitant jet to measure a RV systolic pressure. A chordal systolic anterior motion (SAM) was also noted during the primary transplant without left ventricular outflow obstruction. The CVP improved to 3–7 mm Hg after diuresis with furosemide 20 mg intravenously. The initial hepatectomy and engraftment were uncomplicated with stable hemodynamics without any blood product transfusion. However, the patient became severely hypotensive shortly after reperfusion that was unresponsive to inotropes, vasopressors, and methylene blue, with mean arterial pressures as low as 38 mm Hg. The TEE demonstrated markedly dilated right atrium, chordal SAM physiology (while on norepinephrine drip), good biventricular function, optimal volume status, and no evidence of pulmonary embolism. There was significant intraoperative bleeding from the liver and surgical bed related to high venous pressure and coagulopathy necessitating 12 units packed red blood cell, 20 units fresh frozen plasma, 6 units platelets, and 5 units cryoprecipitate. Within 12 h of LT, he developed hemorrhagic shock requiring triple pressors and additional blood products, as well as volume overload and acute kidney injury requiring continuous renal replacement. On postoperative day (POD) 1, he underwent a washout and evacuation of a hemoperitoneum. The TEE demonstrated an elongated appearance of the heart with bowing of the right atrium into the left atrium during systole (Figure 1A) indicating elevated right-sided pressures.
With a serum alanine aminotransferase 1929 IU/L, international normalized ratio 5.1, and Factor V activity 15%, he was relisted for primary nonfunction and underwent repeat LT on POD 3. Throughout the second LT, there was severe right heart dysfunction and progressive hypoxia necessitating the use of intraoperative inhaled nitric oxide. On reperfusion during retransplant, the CVP was up to 40 mm Hg, and hepatic engorgement and spontaneous capsular tears led to further hemorrhage. Intraoperatively, 17 units packed red blood cells, 32 units fresh frozen plasma, and 4 units platelets were required. On the intraoperative TEE, his pulmonary artery (PA) pulsatility index was 0.5, indicative of RV failure; there was tricuspid regurgitation, and no SAM was appreciated. A PA catheter revealed an elevated PA pressure 76/51 (mean 60 mm Hg) and CVP 44 mm Hg. The biliary anastomosis was delayed, and he was moved back to the intensive care unit for further management. He had a complicated hospital course, including development of dialysis-dependent acute kidney injury and pulmonary aspergillosis on POD 16 (Table 1). He slowly improved and was discharged on POD 39 to a rehabilitation facility with stable allograft function. The pathology of his explanted graft demonstrated extensive, panlobular necrosis, and abundant steatosis.

Eight months after his second LT, the patient underwent a pericardiectomy, wherein a 3-cm rind of fibrous tissue was removed, and the surgical specimen confirmed fibrous pericarditis. The patient made a full clinical recovery on tacrolimus monotherapy and eventually underwent an unremarkable deceased kidney transplant at 12 mo with very stable intraperoperative hemodynamics. He is alive and well 17 mo after his LT.

**DISCUSSION**

The American Association for the Study of Liver Diseases recommends that cardiac stress testing including surface echocardiography with Doppler be performed in all LT candidates to identify reversible coronary ischemia, valvular heart disease, and pulmonary hypertension.1 In light of the increasing age and the presence of medical comorbidities among LT candidates, there will likely be an increasing incidence of cardiac contraindications to LT.2

CP is a rare fibrosing disorder of the pericardium that occurs after pericardial injury or inflammation with an incidence of 0.76 cases per 1000 person-y after an episode of idiopathic or viral pericarditis.3 However, as many as 33% of patients may not have an identifiable trigger, such as acute pericarditis, cardiac surgery, or mediastinal radiation, before developing CP. With CP, the heart is unable to fully relax during diastole because of the fibrous rind and is therefore unable to accommodate large shifts in volume, often resulting in markedly elevated right-sided pressures and a low cardiac output state. There are cases of patients with occult CP who present with cardiac ascites and cryptogenic cirrhosis, wherein the liver biopsy may show bridging fibrosis involving the central veins or other signs of congestive hepatopathy.4 Notably our patient’s liver biopsy 5 y before LT and his initial liver explant did not show any evidence of pericentral injury or hemorrhage, whereas his explanted allograft showed massive necrosis. Furthermore, he had undergone multiple annual echocardiograms during the 3 y on the waiting list that were largely unremarkable. Testing for latent tuberculosis was also negative pre- and postoperatively. Only careful retrospective review of prior computerized tomography imaging of
the chest noted mild thickening of the pericardium and trace pericardial effusion. A right and left heart catheterization performed with a high level of suspicion was necessary to diagnose his CP several months after his second LT. Pericardiectomy in patients with CP and decompensated hepatic function is highly effective but also risky in certain patient subgroups. In a single-center observational study, 12 CP patients with a Model for End-stage Liver Disease score >15 who underwent pericardiectomy had a 1-y survival of only 8.3%, compared to nearly 70% in 53 patients with Model for End-stage Liver Disease score 7.51–15.5. In another observational study, Child-Pugh Score B or C patients with CP had a much lower 5-y survival compared with Child-Pugh A patients (38% versus 81%).

In conclusion, occult CP is exceedingly rare in LT candidates, but it is critical to diagnose and address before LT as exemplified in this case. A review of the 2800 adult LT done in our center over the past 35 y failed to identify another patient with occult CP that had not been recognized with preoperative cardiac testing. The etiology of intraoperative RV dysfunction can be multifactorial, and a discrete etiology can be difficult to elucidate in the highly dynamic setting of LT with rapid blood loss and fluctuating hemodynamics. Nonetheless, if a patient develops immediate, unexplainable right heart failure after reperfusion, there should be a high index of suspicion for fluid overload, pulmonary embolism, or restrictive cardiomyopathy. We now would propose to include possible occult CP if the other more common etiologies are excluded. If one encounters unexplained systemic hypotension with adequate filling pressures in a LT patient, a review of the TEE images is recommended to look for CP. Echocardiographic findings may include a thickened pericardium, a dilated vena cava, hepatic vein flow alterations, and an interventricular septal bounce indicative of ventricular interdependence. Fortunately, intraoperative TEE is used at 95% of LT centers in the United States these days and may help identify individuals with this unusual cardiac condition.

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### TABLE 1.

A 68-y-old man with previously unrecognized constrictive pericarditis

| Hospital day | Event | Comments |
|--------------|-------|----------|
| 1            | Liver transplant #1 | Refractory hypotension after reperfusion, RV failure, and severe intraoperative and postoperative bleeding |
| 2            | Primary nonfunction | Massive pressor requirements, hypotension, acidosis |
| 3            | Liver transplant #2 | Severe intraoperative bleeding and elevated CVP and right heart pressures |
| 6            | Dobutamine added | Low heart rates and elevated SVR |
| 16           | Reintubated | Pulmonary aspergillosis by bronchoscopy |
| 39           | Discharged to inpatient rehabilitation | On intermittent hemodialysis |
| Month 4      | Chest CT | Incidental thickening of pericardium noted |
| Month 4.5    | Cardiology consult | Right and left heart cath confirming the presence of moderate to severe CP |
| Month 8      | Pericardiectomy | 3-cm rind removed with improved hemodynamics |
| Month 12     | Deceased kidney transplant | Uncomplicated intraoperative and postoperative course |
| Month 17     | Follow-up | Alive and well with normal hepatic and renal function |

CP, constrictive pericarditis; CT, computed tomography; CVP, central venous pressure; RV, right ventricular; SVR, systemic vascular resistance.