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CASE REPORTS

INTERMEDIATE

CLINICAL CASE

Constrictive Pericarditis After Lung Transplantation

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ABSTRACT

As a rare complication after lung transplant, cardiac constriction should not be missed. Physical exam, echocardiography, and catheterization are essential for diagnosis A 65-year-old man with previous coronary artery disease and idiopathic pulmonary fibrosis underwent bilateral lung transplant and subsequently presented for progressive dyspnea and volume overload. Cardiac imaging and cardiac catheterization confirmed constriction, and complete pericardiectomy was performed. The patient had rapid resolution of heart failure symptoms. Pericardial constriction is a rare complication following lung transplant, and we provide a review of the literature and discussion of potential contributing factors. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:938–42) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 65-year-old man with a history of coronary artery disease and idiopathic pulmonary fibrosis status post-bilateral lung transplant (LTx) 1 year previously, was referred to cardiology for progressive ascites, lower-extremity edema, and exercise intolerance. LTx surgery was performed through bilateral anterior thoracosternotomy, and pericardium was opened anteriorly for cardiopulmonary bypass with cannulation at the level of ascending aorta and right atrium. The patient had delayed chest closure secondary to intraoperative myocardial edema and volume dependence with normal ventricular function. He required subsequent hospitalizations for recurrent right-sided pleural effusion and trapped right lung, eventually requiring video-assisted thoracoscopic surgery, followed by open right-sided thoracotomy with decortication. After lung mobilization off of the chest wall and removal of pleural rind, complete lung expansion was noted. At 8 months post-LTx, he experienced declining spirometry and received corticosteroids for nonspecific inflammation found on transbronchial biopsy.

LEARNING OBJECTIVES

- To recognize that pericardial constriction can be an early complication of lung transplant.
- To understand the role of invasive hemodynamics in the diagnosis of pericardial constriction.
- To learn the mechanism through which lung transplant may predispose to subsequent pericardial constriction.

PAST MEDICAL HISTORY

The patient's medical history included coronary artery disease status post-percutaneous coronary interventions to the left anterior descending (LAD)

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artery and right coronary artery (RCA), idiopathic pulmonary fibrosis (IPF) status post-bilateral LTx, post-transplant atrial tachycardia, hyperlipidemia, and stage 3 chronic kidney disease.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for dyspnea after LTx included infection, acute rejection, chronic lung allograft dysfunction (i.e., chronic rejection), airway stenosis, pleural complications, thromboembolic disease, and medical complications such as malignancy, cardiovascular, or renal disease (1). Such cardiovascular complications may include tricuspid regurgitation, cardiac tamponade, restrictive cardiomyopathy, cardiac infection, or post-operative heart failure (2,3). Pericardial disease should also be considered when dyspnea is accompanied by symptoms of right heart failure (2,4). Elevated jugular venous pressure without left cardiac disease or pulmonary hypertension raises suspicion for constrictive pericarditis, an infrequent complication with estimated incidence of 0.4% in patients following LTx (1). Since the late 1980s, there have been 20 reported cases of post-LTx cardiac constriction (**Table 1**) (1–6). It is challenging to differentiate post-surgical cardiac septal wall motion and post-operative respirophasic variation from significant constrictive physiology (7). Our differential diagnosis included post-operative abnormal septal motion, venous thromboembolic disease, pleural effusion, pericarditis, and pericardial effusion (8).

INVESTIGATIONS

Examination was significant for elevated jugular venous pressure with rapid x and y descents and bilateral lower-extremity edema. Transthoracic echocardiogram showed normal biventricular size and function, no evidence of elevated left-ventricular filling pressure, mitral valve thickening, and no pericardial effusion. The pulmonary artery systolic pressure was 39 mm Hg. Inspection of M-mode echocardiography was notable for posterior-wall flattening and presence of early diastolic septal notching. Computed tomography (CT) scan of the chest showed diffuse pericardial thickening (**Figures 1A and 1B**), coronary artery disease, stable post-transplant changes in the thoracic cavity, and a small amount of free fluid in the pelvis. Despite unremarkable pericardium on echocardiography (**Figures 1C and 1D**), clinical presentation and

ABBREVIATIONS AND ACRONYMS

CT = computed tomography
IPF = idiopathic pulmonary fibrosis
LAD = left anterior descending artery
LTx = lung transplant
LV = left ventricle
RCA = right coronary artery
RV = right ventricle

TABLE 1 Features of the Previously Reported Cases of Post-LTx Constrictive Pericarditis

Patient #	Age (yrs)/Sex	Indication for Lung Transplant	Time Since Transplant	CPB	RF for Pericarditis	First Author, Year (Ref. #)
1	43/F	Bronchiectasis	4 yrs	Yes	1. Single previous episode of acute cellular rejection 2. Bilateral lung transplant	Afshar et al., 2010 (4)
2	32/F	LAM	1 yr	No	1. CMV viremia 6 months post-transplant 2. Persistent leukopenia 3. Underlying LAM diagnosis 4. Bilateral lung transplant	Billings et al., 2009 (5)
3	34/M	Bronchiolitis obliterans	2 yrs	Yes	1. History of previous bilateral lung transplant for CF 2. Bilateral lung transplant	Karolak et al., 2010 (1)
4	53/M	COPD	6 months	No	1. Bilateral lung transplant 2. Use of powdered gloves intraoperatively	Sayah et al., 2015 (3)
5	47/F	LAM	9 months	No	1. Bilateral lung transplant 2. Use of powdered gloves intraoperatively 3. Underlying LAM diagnosis	Stephens et al., 2015 (6)
6	71/M	Emphysema	8 yrs	No	1. Bilateral lung transplant 2. Use of powdered gloves intraoperatively	Armstrong et al., 2019 (2)
7	70/F	IPF	9 months		1. Voriconazole antifungal ppx 2. Bilateral lung transplant 3. Underlying IPF	
8	49/M	CF	3 months	N	Unknown	
9	46/F	Asthma	19 months	Y	Unknown	

Patient level data not available. Of 1,234 patients who underwent lung transplantation, 10 patients (0.8%) developed constrictive pericarditis. Mean age was 59 ± 10.4 years, 90% were male, and mean time since transplant was 14 ± 9.5 months. Eight of 10 patients had bilateral lung transplant with clamshell thoracotomy. Three patients had their pericardium opened during the procedure. Eight of 10 patients had pulmonary fibrosis at baseline, suggesting that pulmonary fibrosis may be associated with increased risk for constrictive pericarditis.

CF = cystic fibrosis; CMV = cytomegalovirus; COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass; IPF = idiopathic pulmonary fibrosis; LAM = lymphangioleiomyomatosis.

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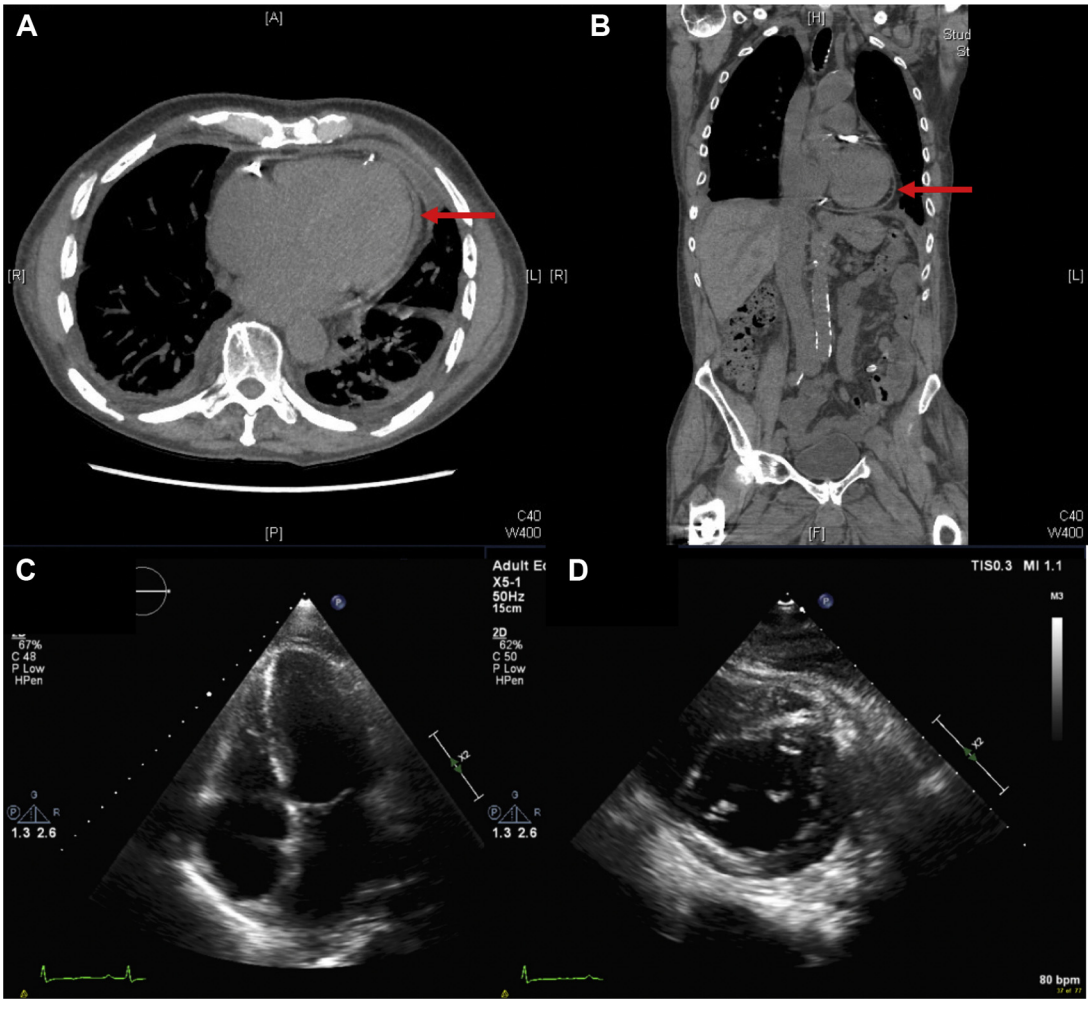
FIGURE 1 Computed Tomography Scan



(A) Axial and **(B)** sagittal slices of patient's noncontrast chest/abdomen/pelvis CT with **red arrows** highlighting thickened pericardium; and **(C)** apical 4-chamber and **(D)** parasternal short-axis views from transthoracic echocardiogram *without* visible pericardial effusion or pericardial thickening.

abnormal pericardial appearance on CT remained concerning for constriction. Simultaneous right- and left-heart catheterization showed end-diastolic pressure equalization and ventricular interdependence with dissociation of intrathoracic and intracardiac pressures (**Figure 2**), consistent with pericardial constriction. There was subtle right ventricle-left ventricle (RV-LV) interaction, with large pulsus paradoxus and ejection-time changes in aortic pressure tracing with respiration. Aortic pulse pressure was decreased with inspiration and pulmonary artery pressure increased. There was end-diastolic pressure equalization of 4 cardiac chambers. Limited coronary angiography showed distal fixation of the epicardial coronary arteries (9).

MANAGEMENT

The patient underwent complete surgical pericardiectomy through redo sternotomy from phrenic to phrenic medially and laterally and from ascending aorta and superior vena cava to diaphragm anteriorly. The operative report details stripping the pericardium off of the right atrium, RV, LV, and behind the left atrium between the pulmonary veins. Cardiopulmonary bypass was not used. Dense adhesions were

found around the heart, and there were several layers of fibrotic material encasing the heart (Figure 3). Central venous pressure decreased from 24 to 9 mm H_2O after pericardiectomy, and symptoms of volume overload improved rapidly.

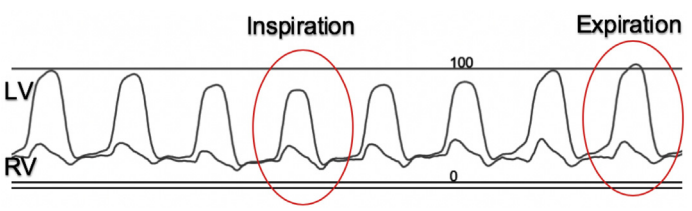
DISCUSSION

Constrictive pericarditis following LTx results from progressive pericardial inflammation and fibrosis, which leads to diastolic dysfunction and reduced cardiac output and occurs at a rate of 0.4% to 0.8% (2,4,6). Recommended therapy is complete surgical pericardiectomy, and post-pericardiectomy prognosis depends on cause of constriction (4). In the modern era, etiology of constriction continues to be a significant predictor of post-operative pericardiectomy survival, with previous chest radiation portending one of the worst prognoses and idiopathic pericarditis the best (10). Approximately 50% of patients with post-LTx constrictive pericarditis will manifest symptoms within the first year. Underlying pre-LTx pulmonary histopathology does not correlate with development of constriction (1).

Predisposing conditions for constrictive pericarditis include infections (tuberculosis, post-viral cases), previous cardiac surgery, preceding myocardial infarction, recent endo/epicardial procedures, chest radiation, rheumatologic conditions, malignancy, and chest trauma (11,12). Risk factors specific to the post-LTx population include cytomegalovirus reactivation post-LTx, uremia, and other infectious or drug-related causes. It has been proposed that the extent of pericardial manipulation (i.e., bilateral vs. unilateral lung transplant) correlates with risk for subsequent pericardial constriction, but a recently published series did not support this (only 3 of 10 patients with post-LTx constriction had their pericardium opened) (2,4). Because of immunosuppression required in the post-LTx patient population, patients may be uniquely vulnerable to constriction-causing infections (3,4). Infection was ruled out in our patient. Potential risk factors that contributed included his need for repeat decortication surgery after transplant, possible relapse of pericarditis triggered by post-transplant course of oral steroids, and cardiopulmonary bypass during his initial LTx surgery (13).

In the diagnosis of pericardial constriction, physical examination remains an essential part of the diagnostic process. Our patient did not demonstrate the characteristic septal bounce on echocardiography despite pericardial thickening visualized on CT. Cardiac catheterization confirmed hemodynamic findings of constriction.

FIGURE 2 Simultaneous Right- and Left-Heart Catheterization

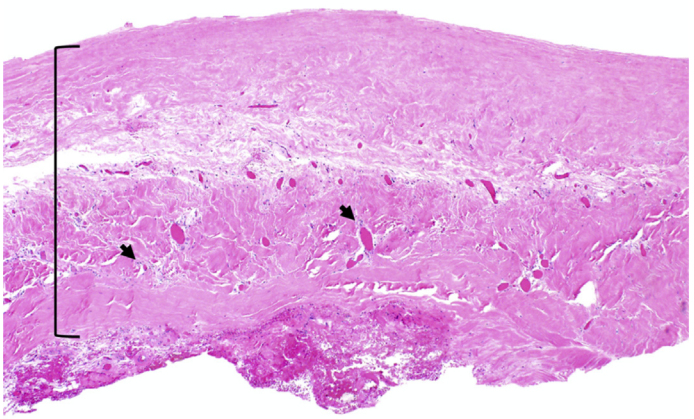


Pressure wires demonstrate ventricular interdependence and discordance of left ventricular (LV)-right ventricular (RV) peak systolic pressures and area-under-the-curve, consistent with pericardial constriction.

FOLLOW-UP

The patient had an uncomplicated post-operative course following pericardiectomy. Diuretics were discontinued after several weeks, without evidence of recurrent fluid retention. He follows closely with cardiology and pulmonary transplant providers for ongoing monitoring following pericardiectomy and previous LTx.

FIGURE 3 Photomicrograph



Dense, fibrotic pericardium after surgical pericardiectomy, showing features consistent with constrictive pericarditis including noncalcific fibrous thickening **(bracket)** and minimal nongranulomatous lymphoplasmacytic infiltrate **(arrows)** (hematoxylin and eosin stain, 40x original magnification). Reprinted with permission of Dr. Melanie Bois, Mayo Clinic Department of Pathology.

CONCLUSIONS

Although post-LTx rejection and opportunistic infection are the most common concerns when a patient in this population presents with progressive shortness of breath, recurrent pleural effusions, and volume overload, careful cardiovascular physical examination and diagnostic imaging are needed (2). Although rare, providers must include pericardial constriction in their differential diagnoses. Pericardial constriction is a rare complication following LTx, and underlying IPF or lymphangioleiomyomatosis, infection, and immunosuppression have been proposed as unique contributing factors in the post-LTx population (2,4).

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