



# Two Cases of Late Shone Syndrome With Pulmonary Hypertension: Heart–Lung Transplant or Valve Surgery?

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## Abstract

Two cases of Shone syndrome with severe mitral and aortic valve problems and pulmonary hypertension were referred for heart–lung transplantation. Severely elevated pulmonary vascular resistance (PVR) was confirmed as was severe periprosthetic mitral and aortic regurgitation. Based on the severity of the valve lesions in both patients, surgery was decided upon and undertaken. Both experienced early pulmonary hypertensive crises, one more than the other, that gradually subsided, followed by excellent recovery and reversal of pulmonary hypertension and PVR. These cases illustrate Braunwald's concept that pulmonary hypertension secondary to left-sided valve disease is reversible.

## Keywords

adult congenital heart disease, mitral valve replacement, pulmonary vascular resistance/hypertension, reoperation

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## Introduction

Shone syndrome represents a spectrum of left-sided cardiac anomalies classically including supravulvar mitral membrane, parachute mitral valve, subaortic stenosis (membranous or muscular), and coarctation of the aorta<sup>1</sup> (Figure 1). After initial description in 1963 by Shone, the reported outcomes of surgical repair were poor.<sup>2,3</sup>

Outcomes have improved due to better diagnostic imaging, care, and surgical management. As more data have become available, it appears that severity of mitral valve obstruction is a major predictor of poor long-term survival, and when patients develop pulmonary hypertension, prognosis is even more dismal.<sup>4</sup>

We present two young adults with Shone syndrome presenting with severe pulmonary hypertension and severe left-sided valve lesions referred to our institution for consideration of combined heart–lung transplant. In the setting of multidisciplinary discussion, it was decided to perform high-risk valve surgery.

## Case I

A 25-year-old male presented with New York Heart Association Class IV symptoms and severe pulmonary hypertension. He had undergone aortic valvotomy at age 1 month, aortic

valve replacement at 6 years, mitral valve replacement at 10 years, and aortic and mitral valve replacements with mechanical St Jude valves with aortic and mitral annulus enlargement at 14 years.

Echocardiography demonstrated paravalvar leaks around both prostheses. The leaks were deemed mild to moderate but difficult to quantify because of shielding. Gradients across aortic and mitral prostheses were low, 10 mm Hg and 7.5 mm Hg, respectively. On right heart catheterization, pulmonary vascular resistance (PVR) was 15 Wood units (Wu), with a pulmonary artery (PA) pressure of 103/52 mm Hg, mean 72 mm Hg, and a transpulmonary gradient of 50 mm Hg. Pulmonary vascular resistance remained elevated at 16.6 Wu after 100% oxygen

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**Abbreviations and Acronyms**

AR	aortic regurgitation
LVEF	left ventricular ejection fraction
MR	mitral regurgitation
NO	nitric oxide
PA	pulmonary artery
POD	postoperative day
PVR	pulmonary vascular resistance
Wu	Wood units

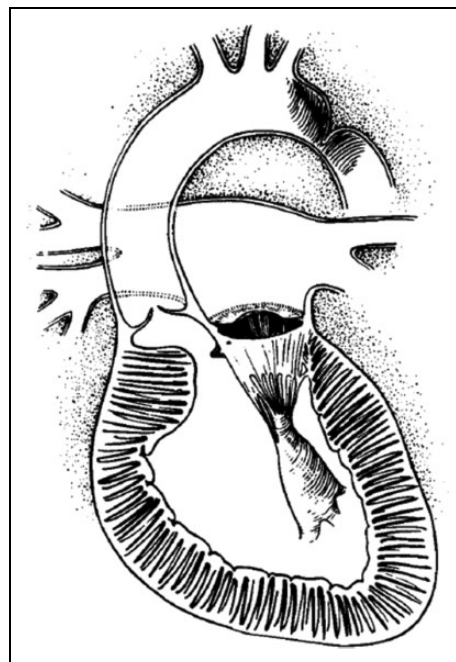
for 10 minutes but decreased to 7.0 Wu after 100% oxygen + 40 ppm nitric oxide (NO). Cardiac index by thermodilution was  $1.92 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$  at baseline (room air),  $1.95 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$  on 100% oxygen, and  $4.27 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$  on 100% oxygen + 60 ppm NO.

Over the next month, he deteriorated further and was started on milrinone, and sildenafil was increased, hoping to make heart transplant only possible. However, repeat right heart catheterization after 3 months showed PVR still 15 Wu, transpulmonary gradient of 42 mm Hg, and cardiac index of  $1.58 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ . He was readmitted to the hospital to complete heart–lung transplant assessment.

Transthoracic echocardiography revealed normal left ventricular ejection fraction (LVEF) of 57%, dilated right ventricle with moderate dysfunction, 1+ mitral regurgitation (MR; maybe underestimated due to shielding) with peak and mean gradients of 27 and 13 mm Hg, respectively. The aortic valve was reported to have 1 to 2+ paravalvular aortic regurgitation (AR) with peak and mean gradients of 15 and 10 mm Hg, respectively. A transesophageal echocardiogram the following day showed very different results: LVEF was 60%, and MR was read as severe 4+ paravalvular leak. The AR was also read as 4+. Repeat valve surgery was decided.

A fifth-time sternotomy was performed. The mitral valve prosthesis was found dehisced corresponding to one-third of annulus circumference, and the aortic valve prosthesis had a 1-cm wide anterior leak. Reusing the previously reconstructed intervalvular fibrosa, the mitral valve was replaced with a 25-mm On-X valve (Life Technologies, Inc, Austin, Texas, USA) and the aortic valve replaced with 23-mm On-X valve. The patient had a relatively smooth postoperative course with manageable pulmonary hypertension responding to treatment, extubated on day 2, intensive care unit stay of 5 days, and hospital stay of 2 weeks. He was managed with milrinone in the operating room and immediately postoperatively. On postoperative day (POD) 3, the milrinone was stopped, but systolic PA pressures increased to 90 to 100 mm Hg. Milrinone was restarted and sildenafil was initiated at a dose of 50 mg twice a day. This was increased to 40 mg three times a day on POD 4, and the following day the milrinone was stopped and PA pressures remained stable (approximately 75/35 mm Hg).

Right heart catheterization after 18 months showed PA pressure of 58/23 mm Hg, transpulmonary gradient of 16 mm Hg, PVR of 2 Wu, and cardiac index of  $4.01 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ . The patient is three years postoperative and has had no readmissions



**Figure 1.** Original drawing describing the lesions associated with Shone syndrome including supravalvar mitral membrane, parachute mitral valve, subaortic stenosis (membranous or muscular), and coarctation of the aorta.

and does not want additional cardiac catheterizations. His breathing ability and energy level are good, has no limitations, and has graduated from college.

## Case 2

A 22-year-old woman presented with Shone syndrome, including bicuspid aortic valve, subvalvular and supravalvular aortic stenosis, mitral stenosis, and coarctation of the aorta. The coarctation was repaired at age 11 months. Five years later, she had a 10 mm Hg residual coarctation gradient, moderate supravalvular, valvular, and subvalvular aortic stenosis, mild mitral stenosis, and a positive stress test. She underwent resection of a subaortic membrane and repair of supravalvular aortic stenosis and an open mitral valvotomy. Subsequently, she developed increasing AR and underwent aortic valve repair with autologous pericardial extension of the aortic cusps at age 16 years.

At age 20 years, the patient returned with progressive dyspnea during pregnancy. A limited right heart catheterization demonstrated PVR of 13 Wu on room air and 12 Wu on 100% oxygen. She was treated with vasodilator therapy including hydralazine, nitrates, and carvedilol and delivered a healthy baby via planned C-section. Patient was lost to follow up until thirteen months later when she was hospitalized with group B streptococcal sepsis at which time a transesophageal echocardiogram showed no evidence of endocarditis but severe MR (two regurgitant jets, one central and one suggesting a hole in the anterior leaflet), moderate AR, and evidence of severe pulmonary hypertension. The right ventricle was enlarged with

significant dysfunction. On repeat catheterization, PVR was 22.8 Wu on room air with good response to both oxygen (PVR 12.6 Wu) and NO (PVR 8.0 Wu), no gradient across the mitral valve, aortic valve, or the coarctation but markedly elevated PA wedge pressure (27 mm Hg) and left ventricular end diastolic pressure (25 mm Hg). She was hospitalized and referred for heart–lung transplant. Based on the severity of the MR, it was decided, after extensive discussions, to offer conventional valve surgery.

Preoperatively and on intraoperative transesophageal echocardiography, the AR was deemed not severe enough to justify replacement. On exploration, the patient was found to have complete avulsion of the P1 scallop from the annulus of the mitral valve leaflet. The valve was repaired with an autologous pericardial patch with no residual MR. After protaminization, a pulmonary hypertensive crisis resulted in circulation collapse and required recannulation and return to cardiopulmonary bypass. The mitral valve repair was inspected and found intact, and we decided to replace the aortic valve with a 19-mm On-X mechanical valve. Inhaled NO and milrinone were started in the operating room. She was transferred to the intensive care unit on 100% fraction of inspired oxygen (FIO<sub>2</sub>), inhaled NO, and significant inotropic support. During the first postoperative week, the patient had pulmonary hypertensive crises, and junctional ectopic tachycardia and ventricular tachycardia were treated with amiodarone. On POD 1, the patient had a coughing episode that resulted in systemic PA pressures. Chemical paralysis and increased sedation were initiated. Inhaled epoprostenol and diuresis were added with good responses. On POD 5, the patient had a second pulmonary hypertensive crisis. Intravenous epinephrine and enteral sildenafil were started. On POD 6, inhaled NO was discontinued, and on POD 7 inhaled epoprostenol was stopped. By POD 8, her pulmonary hypertension was well controlled and her rhythm was stable, so she was extubated. Intensive care unit stay was 13 days and hospital stay 19 days.

After discharge, recovery to full functionality was rapid, and repeat echocardiogram and heart catheterization six months postoperatively demonstrated normalized heart function and well-functioning valves and almost normalized pulmonary pressures (33/16 mm Hg, PVR 2.3 Wu on 100% O<sub>2</sub>).

## Comment

We presented two cases of Shone syndrome with severe pulmonary hypertension and high PVR referred for heart–lung transplantation. Conventional valve surgery addressing the severe left-sided valve lesions (dominated by severe MR) resulted in rapid reversal of the pulmonary hypertension and PVR in both.

There are several publications testifying to the complexity of patients with Shone syndrome. Bolling et al<sup>5</sup> described 28 patients treated with surgical correction over 23 years, 19 had the full syndrome and ultimately underwent a total of 84 operations without mortality and low late mortality with mean follow-up of 5.7 years.

Later management is, however, ill defined, with a general goal to delay development of severe pulmonary hypertension and move to transplant when needed. The severity of mitral valve involvement seems most important in determining the long-term outcome.<sup>1,5</sup> In Bolling's series, severity of left ventricular inflow obstruction was inversely related to long-term outcomes. Delmo Walter et al<sup>6</sup> examined the long-term outcomes of mitral valve repair in 45 children with Shone syndrome. Survival was 98% at 30 days and 70% at 15 years, and freedom from reoperation was 53% at 15 years (mean follow-up 17.5 ± 1.5 years). Growth of the mitral annulus was demonstrated and most patients had only mild stenosis. If the mitral valve grows, replacement should be delayed if possible.<sup>7</sup> It seems clear that the pulmonary hypertension is secondary to mitral valve dysfunction, which in most cases is stenosis but in both our cases was regurgitation. Regurgitation is easier to deal with surgically!

Our first case also illustrates the difficulties in diagnosing MR and AR in patients with mechanical prostheses. With this severity of regurgitation, both pulmonic and systemic circulations are driven by the right ventricle, a kind of “reversed Fontan circulation” limiting the regurgitant volumes across left-sided valves. Once severity of the valvular lesions was clear, the decision to perform valve surgery was still controversial in the first case but easy in the second. However, heart–lung transplantation is not readily available and any chance to avoid that should be attempted. Both our cases confirmed that even very severe pulmonary hypertension with an important arterial component is reversible when secondary to mitral valve disease. Since Braunwald's publication in 1965 about reversibility of severe pulmonary hypertension in patients with mitral stenosis after mitral surgery, almost no degree of pulmonary hypertension secondary to mitral valve disease is considered a contraindication to surgery provided the valve lesion is severe enough.<sup>8</sup>

The proposed pathophysiology of pulmonary venous hypertension, or postcapillary hypertension, involves passive increases in left atrial and pulmonary venous pressure. This results in congestion of the pulmonary venous bed, leading to endothelial dysfunction (decreased NO and increased endothelin 1 which both contribute to vasoconstriction) and eventual right ventricular failure.<sup>9</sup> Interestingly, the response to vasodilators in postcapillary pulmonary hypertension is mixed (unlike reactive pulmonary hypertension), and currently it is not recommended to use prostaglandins in the diagnosis, as they may worsen the hypertension and cause rapid pulmonary edema. It has been suggested that the diagnosis of isolated postcapillary pulmonary hypertension can be made when the pulmonary capillary wedge pressure is >15 mm Hg and the diastolic pressure difference (diastolic PA pressure – mean pulmonary capillary wedge pressure) is <7 mm Hg.<sup>10</sup> The variable response to vasodilators and the relatively rapid reversal of the vasculopathy may be due to the heterogeneous etiologies of the disease (valvular, left ventricular diastolic dysfunction, and heart failure), the passive nature, a less robust vasoactive response in the pulmonary venous system, and relatively long period over which pulmonary venous vascular remodeling occurs.

Technically, these operations can be anticipated to be difficult because of multiple previous operations and possible need for enlarging both valve annuli. Peri- and postoperatively, we had to deal with the pulmonary hypertension and pulmonary hypertensive crises.

With better early management, we will encounter more patients with Shone syndrome presenting with complex pathologies. It is good to know that despite severe secondary pulmonary hypertension and elevated PVR, conventional valve surgery can result in reversal and excellent outcomes.

### Declaration of Conflicting Interests

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