Severe mitral regurgitation unmasked after bilateral lung transplantation

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Abstract: A 33-year-old female patient with advanced idiopathic pulmonary artery hypertension underwent bilateral lung transplantation. The postsurgical course was complicated by prolonged mechanical ventilation and acute hypoxemia with recurrent episodes of pulmonary edema. An echocardiogram revealed improved right-sided pressures along with a dilated left atrium, a structurally normal mitral valve, and a new posterior-oriented severe mitral regurgitation. The patient's condition improved after treatment with arterial vasodilators and diuretics, and she has remained in World Health Organization functional class I after almost 36 months of follow-up. We hypothesize that cardiac ventricle remodeling and a geometric change in mitral valve apparatus after transplantation led to the hemodynamic changes and recurrent pulmonary edema seen in our patient. Our case is, to our knowledge, the second report of severe valvular regurgitation in a structurally normal mitral valve apparatus in the postoperative period and the first of a patient to be treated without valve replacement.

Keywords: idiopathic pulmonary arterial hypertension, hypoxemia, pulmonary edema, cardiac ventricle remodeling.

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INTRODUCTION

Lung transplantation remains the only treatment option for selected patients with advanced idiopathic pulmonary arterial hypertension (IPAH) who continue to experience deterioration despite optimal pulmonary vasodilator therapy. Early postoperative pulmonary complications include primary graft dysfunction, infection, and pulmonary edema. Mitral regurgitation (MR) is an important cause of pulmonary edema, and the etiology includes infectious¹ and non-infectious²⁻⁴ causes; however, the true incidence is unknown. MR has been associated with acute allograft rejection and increased mortality in heart trans-

plant recipients. It could have similar implications for lung transplant recipients. We present, to our knowledge, the second reported case of severe valvular regurgitation in a structurally normal mitral valve apparatus in the posttransplantation period; our patient is the first to be treated with medical therapy and did not require mitral valve replacement.

CASE HISTORY

A 33-year-old black female with a history of IPAH was referred for lung transplantation evaluation. She

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was receiving 3 L/min of supplemental oxygen and was in World Health Organization (WHO) functional class IV despite receipt of aggressive medical therapies with multiple diuretics, bosentan, sildenafil, epoprostenol, and dopamine. Physical examination findings showed an ill-appearing woman with signs of cor pulmonale, hepatic congestion, and significant lower extremities edema. Echocardiogram findings revealed a small left ventricle (LV) with normal function, severely dilated right ventricle (RV) and right atrium (RA), elevated pulmonary artery (PA) pressure, and mild MR. Right-sided heart catheterization showed elevated PA pressure of 78/45 mmHg with a mean of 56 mmHg and a decreased cardiac index (Fick cardiac index, 1.91 L/min/m²) without any evidence of intracardiac shunt or elevated pulmonary capillary wedge pressure.

The patient underwent bilateral sequential lung transplantation (BLTx) with cardiopulmonary bypass. The total allograft ischemic time was 5 hours (the right and left lungs required 3 and 5 hours, respectively). The surgical procedure was complicated by coagulopathy and bleeding that required transfusion of multiple blood products. Intraoperative transesophageal echocardiography revealed severely dilated RA and RV causing septal bowing into the LV cavity, mild-to-moderate MR, structurally normal chordae tendineae, and normal mitral valve annulus and leaflets. In her early postoperative course, the patient was treated for the complication of allograft methicillin-susceptible *Staphylococcus aureus* pneumonia. She continued to be hypoxemic with an elevated alveolar-arterial oxygen gradient. Transfusion-related lung injury was also considered as a possible etiology for her continued hypoxia; she was receiving supportive treatment and was already receiving corticosteroids.

Her hypoxemia improved slowly, but several spontaneous breathing trials and extubation attempts were unsuccessful because of tachypnea, acute oxygen desaturation, and recurrent pulmonary edema necessitating percutaneous tracheostomy on postoperative day (POD) 15. Serial brain natriuretic peptide value was elevated (maximum value, 4,000 pg/mL) despite aggressive diuresis. Plain chest radiograph findings showed resolving multifocal pneumonia but with persistent pulmonary edema pattern (Figure 1B, 1C). A transbronchial lung biopsy specimen was obtained,

Figure 1. Chest radiographs obtained on (A) postoperative day (POD) 1, showing bilateral pulmonary edema pattern; (B) POD 14, after completion of an antibiotic course for allograft infection; (C) POD 34, showing a new pulmonary edema pattern after new posterior-oriented severe mitral regurgitation was seen on transthoracic echocardiogram; (D) POD 37, showing improved lung radiograph findings.

and it showed no acute lung injury pattern or evidence of acute cellular rejection.

Three weeks after receipt of her transplant, our patient became hypotensive, and milrinone therapy was initiated. Potential causes of hypotension, such as sepsis and cardiogenic shock, were excluded. Preoperative evaluation did not reveal any coronary artery disease, and recent cardiac enzymes and electrocardiogram findings were negative. An additional echocardiogram obtained on POD 34 showed improved RA and RV pressures, a dilated left atrium (anterior-posterior diameter, 46 mm), and a new posterior-oriented severe MR on color flow Doppler (Figure 2A, 2B). The mitral valve apparatus appeared to be normal, but there was no coaptation between the anterior and posterior mitral leaflets. Milrinone was discontinued in favor of an arterial vasodilator with nitroprusside and captopril, which led to improvement in the patient's blood pressure. Her diuretics were restarted, and an additional echocardiogram on POD 37 showed continued improvement in the anterior-posterior diameter (37 mm) of the left atrium.

The intensity of the patient's MR decreased, and her hypoxemia and chest radiograph findings improved (Figure 1D). She was weaned to tracheostomy

Figure 2. Parasternal long-axis view from transthoracic echocardiogram with color Doppler imaging. A, Pretransplant image showing enlarged right ventricle (RV) and bowing of the interventricular septum. The red arrow shows tethered posterior mitral valve leaflet. B, Posttransplantation image showing improved ventricle sizes with white arrow indicating resulting severe mitral regurgitation. LA, left atrium; LV, left ventricle.

collar on POD 38, and her tracheostomy tube was decannulated 4 days later. Echocardiogram findings obtained 54 days after receipt of her transplant continued to show decreasing left atrium size, which suggested sustained improvement of her MR. After weeks of physical therapy, the patient regained almost all of her functional status and was discharged from the hospital on POD 62. She continues to remain compliant with her medication regimen and is currently in WHO functional class I after almost 36 months of follow-up.

DISCUSSION

Pulmonary edema is one of the early postoperative pulmonary complications in lung transplant recipients. MR is an important cause of pulmonary edema that can result in respiratory failure, hypoxemia, and prolonged mechanical ventilation and can also contribute to the transplant recipients' morbidity and mortality. We have described a second case of severe mitral valve regurgitation in a structurally normal mitral valve apparatus occurring in the postoperative period and the first such patient to be treated without valve replacement.

The exact cause and true incidence of left-sided valvular complications after lung transplantation are unknown. Mitral valve regurgitation can result from any disease affecting any part of the valve apparatus or from structural changes in the cardiac ventricle that prevent adequate coaptation of the mitral leaf-

lets.² The mitral valve apparatus consists of the annulus, anterior and posterior leaflets, chordae tendineae, and papillary muscles.² MR has been associated with noninfectious^{1,2} and infectious^{3,4} etiologies in lung transplant recipients. Recurrent pulmonary congestion causing acute hypoxemia is the most feared clinical consequence of MR irrespective of the etiology.

We hypothesize that structural and geometric changes in cardiac ventricles in the posttransplantation period resulted in our patient's severe MR. Before BLTx, the mitral regurgitant volume was graded as mild on echocardiograms because of a small mitral orifice caused by the dilated RV bowing into the LV cavity and decreasing its effective chamber volume. Similar to what was reported by Bermudez et al.,¹ the reduction in our patient's pulmonary and RV pressures after transplantation led to a reduction in the size of the RV and, inversely, to a larger LV cavity and a change in mitral annulus. There was also a loss of coaptation of the anterior and posterior mitral leaflets, mostly because of the apical displacement of the papillary muscles from both regional and global LV geometric changes after transplantation.^{5,6} The associated hemodynamic changes and pulmonary congestion are related to the regurgitant orifice area and volume. The regurgitant volume is determined by the magnitude of the systolic pressure gradient across the mitral valve during systole.^{6,7} The increased mitral orifice area was then able to accommodate an increase in regurgitant volume and flow

across the mitral valve leading to an increase in the left atrium diameter, pulmonary congestion, and oxygen desaturation.

Pulmonary edema can also occur from excessive intravenous fluid (including blood products) administration during surgery and surgical complication (i.e., pulmonary vein stenosis). However, these would be expected to present in the immediate postoperative period and not in the late period, as in our patient. Primary graft dysfunction, allograft infection, transfusion-related acute lung injury, and acute cellular rejection are plausible causes for our patient's respiratory failure in the early and late posttransplantation period. Our prompt evaluation excluded any of these potential diagnoses. It was her failure to tolerate multiple mechanical ventilator weaning trials and the subsequent evaluation with echocardiogram that led to the discovery of the new severe MR caused by a structurally normal valve.

Asymptomatic MR before lung transplantation in patients with severe pulmonary hypertension should not be overlooked, because it can progress to severe MR with its associated clinical symptoms in the postoperative period. Significant MR seen in the late postoperative period is associated with acute rejection and mortality in heart transplant recipients.⁸ Therefore, recurrent pulmonary edema in the period after lung transplantation may have similar consequences for allograft function and patient morbidity. Other authors have shown satisfactory results with mitral valve repair¹ or replacement² for severe MR, either before or at the time of transplantation. Alternatively, we have shown that such patients could be managed using a conservative medical approach.

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