

Received: 2017.06.11
Accepted: 2017.07.06
Published: 2017.12.05

Pulmonary Vein Stenosis Following Single-Lung Transplantation Successfully Treated with Intravascular Ultrasound-Guided Angioplasty and Stent Placement

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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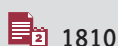
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Conflict of interest: None declared

Patient: Female, 60
Final Diagnosis: Pulmonary vein stenosis following single lung transplant
Symptoms: Dyspnea on exertion and dry cough
Medication: —
Clinical Procedure: Balloon angioplasty and stenting of the left common pulmonary vein
Specialty: Cardiology

Objective: Unusual clinical course
Background: Pulmonary vein stenosis (PVS) is a rare event following lung transplantation, but is a serious complication that requires prompt diagnosis and treatment.
Case Report: We describe the case of a 60-year-old woman who underwent single-lung transplantation for idiopathic pulmonary fibrosis (IPF). One year following her single-lung transplant, she was admitted to the hospital for hypoxemic respiratory failure. The results of quantitative lung perfusion scintigraphy (LPS) raised the possibility of a diagnosis of PVS. Computed tomography angiography (CT angiography) of the chest identified more than 50% stenosis of the left common pulmonary vein at the anastomotic site with the left atrium. She was successfully treated with angioplasty and stent placement guided by intravascular ultrasonography. Post dilatation of the PVS, the pulmonary venous pressure gradient decreased from 12–16 mm Hg to 3–4 mm Hg. At three-month follow-up, the patient reported resolution of her shortness of breath. In support of this case report, we review the management of four previously reported cases from the literature of lung transplantation associated with PVS.
Conclusions: PVS should be considered in the differential diagnosis of lung transplant patients who present with worsening dyspnea. Quantitative LPS and CT angiography are important in the diagnosis of PVS. Successful management of PVS, with salvage of the transplanted lung and the prevention of further surgical interventions, may be achieved with intravascular ultrasound-guided angioplasty and stent placement.

MeSH Keywords: Angioplasty • Lung Transplantation • Postoperative Complications • Stents • Ultrasonography, Interventional

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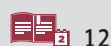
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Background

Worldwide, as of 2015, more than 55,000 adult lung transplantations had been performed [1]. The most common indication for lung transplantation is chronic obstructive pulmonary disease (COPD) [1]. However, variants of interstitial lung disease (ILD) account for approximately 30% of all lung transplantations; ILD includes idiopathic pulmonary fibrosis (IPF), a condition formerly known as usual interstitial pneumonia (UIP) [1]. Although the overall patient survival rates following lung transplantation continue to improve, there remain certain complications of lung transplantation surgery that can lead to graft failure or patient mortality [1]. Clinicians involved in the care of patients undergoing lung transplantation are advised to be aware of the common and the uncommon causes of postoperative complications [1].

Although pulmonary vein stenosis (PVS) is a well-recognized complication of catheter ablation procedures currently used to treat atrial fibrillation, PVS following lung transplantation is a rare, but potentially fatal complication, which requires swift identification and treatment [2]. Left untreated, PVS can lead to failure of the transplanted lung [3]. Clinically, PVS is a challenging diagnosis as it presents with similar clinical symptoms to other post-transplantation complications, such as reperfusion edema, infection and acute graft rejection [4,5]. The sutured surgical junction between the allograft pulmonary vein and the recipient atrium is a particularly vulnerable site for PVS due to fibrosis [3]. Currently, there are no clear guidelines on the management of patients with PVS following lung transplantation, but rapid identification of PVS and other vascular complications prevent the need for re-transplantation or surgical revision [3].

We describe a case of PVS in a 60-year-old woman who underwent single-lung transplantation for IPF successfully treated with intravascular ultrasound-guided angioplasty and stent placement.

Case Report

A 60-year-old woman from Kuwait, who was a life-long non-smoker, initially presented in 2012 for clinical evaluation following a previous diagnosis of idiopathic pulmonary fibrosis (IPF), made on surgical lung biopsy at another institution. Her symptoms included dyspnea on exertion and a dry cough, which failed to improve, despite long term use of prednisone, azathioprine and continuous home oxygen therapy.

Her past medical history included hypertension and a previous total abdominal hysterectomy complicated by postoperative pulmonary embolism, for which she was treated with

warfarin. Her family history was significant for IPF, which was diagnosed in one of her sisters.

At our institution, initial pulmonary function tests showed a severe restrictive pattern of pulmonary function, with a forced vital capacity (FVC) of 31% predicted (0.8 L). A chest X-ray showed reduced lung volumes and bilateral reticular lung changes, consistent with pulmonary fibrosis. Her initial echocardiogram at presentation was significant for an estimated ejection fraction (EF) of 63%, and grade 1 diastolic dysfunction that indicated mild diastolic heart failure, and normal right ventricular systolic function, with no intracardiac shunts. The estimated right ventricular systolic pressure was 33 mm Hg consistent, with normal pulmonary artery pressure (PAP).

Approximately two years after her inclusion on the lung transplant waiting list, the patient underwent left single-lung transplantation without cardiopulmonary bypass. Following transplantation, she was doing well at the time of hospital discharge, and by day 24, she no longer required supplemental oxygen.

At about a year following single-lung transplantation, the patient was admitted for acute hypoxemic respiratory failure, which was initially thought to be due to pneumonia and graft rejection. She required intermittent high-flow oxygen and noninvasive positive-pressure ventilation to relieve her symptoms. Systemic steroids and diuretic treatment produced little clinical response. Repeat bronchoscopy demonstrated normal bronchial surgical anastomosis and scant mucoid secretions throughout the tracheobronchial tree. Right heart catheterization showed normal cardiac output, mild pulmonary hypertension, and a slightly elevated pulmonary capillary wedge pressure. A quantitative perfusion lung scan (PLS) showed 46% perfusion to the transplanted left lung. Computed tomography (CT) angiogram of the chest identified stenosis of the left common pulmonary vein (Figure 1).

In the transplanted left lung, although the bronchial anastomosis was patent, there was a greater than 50% luminal stenosis at the junction of the left pulmonary vein and the atrium, which was presumed to be at the only anastomotic site. This impedance to pulmonary venous return was thought to be the cause of the perfusion defect that caused reduced blood flow to the allograft. Transthoracic echocardiography (TTE) showed normal left ventricular systolic function, and an EF of $66 \pm 5\%$ (2D Simpson's biplane) with baseline left ventricular diastolic function consistent with abnormal relaxation (grade 1 diastolic heart failure). No transesophageal echocardiography (TEE) was performed at this time.

The patient successfully underwent percutaneous balloon angioplasty and stenting of the left common pulmonary vein (Figure 2). A 9 French long sheath was placed in the left femoral

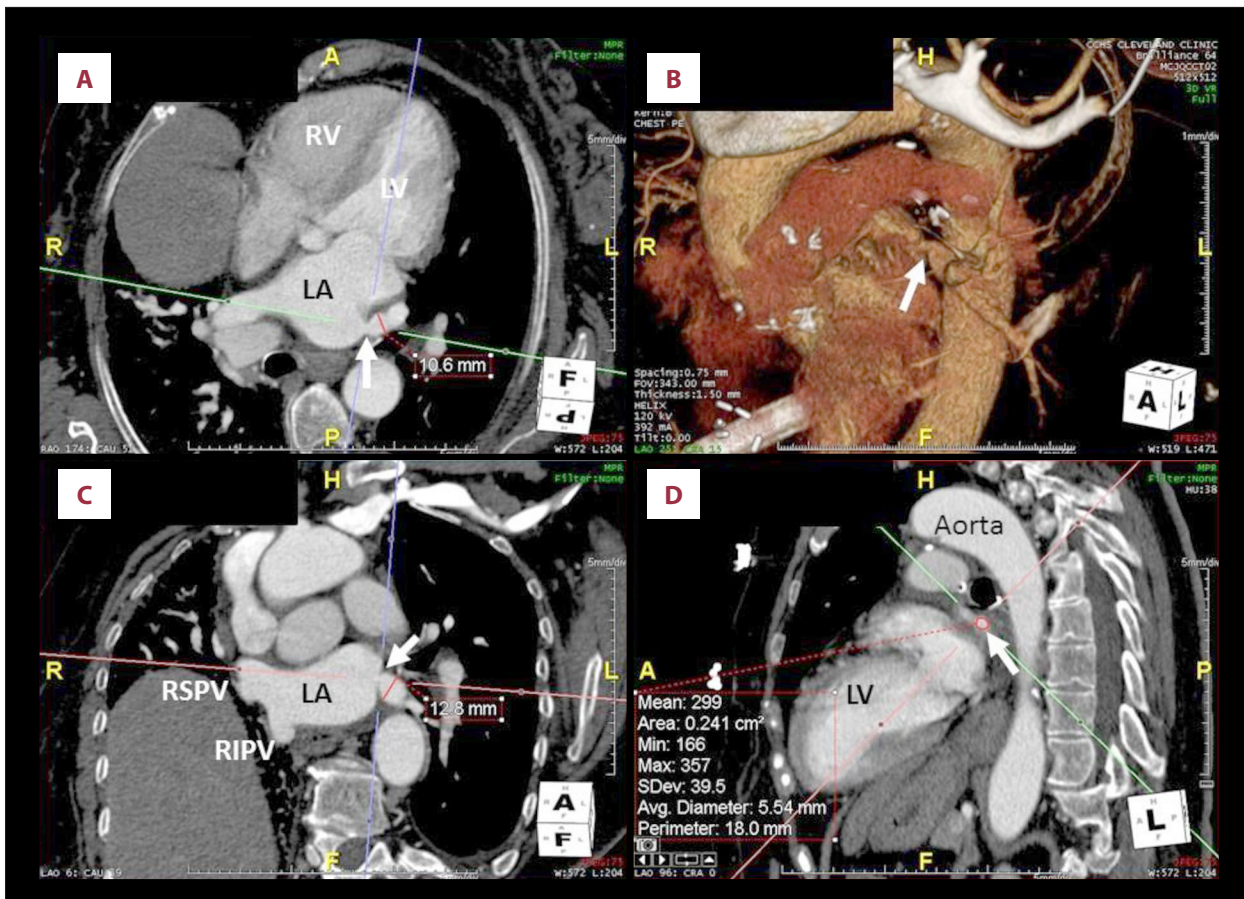


Figure 1. Contrast-enhanced computed tomography (CT) angiograms. Stenosis of the common pulmonary vein (white arrow) is seen in: (A) The transverse plane with the post-stenotic segment measuring 10.6 mm; (B) The three-dimensional (3D) reconstruction; (C) The coronal plane with the post-stenotic segment measuring 12.8 mm; (D) The sagittal plane with the post-stenotic area of 0.24 cm², average diameter of 5.54 mm and perimeter of 18.0 mm. RIPV – right inferior pulmonary vein; RSPV – right superior pulmonary vein; RV – right ventricle; LV – left ventricle; LA – left atrium.

vein and an AcuNav™ (Siemens Medical Solutions, USA) intracardiac echocardiography probe was advanced into the right atrium. The atrial septum was punctured with a Brockenbrough® curved needle (Medtronic Inc., MN, USA) and crossed using a Mullins® introducer sheath (Medtronic Inc., MN, USA). The Mullins® sheath was then removed and exchanged for a dilator over a Torayguide® guidewire (Toray International Inc., NY, USA). The interatrial septum was dilated, and an Agilis® medium (22.4 mm) curve sheath (St Jude Medical, MN, USA) was inserted. Through the Agilis® sheath, a 4 French guide catheter with a loaded 300 cm Balance Middle Weight (BMW®) 0.014" outer diameter wire (Abbott vascular, Santa Clara, CA, USA) was advanced. The left common pulmonary vein was selectively engaged, and angiography showed an almost occlusive stenosis at the ostium of the left pulmonary vein. A pressure gradient of 12–16 mmHg was found between the left pulmonary vein and left atrium. The BMW® coronary wire was advanced distally, and the guide catheter was removed.

To better understand the nature of the lesion and estimate the appropriate stent size, an intravascular ultrasound (IVUS) was performed, which showed a critical ostial stenosis with surrounding fibrotic changes (Figure 3). The BMW® wire was initially in a small branch of the pulmonary vein; based on IVUS navigation, it was rewired into a larger branch that was 9.5–10 mm in size. This vessel was stented with a 10×29 mm Palmaz® Genesis® (Cordis, Cardinal Health, Fremont, CA, USA) balloon expandable stent at 4 atmospheric pressure (atm). The ostium was flared to 6 atm. Post dilatation, the vein stenosis was reduced to less than 10% and the pressure gradient between the left pulmonary vein and left atrium was reduced to 3–4 mm Hg. The patient tolerated the procedure well. She was treated for one month with triple antithrombotic therapy that included aspirin, clopidogrel, and warfarin followed by long term treatment with aspirin and warfarin.

Following intravascular ultrasound-guided angioplasty and stent placement, the patient reported a significant improvement in

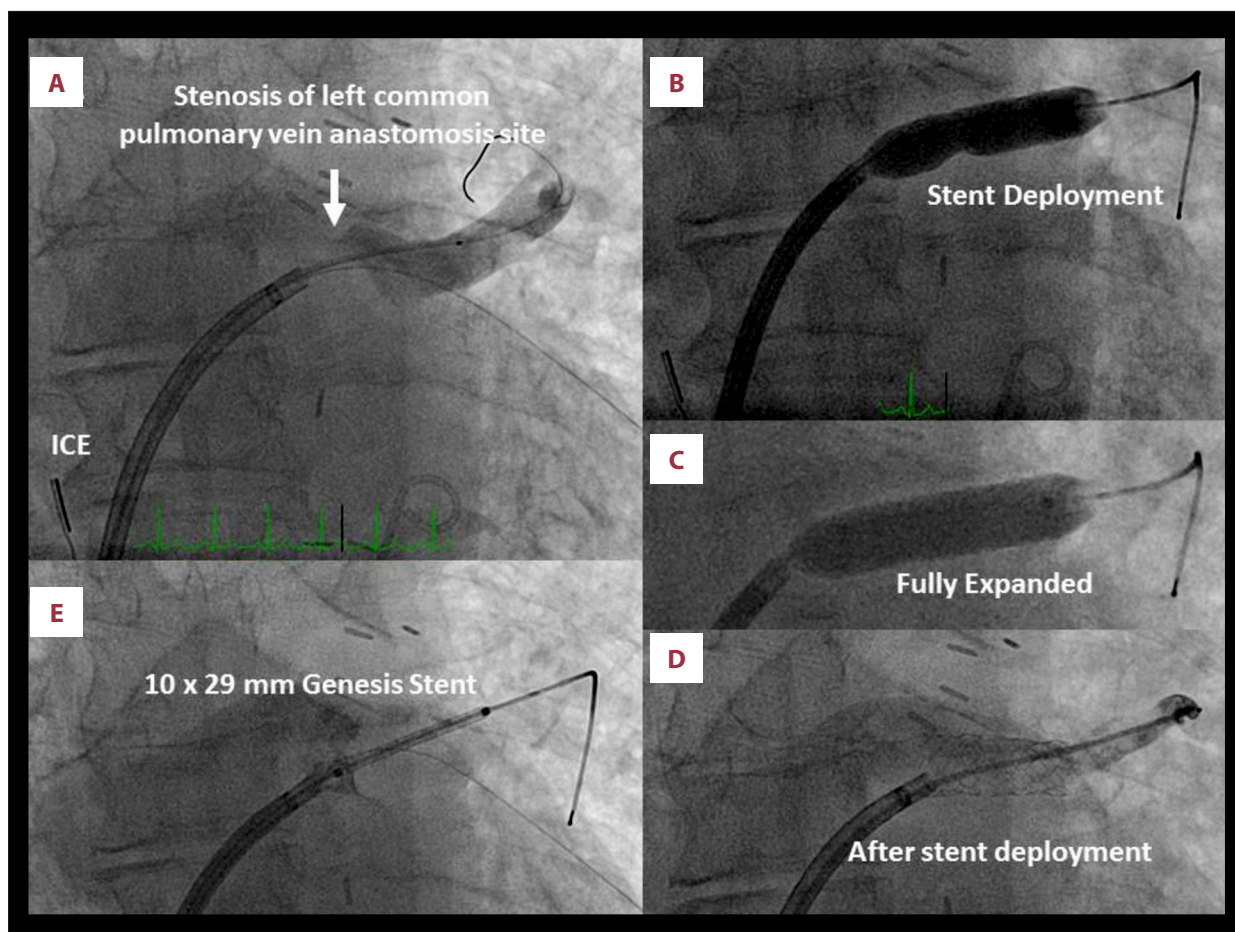


Figure 2. Pulmonary venous angiograms. (A) Stenosis of the left common pulmonary vein anastomosis site is shown (white arrow); (B) Stent deployment is shown; (C) The fully expanded balloon is shown; (D) The angiogram appearance following stent deployment; (E) The 10x29 mm Genesis® (Cordis, Cardinal Health, Fremont, CA, USA) balloon expandable stent is shown in place.

her respiratory symptoms and was discharged three days later, and required a markedly lower oxygen requirement than on initial presentation. The patient reported resolution of her shortness of breath at three-month follow-up.

Discussion

Pulmonary vein stenosis (PVS) following lung transplantation is a rare event, which may explain the lack of consensus regarding the optimal management. The treatment options for PVS include conservative measures, revision at the site of anastomosis, re-transplantation, or percutaneous balloon angioplasty and stent placement [3].

There have been a few cases of stent implantation in PVS following lung transplantation. In support of this case report, the management of four previously reported cases from the literature of lung transplantation associated with PVS have been reviewed.

Mydin et al. described the case of a 62-year-old man who had right PVS following a single-lung transplantation for IPF [6]. In this case, balloon angioplasty was performed, but stenting was unsuccessful due to technical issues, and the patient's symptoms recurred after two months [6]. Gaubert et al. reported a patient with left pulmonary artery stenosis, which recurred with balloon angioplasty alone [7]. However, repeat angioplasty followed by stent placement lead to resolution of stenosis [7]. A case report published in 2009 showed similar findings following stent insertion [8]. Stenting of pulmonary veins has been successful when large stents (≥ 10 mm) are used in patients with post-ablation stenosis [9]. On review of the literature, we found that the timing of onset of PVS following lung transplantation was quite variable and has been reported to occur both early and late following transplantation (Table 1). Our patient was diagnosed with PVS nearly one year after lung transplantation.

In most previously reported cases of post-lung transplant PVS, patients deteriorated in the early postoperative period

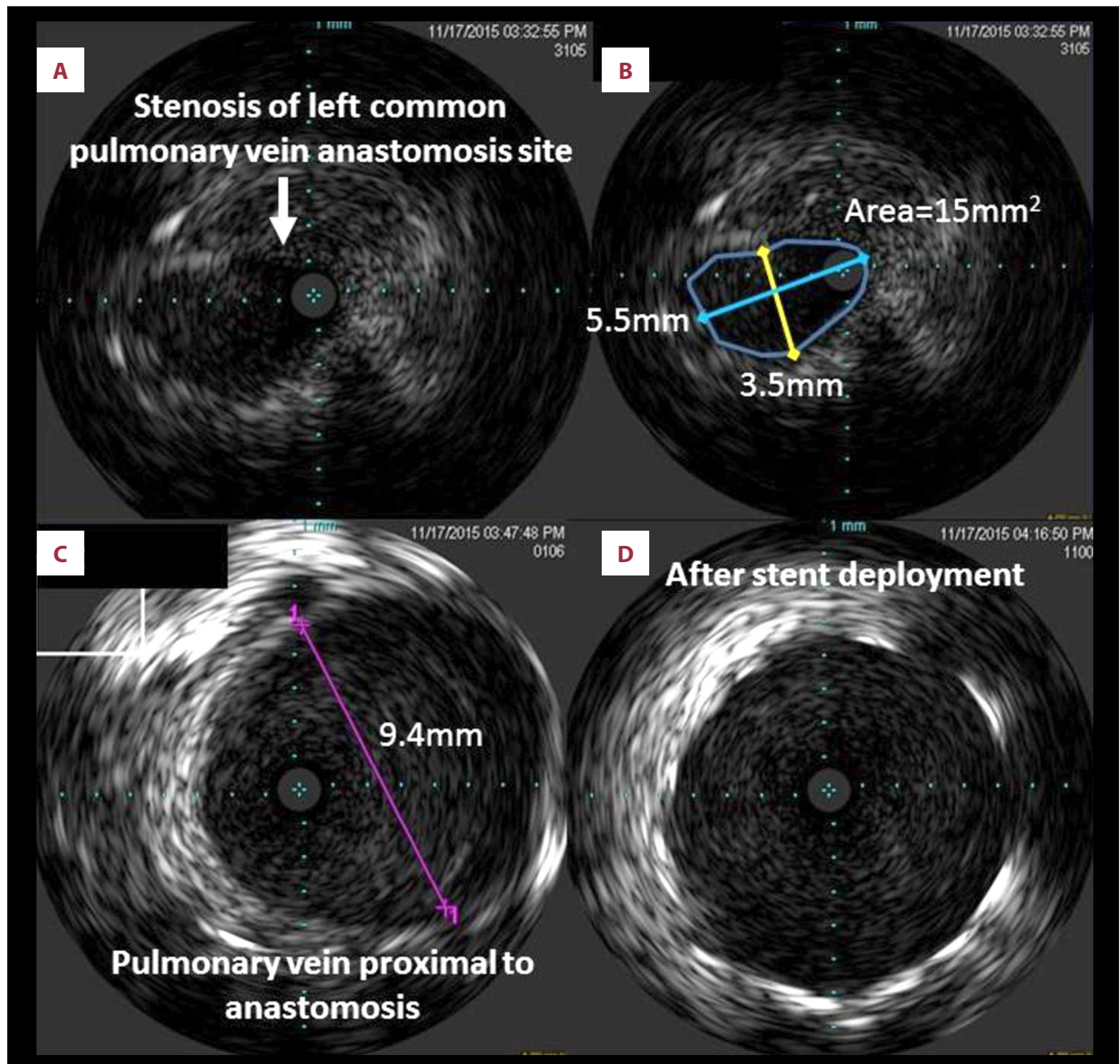


Figure 3. Intravascular ultrasonography (IVUS) images of the left common pulmonary vein. (A) showing stenosis of the left common pulmonary vein anastomosis site (white arrow); (B) showing the stenotic segment area of 15 mm², maximum diameter of 5.5 mm and minimum diameter of 3.5 mm; (C) Pulmonary vein proximal to the anastomosis measuring 9.4 mm and (D) after stent deployment.

as early as two weeks after surgery. It is unclear why the stenosis appeared more rapidly in these patients, although some cases reported technical difficulties during the surgery itself that were related to anatomic challenges. González-Fernández et al. suggest that transesophageal echocardiography (TEE) is a useful, noninvasive imaging modality that can rapidly identify postoperative anastomotic compromise, as rapid identification of PVS by TEE can allow for rapid surgical intervention, avoiding a delay in diagnosis and management [10]. Michel-Cherqui et al. also found utility in the use of TEE intraoperatively during lung transplantation surgery itself, as it allowed

measurements of peak systolic flow velocity in the pulmonary vein and, if elevated, the pressure gradient across the anastomosis, to allow immediate identification and correction of the PVS [11]. However, it should be noted that the use of TEE in this previous study allowed for greater visualization of the right-sided anastomosis compared with the left [11].

As the present case has shown, the use of intravenous ultrasound (IVUS) is helpful to correctly deploy the venous stent in the optimal location covering the ostium and also confirms optimal stent expansion. IVUS can also help to understand the

Table 1. Characteristics of four previously reported cases and the present case of pulmonary vein stenosis (PVS) following lung transplantation treated with balloon angioplasty or stenting.

Author (Ref #)	Age (yrs) Gender	Transplantation	Level of Stenosis	Possible Etiology	Timing of diagnosis	Stenosis size seen on CT	Gradient across stenosis (mm of Hg)	Intervention*	Outcome
Mohamed [6]	62 M	Rt. Single	RIPV	Fibrosis and shrinkage of pericardial repair of anastomosis	12 months	2 mm	7	Balloon dilatation	Recurrence at 2 months
Zimmerman [5]	42 M	Rt. Single	RSPV	Intra-op revision of PV anastomosis	16 days	NA	NA	Balloon dilation and a bare metal stent placement	Resolution of symptoms at 6 mths F/U
Pazos-Lopez [12]	31 F	Lt. Single	LPV	NA	15 days	50%	20	Bare metal stent placement	Resolution of symptoms at 20 days F/U
Loyalka [4]	56 M	Lt. Single	LIPV	NA	Early postoperative period	0.17 cm ²	8	Balloon dilation and a bare metal stent placement	Resolution of symptoms at 1 mmth F/U
Our case	60 F	Lt. Single	Lt. common PV	Severe intimal hyperplasia consistent with scar formation after suturing at anastomotic site	14 months	>50%	12–16	Stent placement	Resolution of symptoms at 3 mths F/U

Rt. – right; Lt. – left; PVS – pulmonary vein stenosis; RIPV – right inferior pulmonary vein; RSPV – right superior pulmonary vein; LIPV – left inferior pulmonary vein; atm – atmosphere; F/U – follow-up. * Refer to the individual case for the type of balloon catheter and stent used.

mechanism of stenosis of the pulmonary vein by direct visualization of the stenotic lesion. In our patient, there was severe intimal hyperplasia consistent with fibrosis or scar formation after suturing, rather than complications of the surgical anastomosis. Loyalka et al. confirmed benefit from the use of IVUS in the management of a case of lower left PVS which was treated with percutaneous stenting [4]. Another imaging modality that has been shown to be useful, is TEE, both in the diagnosis of PVS and for visual guidance during angiography and stent placement [12]. With the technique of TEE, peak echo gradients can be monitored to ensure successful stent placement and postoperative vein patency. In this case, we used intracardiac echocardiography, which was helpful for trans-septal puncture and stent placement and allowed for the procedure to be completed with conscious sedation.

Conclusions

Pulmonary vein stenosis (PVS) is a rare complication of lung transplantation and can mimic other postoperative complications. The complication of PVS has greater clinical relevance in recipients of single-lung transplantation with single venous anastomosis. Quantitative perfusion lung scan can aid the diagnosis of PVS, and the diagnosis can be confirmed by computed tomography (CT) angiography. Although guidelines for the optimum treatment of post lung transplantation PVS are still awaited, percutaneous angioplasty and stent placement offer a less invasive treatment approach and potential salvage of the lung allograft that can avoid re-transplantation.

Conflicts of interest

None.

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