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Case Report

Normalization of Pulmonary Hypertension by the Use of Left Ventricular Assist Device in Patients with End-stage Heart Failure: A Possible Contribution to Donor Pool Expansion in Lung Transplantation☆

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SUMMARY

Heart transplantation alone has been recognized to be contraindicated when pulmonary hypertension (PH) and elevated pulmonary vascular resistance (PVR) are irreversible, irrespective of any medical intervention by the use of inotropic agents or pulmonary vasodilators, because such patients are at an increased risk of post-transplantation right ventricular failure and mortality. Therefore, end-stage heart failure patients with concomitant fixed PH and irreversibly high PVR are considered to be heart–lung transplant candidates. Recently, left ventricular assist device (LVAD) therapy has been reported to normalize PVR through persistent unloading of the left ventricle, even in patients with medically refractory PH. Therefore, LVAD therapy could make such patients suitable for "heart-only" transplants, which contributes to appropriate donor lung allocation for lung-only candidates. We review the literature regarding LVAD use for secondary PH and present a case with end-stage heart failure that could avoid a heart–lung transplant owing to LVAD therapy.

1. Introduction

Heart transplantation alone has been recognized to be contraindicated when the minimum trans-pulmonary gradient is greater than 15 mmHg or pulmonary vascular resistance is greater than 6 Wood units and irreversible, irrespective of any medical intervention by the use of inotropic agents or pulmonary vasodilators; this is because such patients are at an increased risk of post-transplantation right ventricular failure or mortality[1,2]. Secondary pulmonary hypertension (PH) is a common consequence of end-stage heart failure, mainly related to increased left ventricular filling pressure. It has been reported that up to 40% of potential heart transplant candidates develop secondary PH at the time of evaluation[3,4].

Due to high early mortality and poor outcome after "heart-only" transplants[5–7], end-stage heart failure patients concomitant with fixed PH and irreversibly high pulmonary vascular resistance (PVR) are considered to be heart–lung transplant candidates. According to the International Society for Heart and Lung Transplantation Registry Report in 2009, the five leading indications for heart–lung transplantation were congenital heart disease with Eisenmenger syndrome (34.9%), idiopathic pulmonary arterial hypertension (27.2%), cystic fibrosis (14.1%), chronic obstructive pulmonary disease/emphysema (3.8%), and acquired heart disease (2.9%)[8]. Therefore, nearly 3% of heart–lung recipients who required simultaneous lung and heart transplants might have medically

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refractory PH and/or high PVR due to severe heart failure as a primary reason for their transplants. However, the world-wide number of combined heart–lung transplants has remarkably reduced and stabilized since 2001, ranging from 75 to 86 cases per year[8]. This procedure involves competition with heart-only, single-lung, and double-lung transplant candidates under circumstances of global donor shortage.

Left ventricular assist device (LVAD) therapy has been reported to lower pulmonary pressures through persistent unloading of the left ventricle. Some observational studies have shown that in patients who were initially nontransplant candidates due to severe PH secondary to heart failure, LVAD implantation decreased pulmonary pressures, allowing patients to undergo cardiac transplantation[9–12]. Thus, the appropriate use of LVAD would allow a certain proportion of heart–lung recipients whose primary disease is end-stage heart failure to become only-heart candidates, thus contributing to appropriate distribution of donor lungs to patients who are on the lung-only waiting lists.

2. Case report

A 36-year-old Japanese female with end-stage heart failure due to dilated cardiomyopathy was listed for heart transplant in 2005. At the time of evaluation in 2005, when under an intravenous milrinone and dobutamine infusion, her ejection fraction, measured by echocardiography, was 20%; her cardiac index, 1.5 L/min/m^2; her serum creatinine concentration, 2.6 mg/dL; and her PVR, 4 woods. She was successfully weaned from the milrinone and dobutamine infusion and became ambulatory; however, she again developed acute decompensated heart failure and was admitted 3 months after she was discharged. In spite of the dobutamine, milrinone, and dopamine infusion, her PVR remained over 6 woods and her mean pulmonary artery pressure over 50 mmHg for 2 months. Reversibility of PH was assessed by nitroglycerin and prostaglandin. The possibility of the patient having coexisting pulmonary thromboembolism was excluded by imaging study. The PH of the patient was not normalized by this assessment. Therefore, the transplant team needed to consider withdrawing the patient from the heart transplant waiting list and putting her on the heart–lung waiting list, instead of the heart-only waiting list.

After considerable discussion with the patient's family, her transplant team decided to perform extracorporeal pulsatile LVAD surgery on the patient, with the hope that the LVAD would lower her PVR. The patient's body size was too small to undergo implantable devise surgery. Two months after the LVAD implantation, she was successfully weaned from any inotropic agents including phosphodiesterase type 3 inhibitors with a stable PVR between 2 and 3 Wood units. Five months after the surgery, her PVR was stabilized between 1 and 1.5 Wood units. The patient successfully underwent heart-only transplantation 2 years after the LVAD surgery. The clinical course of the present case is shown in Fig. 1.

3. Discussion

Lung transplant is an effective treatment for patients with end-stage lung disease; however, it is severely limited because of the shortage of acceptable donor organs. Although the number of heart–lung transplantations has been small compared with single-lung or double-lung transplantations, we could better distribute the donor lungs if we could avoid heart–lung transplantation for patients whose primary disease is end-stage heart failure with secondary PH.

We presented a case with end-stage heart failure concomitant with secondary PH that was successfully treated by LVAD implantation. Not only did LVAD acutely reduce PVR, but the patient demonstrated subacute and chronic effects of LVAD on gradual PVR reduction. The patient showed greater than 6 woods PVR for 2 months under inotropic support, irrespective of any medical intervention prior to the surgery; however, the PVR decreased by around 3 Wood units in the 2 months after the surgery. The PVR even continued to reduce 5 months after the surgery, and finally normalized. Zimpfer et al[11] reported that both continuous and

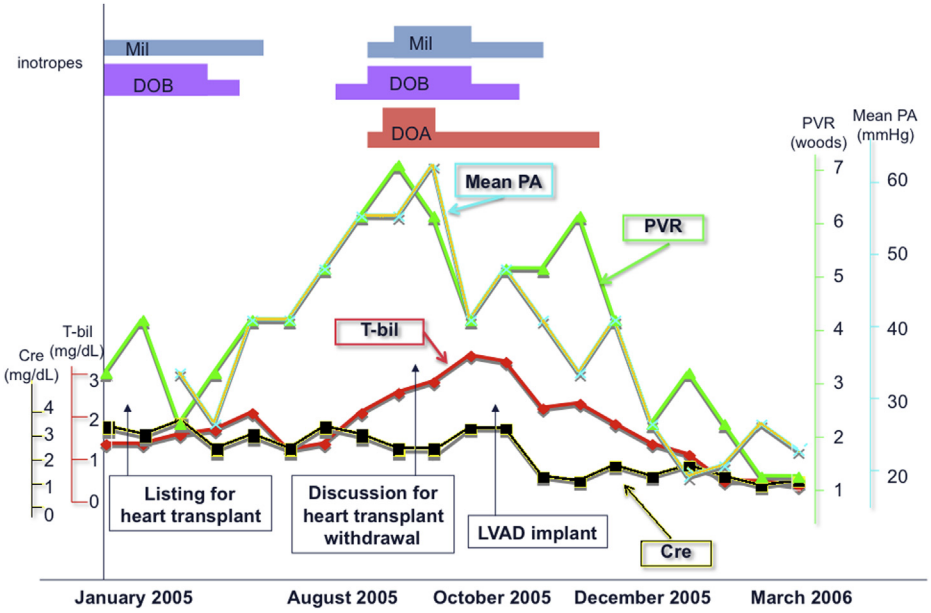

Fig. 1. Clinical chart of the patient with end-stage heart failure and persistent pulmonary hypertension who was treated with LVAD therapy. Cre = serum creatinine concentration; DOA = dopamine; DOB = dobutamine; LVAD = left ventricular assist device; Mean PA = mean pulmonary artery pressure; Mil = milrinone; PVR = pulmonary vascular resistance; T-bil = total bilirubin concentration.

pulsatile LVAD could reduce fixed PH in patients with end-stage heart failure during a 6-week period. We believe that the present case demonstrated resolution of pulmonary hypertension within a short-to-intermediate follow-up period, accompanied with the serial hemodynamic examinations and clinical presentations.

Secondary PH is the consequence of elevated left atrial filling pressures, and LVAD therapy might reverse this process by continuously unloading the left ventricle. A previous study revealed that left ventricular unloading was more efficiently done by continuous flow devices[13]. Therefore, continuous flow LVAD had more potential to be highly beneficial for end-stage heart failure patients with severe secondary PH. The presented case underwent extracorporeal pulsatile LVAD surgery due to her small body size, but nevertheless successfully demonstrated a remarkable decrease in PVR.

In conclusion, LVAD therapy could be considered for end-stage heart failure patients who had medically refractory secondary PH, in order to make such patients suitable for "heart-only" transplants. Avoidance of heart–lung transplantation for these patients through LVAD therapy would contribute to appropriate donor lung allocation for lung-only candidates.

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