SUCCESSFUL RIGHT VENTRICULAR MECHANICAL SUPPORT AFTER COMBINED HEART-LIVER TRANSPLANTATION

Michael G. Fitzsimons, MD,* Fumito Ichinose, MD,† Parsia A. Vagefi, MD,† James F. Markmann, MD,† Eric T. Pierce, MD, PhD,* Thomas E. MacGillivray, MD,‡ Martin Hertl, MD,† Cosmin Gauran, MD,§ Joren C. Madsen, MD,† and Joshua Baker, MD‡

CASE REPORT

A 45-year-old male with a history of right-sided congestive heart failure associated with cirrhosis presented for combined heart-liver transplantation. At age 28 he was diagnosed with a right-sided cardiac mass. At that time he underwent a massive debulking of the mass associated with excision of the tricuspid valve. Pathology showed thrombus and a benign fibroproliferative process. After his operation he lived with severe tricuspid regurgitation, eventually leading to cardiac cirrhosis associated with recurrent ascites, pleural effusions, a chronic cough, and decreased exercise tolerance. He presented for consideration for combined heart and liver transplantation.

Echocardiography performed during his transplant evaluation revealed normal left ventricular size and function, an ejection fraction of 64%, tricuspid regurgitation, and a small and hypokinetic right ventricle with only a small remnant of the tricuspid valve. There was dilation of the right ventricle and inferior vena cava with associated hepatic vein dilation. The interatrial septum was shifted toward the left, consistent with right atrial volume overload. There was evidence of a patent foramen ovale. Right and left cardiac catheterization at the time of initial evaluation demonstrated no evidence of coronary artery disease. Superior vena cava pressure was 24 mmHg, mean right atrial pressure was 26 mmHg, mean pulmonary artery pressure (PA) was 26 mmHg, and pulmonary capillary wedge pressure was 15 mmHg with spontaneous ventilation. Cardiac output was 2.45 L/min and cardiac index 1.3 L/min/m² by thermodilution. Pulmonary vascular resistance (PVR) was reported as 359.2 dynes-sec-cm⁻⁵ (4.49 Woods units). Liver biopsy was consistent with cirrhosis. Several attempts at radiofrequency ablation for atrial fibrillation were unsuccessful. His condition progressed such that he required intensive care management with sildenafil, intravenous milrinone (0.1 µg/kg/min), dobutamine (70 µg/min), and phenylephrine (10 µg/min) before surgery and was thus admitted to the intensive care unit and listed as status 1A for combined heart-liver transplantation.

Sixty-three days after his admission, a suitable 25-year-old brain-dead donor became available and the patient was brought to the operating room for combined heart-liver transplantation. The patient’s MELD score at the time of transplant was 25, creatinine 1.34, sodium 131, albumin 3.6, INR 1.3.

Baseline hemodynamics with spontaneous ventilation revealed blood pressure of 132/57 (mean 68) mmHg, PA pressure 28/22 (mean 25), central venous pressure 29 mmHg, and heart rate of 63 beats/minute. General anesthesia was induced with etomidate, 20 mg, rocuronium, 90 mg, and fentanyl, 100 µg, and the trachea was intubated. The patient also was administered 1,000 µg of methylprednisolone. Anesthesia was maintained with isoflurane. The patient received a total of 450 µg of fentanyl and 2 mg of dilaudid. A propofol infusion was used to maintain sedation for transfer to the intensive care unit. Transeosophageal echocardiography (TEE) confirmed the expected findings based on preoperative evaluation. The right ventricle was small and hypokinetic with only a small remnant of the tricuspid valve (Video clip 1).

Repeat median sternotomy was accomplished safely, followed by systemic heparinization, initiation of bypass, and cooling of core temperature to 25°C. Implantation of the donor heart was accomplished in the standard fashion, with the left atrial anastomosis followed by the inferior vena cava to the donor right atrium, the pulmonary arteries, and then the aortic anastomosis. Air was removed from the heart with TEE assistance followed by removal of the aortic cross-clamp and return of a junctional rhythm before a sinus rhythm. The total ischemic time for the heart was 4 hours and 43 minutes. The superior vena cava to donor right atrium anastomosis was completed. Protamine, 250 mg, was administered. Cardiopulmonary bypass easily was weaned with norepinephrine, 12 µg/min, milrinone, 0.5 µg/kg/min, vasopressin, 0.04 unit/min, and calcium. TEE suggested a small gradient across the pulmonary artery anastomosis and mild right ventricular dilation. The peak gradient across the pulmonary artery anastomosis was estimated by TEE at 18 mmHg. Direct pressure measurement...
revealed a pressure gradient of 2 to 3 mmHg. The pulmonary artery catheter could not be advanced into the pulmonary artery initially but ultimately was positioned. Initial systemic blood pressure was 91/47 mmHg (mean 60), pulmonary artery pressure 27/14 mmHg (mean 20), central venous pressure 12 mmHg, and heart rate 112 bpm. Cardiac output was 4.3 to 4.6 L/min. Pacing was not necessary. TEE demonstrated normal function of the right ventricle (Video clip 2). Norepinephrine was increased to as high as 100 µg/min and vasopressin to 0.08 units/min. The chest was left open during liver implantation, and the superior vena cava cannula was left in place for venovenous bypass.

Liver transplantation was performed in the standard fashion with a bivacal anastomosis. Venovenous bypass through a femoral venous catheter with blood return to the superior vena cava cannula was used. The liver was flushed with 2 L of lactated Ringer’s and albumin before reperfusion. Total cold ischemic time was 10 hours and 23 minutes. Total warm ischemic time was 54 minutes. After liver graft reperfusion, the right ventricle began to demonstrate a further decrease in function, primarily indicated by dilation and hypokinesis (Video clip 3), whereas the function of the left ventricle remained vigorous. Escalation of vasopressor and inotropic support was required to maintain blood pressure. Epinephrine was increased to 2 µg/min, norepinephrine, 70 µg /min, vasopressin, 0.08 units/min, and milrinone, 0.38 µg/kg/min. Inhaled epoprostenol was started without improvement. It was determined that support of the right ventricle was indicated based on a progressive decrease in right ventricular function as a result of failure associated with a long cardiac ischemic time and the stress of liver transplantation. The left ventricle remained vigorous. A 30-French inflow basket-tipped cannula was placed through the right anterior chest wall into the right atrium. An 18-French Fem-Flex© inflow cannula (Edwards Lifesciences, Irvine, CA) was placed through the left anterior chest wall into the pulmonary artery. The CentriMag® (Thoratec Corp., Pleasanton, CA) right ventricular assist device (RVAD) flow was initiated at 4 L/min. The left atrial pressure increased and the right atrial pressure decreased. Vasoactive medications were weaned and the patient was brought to the cardiac surgical intensive care unit (ICU) in critical condition. Total transfusion requirements were cryoprecipitate 10 units, platelets 30 units, red blood cells 14 units, fresh frozen plasma 20 units, and 5,200 mL of cell saver.

Anticoagulation was initiated with heparin to maintain a partial thromboplastin time (PTT) of 44 to 55 seconds (normal, 22-35 seconds). Flows via the RVAD were maintained at 3.5 to 4.5 L/min.

The patient developed mild renal insufficiency with a peak creatinine of 2.1 on postoperative day (POD) 3. On POD 4, TEE revealed normal left ventricular size and function, trace tricuspid regurgitation, and a mildly hypokinetic right ventricle. The ventilator assist device flow was decreased from 3 L/min down to 1 L/min with no decrease in right ventricular function or increase in tricuspid regurgitation. The patient was taken back to the operating room, where the RVAD was successfully removed (Video clip 4). The patient was discharged from the hospital on POD 30 and has remained free of complications since that time. The patient is currently 1.5 years post-transplant with normal allograft function of both his heart and liver and with no evidence of rejection. There is no gradient across the pulmonary anastomosis.

**DISCUSSION**

Combined heart-liver transplantation has proven to be a viable option for patients with combined disease of the heart and liver. The most common indication for heart transplantation in this patient population is amyloidosis, followed by congenital heart disease and idiopathic dilated cardiomyopathy.1-2 The most common indication for liver transplantation in such patients is amyloidosis, hepatitis C, and hemochromatosis.

Right ventricular failure after heart transplantation complicates approximately 12% of cardiac transplants. The etiology is multifactorial, likely a combination of inadequate myocardial protection coupled with an inability to respond to increased pulmonary vascular resistance.5 Dilation, decreased contractility, and tricuspid regurgitation result in decreased cardiac output. Management of right-sided heart failure includes increasing perfusion pressure, decreasing PVR (milrinone, inhaled nitric oxide, inhaled prostacyclin), increasing myocardial inotropy (dobutamine, dopamine, isoproterenol, milrinone), and increasing right ventricular coronary perfusion pressure. An intraaortic balloon pump has been used successfully in the management of predominantly right-sided ventricular failure after heart transplantation.6 Improvement in cardiac index and mixed venous oxygen saturation has been demonstrated. Extracorporeal membrane oxygenation (ECMO) has been used to salvage patients with early graft dysfunction after heart transplantation. Those requiring ECMO had higher mortality at 30 days and 1 year. ECMO also has been used successfully as a planned intervention when a prolonged ischemic time was anticipated during transplantation.7

Severe heart failure after liver transplantation occurs in approximately 3.3% to 7% of patients.9,10 Risk factors include older age and elevated preoperative right-sided heart pressures on the recipient side and marginal graft quality on the recipient side.9 The actual cause of failure is largely unknown, but upregulation of metalloproteinases and other vasoactive substances released by the liver are thought to contribute to cardiac hypokinesis.10,11 Postreperfusion syndrome (PRS) is marked by a significant fall in blood pressure associated with unclamping of the portal vein and liver reperfusion and occurs in approximately 25% of liver transplants.12 The absence of a portal caval shunt and longer duration of cold ischemia are known risk factors.12,13 Intraoperative hypotension, defined as a mean arterial pressure less than 40 mmHg at least once during a liver transplant, has been identified as an independent risk factor for mortality.14

This patient was noted to have right ventricular dilation at the end of the heart transplantation. This was felt to be due to an ischemic time greater than 4 hours along with elevated preoperative PVR likely secondary to hepatopulmonary syndrome. It was felt that the risk associated with hepatic decompensation if liver transplantation was not pursued greatly outweighed the added potential risk associated with hepatic reperfusion, including hypothermia, hyperkalemia, fluid overload, and acidosis.15 Thus, dual-organ transplantation was performed. Given persistent impaired right ventricular function and failure to improve with pharmacologic support, mechanical support was sought. Intra-aortic balloon pump (IABP) and ECMO have both been used successfully after heart transplantation circulatory failure.6,7 It was not felt that an IABP would decrease the right-sided pressure enough to maintain adequate hepatic perfusion. ECMO can provide support to both the left and right ventricles along with the lungs, which was unnecessary. ECMO would have required anticoagulation and risked increased bleeding. RVAD implantation would provide significant support to the right ventricle without anticoagulation while allowing protamine reversal of heparin.
In patients undergoing combined heart-liver transplantation, right ventricular failure after heart transplantation risks hepatic congestion and subsequent graft failure. Extracorporeal membrane oxygenation requires anticoagulation, and intra-aortic balloon counterpulsation may not unload the right ventricle. The use of a right ventricular assist device after combined heart-liver transplantation may provide temporary support and allow adequate return of right ventricular function without compromise of a newly implanted liver.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1053/j.jvca.2013.10.013.

REFERENCES