Pulmonary Tuberculosis After Lung Transplantation*

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During a 5-year study period, we diagnosed pulmonary tuberculosis in two (2%) of 94 lung and heart-lung transplant recipients. Each infection occurred 3 months after bilateral lung transplantation in the presence of evidence implicating donor-to-recipient transmission of the pathogen. The radiographic patterns of pulmonary tuberculosis were subtle: narrowing of the middle lobe bronchus of the right lung caused by an endobronchial granulomatous mass (n=1) and a focal cluster of small nodules in the upper lobe of the left lung and small bilateral pleural effusions (n=1). Each patient achieved complete clinical and radiographic response after antituberculous therapy. We conclude that *Mycobacterium tuberculosis* may be transmitted directly by a donor lung and may involve bronchial mucosa, pulmonary parenchyma, and pleura.

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Key words: immune suppression; lung infection; lung transplantation

Abbreviations: PPD= purified protein derivative

The donor lung is unique in its ability to transmit respiratory infections directly into the recipient thorax.\textsuperscript{1,2} Reactivation of pulmonary tuberculosis in donor lungs is a potentially serious complication after lung transplantation, but has been reported infrequently.\textsuperscript{3-6} In the present series, we report 2 (2%) of 94 lung and heart-lung transplant recipients who developed pulmonary tuberculosis in the early postoperative period after lung transplantation and in whom evidence implicated donor-to-recipient transmission of the infection.

**Methods**

The study population consisted of 94 consecutive adult patients who underwent successful lung or heart-lung transplantation at our institution between 1989 and 1994. Of these 94 patients, 62 received a single-lung transplant for emphysema (n=51), pulmonary fibrosis (n=7), or pulmonary hypertension (n=4). Twenty-four patients received bilateral lung transplants for cystic fibrosis (n=17), pulmonary hypertension (n=5), or bronchiectasis (n=2). Eight patients received combined heart-lung transplants for pulmonary hypertension. Fifty-one (54%) transplant recipients were women and 43 (46%) were men. Mean age at the time of surgery was 43.5±15 years (range, 17 to 66 years).

All patients except one were purified protein derivative (PPD)-negative before transplantation. (The only PPD reactor was a single-lung transplant recipient who had completed 1 year of isoniazid prophylactic therapy 10 years before transplantation). PPD testing was not routinely performed after transplantation. Duration of follow-up for all patients was 2.1±1.4 years (range, 0.5 to 5.1 years) and follow-up was complete in each patient. During the study period, 2 of 94 (2%) lung transplant recipients developed pulmonary tuberculosis.

**Case Reports**

**Case 1**

A 27-year-old man underwent bilateral lung transplantation for severe bronchiectasis as a consequence of cystic fibrosis. The donor was a 19-year-old New York City resident who sustained a gunshot wound to the head while intoxicated. The explanted recipient lungs showed severe bronchiectasis and acute and chronic pneumonitis. Cultures of the explanted lungs grew two species of mucoid Pseudomonas. There was no evidence of granuloma formation, and cultures for fungi and mycobacteria were negative. The patient received a standard immune suppression regimen of cyclosporine, azathioprine, and prednisone.\textsuperscript{9} During his 4-week hospitalization, the patient was housed in a single room on a cardiac surgical floor. Postoperative recovery was uneventful except for a single episode of mild acute rejection (grade A\textsuperscript{2})\textsuperscript{10} 3 weeks after surgery for which the patient received an infusion of methylprednisolone (1 g/d) for 3 days followed by oral prednisone, tapered over 10 days, back to a baseline dosage of 0.1 mg/kg/d.

Three months after surgery, he complained of high fevers and myalgias but had no specific respiratory symptoms. Fiberoptic bronchoscopy revealed a smooth, round endobronchial mass protruding from the orifice of the right middle lobe (Fig 1, bottom). In retrospect, the chest radiograph showed subtle middle lobe bronchial narrowing of the right lung (Fig 1, top). Biopsy of the mass revealed caseating granulomata with acid-fast organisms, and airway cultures were positive for pan-sensitive *Mycobacterium tuberculosis*. The patient was treated initially with a four-drug antituberculous regimen of isoniazid, ethambutol hydrochloride, pyrazinamide, and streptomycin. After 1 month of therapy, he was asymptomatic and sputum cultures were sterile. After 3 months of therapy, the middle lobe lesion in the right lung resolved completely, as evidenced both endoscopically and radiographically. He completed 18 months of therapy with isoniazid and ethambutol without complications.

**Case 2**

A 57-year-old man underwent bilateral lung transplantation for idiopathic bronchiectasis. The donor was a 25-year-old South American man who had immigrated to New York City 2 years earlier and who sustained fatal blunt head trauma during an episode of alcoholic intoxication. The explanted recipient lungs showed severe bronchiectasis and chronic parenchymal fibrosis. Cultures of the explanted lungs grew *Serratia marcescens*. There was no evidence of granuloma formation, and cultures for fungi and mycobacteria were negative. The patient received a standard immune suppression regimen of cyclosporine, azathioprine, and prednisone.\textsuperscript{9} During his 3-week hospitalization, he was housed in a single room on a cardiac surgical floor.

Two months after surgery, the patient had asymptomatic mild acute rejection (grade A\textsuperscript{2}) diagnosed by surveillance bronchoscopy. He was treated as an outpatient with infusion of methylprednisolone (1 g/d) for 3 days followed by oral prednisone, tapered over 10 days, to 0.1 mg/kg/d.

Three months after surgery, he complained of headaches, myalgia, and low-grade fever. On the following day, he noted the

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onset of pleuritic chest pain on the right side. Chest radiographic examination revealed a new cluster of small nodules in the lateral aspect of the upper zone of the left lung and new small bilateral pleural effusions (Fig 2). Fiberoptic bronchoscopy showed well-healed bronchial anastomoses and minimal secretions. BAL fluid from the upper lobe of the left lung revealed multiple acid-fast organisms, and cultures were positive for pansensitive M tuberculosis. Transbronchial biopsies from the same region showed a single poorly formed granuloma and no evidence for rejection. The patient was treated with a four-drug antituberculous regimen of isoniazid, ethambutol, pyrazinamide, and streptomycin. After 1 month of therapy, he was asymptomatic, sputum cultures were sterile, and the pleural effusions resolved completely. Nodules of the upper lobe of the left lung disappeared slowly during the next 6 months. He completed 18 months of therapy with isoniazid and ethambutol without complications.

**Discussion**

This report correlates the clinical and radiographic findings of pulmonary tuberculosis in 2 (2%) of 94 patients after lung transplantation. This rate of pulmonary tuberculosis is at the upper end of the range of 0.65 to 1.7% reported after renal transplantation, and 100 times higher than the rate in the general population.11,12 The exact incidence of pulmonary tuberculosis after lung transplantation is unknown but is presumably very low since to our knowledge only nine instances of M tuberculosis infection after lung transplantation have been reported in the medical literature.3-8

The two instances of pulmonary tuberculosis in the present series were probably transmitted via the donor allograft. In each instance, there was no evidence of M tuberculosis in the explanted recipient lungs. Hospital-acquired infection was unlikely since recipients were housed in single rooms on a cardiac surgical floor. On the other hand, the donors had risk factors for tuberculosis including alcoholism, residency in New York City, and recent immigration from South America.13,14

The source of M tuberculosis in a transplant recipient may be hard to identify. Most instances of pulmonary tuberculosis after renal transplantation represent reactivation of endogenous infection,11,12 although there are two well-documented instances of donor-to-recipient transmission of disseminated tuberculosis via the renal allograft.15,16 Some instances of pulmonary tuberculosis after lung transplantation may also represent reactivation of endogenous infection.3,6 One report documented tuberculous lymphadenitis in a bilateral lung transplant recipient as the source of infection,9 and another report implicated the native emphysematous lung as the source of infection after single-lung transplantation.6 Yet another case report linked the source of infection to a hospital roommate.3 However, three reports have implicated the donor lung as the source of M tuberculosis.3,4,8 In one instance, postmortem examination revealed calcified hilar nodes and a Ghon complex in the donor lung as supporting evidence for previous infection.3 In the second instance, conclusive evidence was not available, but transmission was suspected based on the recipient’s negative pretransplant PPD at a time when the recipient was immunocompetent.4 In the third instance, two recipients who had received a single lung from the same donor had identical isolates of M tuberculosis, which suggested a common source of infection.8

The timing of M tuberculosis after lung transplantation is fairly predictable. In the present series, both episodes of pulmonary tuberculosis occurred 3 months after transplantation. The mean time from lung transplantation to the onset of pulmonary tuberculosis in other reports was 5±2.5 months (range, 1.5 to 9 months; median, 3.5 months).3-8 In the present series and in nearly all instances reported in the medical literature, diagnosis of tuberculosis followed augmentation of corticosteroid administration.3-7

Tuberculosis in transplanted lungs, however, has no characteristic radiographic pattern.3,5 In the present se-
ries, radiographic manifestations of pulmonary tuberculosis varied from subtle bronchial narrowing (Fig 1) to focal nodular clustering and small, bilateral pleural effusions (Fig 2). Carlsen and Bergin\(^2\) described multiple bilateral small nodules and a unilateral pleural effusion in a heart-lung transplant recipient. Miller et al\(^4\) reported multiple bilateral upper and lower lobe cavitory lesions without pleural effusions in a bilateral lung transplant recipient. Dromer et al\(^5\) reported single instances of pulmonary consolidation with perihilar lymph node enlargement, pulmonary consolidation without lymph node enlargement, mediastinal lymph node enlargement without parenchymal abnormality, and a solitary pulmonary nodule.

Given the potentially ominous implications of \textit{M. tuberculosis} and other opportunistic respiratory pathogens after lung transplantation,\(^1\)\(^,\)\(^,\)\(^3\)\(^,\)\(^5\) it is essential for the clinician and radiologist to maintain vigilance in monitoring these patients to allow early diagnostic and therapeutic intervention. In the present series, the two instances of pulmonary tuberculosis did not adversely affect graft function. This observation suggests that awareness of the varied clinical and radiographic patterns of pulmonary tuberculosis after lung transplantation can facilitate prompt initiation of diagnosis and therapy to minimize complications of these pulmonary infections.

**REFERENCES**


**FIGURE 2.** \textit{M. tuberculosis} infection in a 57-year-old man. \textit{Left:} control radiograph 2 months after bilateral lung transplantation for idiopathic bronchiectasis. \textit{Right:} a cluster of irregular nodular opacities is evident laterally in the upper zone of the left lung 3 months after transplantation.
The term “restrictive cardiomyopathy” defines a group of disorders characterized primarily by diastolic dysfunction, with impairment of ventricular filling by unyielding endocardial, subendocardial, or myocardial tissue. A restrictive hemodynamic pattern may be due to infiltrative and storage diseases or to endomyocardial fibrosis; or the pattern may be primary. If a restrictive cardiomyopathy is clinically suspected, cardiac hemodynamics, angiography, and MRI implemented by ventricular endomyocardial biopsy enable it to be differentiated from constrictive pericarditis and allow identification of the underlying myocardial disorder. Confirmation of the latter pathologic finding is crucial in order to provide appropriate treatment and improve prognosis, particularly for patients with sarcoidosis or an eosinophilic endomyocardial disease. In this case report, we present a previously unreported case of idiopathic myocardial vasculitis, presenting as a restrictive cardiomyopathy with severe heart failure, which needed a thoracotomy and surgical cardiac biopsy for both diagnosis and treatment.

**CASE REPORT**

A 61-year-old woman was admitted to the hospital because of severe congestive heart failure unresponsive to digitals, angiotensin-converting enzyme inhibitors, and diuretic therapy. Two years earlier she had developed chest pain and dyspnea on effort, which became progressive and resistant to therapy.

Physical examination showed a seriously ill patient, with dyspnea at rest, systemic venous congestion, peripheral edema, an enlarged liver, and ascites. Cardiac auscultation revealed a protodiastolic gallop rhythm (130 beats per minute) unaccompanied by murmurs. Blood pressure was 90/60 mm Hg. Results of routine laboratory tests (hematologic, biochemical, and urine analysis, including thyroid function tests) were within normal limits. Serum and urine immunoelctrophoresis showed mild hypogammaglobulinemia (IgG, 645 mg/100 mL; normal value, 800 to 1800). Chest x-ray film showed a mildly enlarged cardiac silhouette due to prominence of the third left arch.

The ECG showed sinus rhythm with first-degree atrioventricular block and diffuse low QRS voltages. A two-dimensional echocardiogram revealed mild increased thickness of the ventricular wall (ventricular septum, 12 mm; left ventricular [LV] posterior free wall, 11 mm), normal ventricular dimension (LV end-diastolic diameter, 42 mm; LV end-systolic diameter, 36 mm), dilated atria (left atrial diameter, 46 mm), normal LV contractility (LV ejection fraction, 0.60); mild pericardial effusion, Doppler evidence of marked abnormality of diastolic function (shortening of the isovolumic relaxation period, increased and rapid E wave with enhanced E/A ratio, shortening of the deceleration time), and mild tricuspid regurgitation with pulmonary artery systolic pressure of 42 mm Hg. The myocardial mass, assessed using the echocardiographic method of Devereux and Reichek,2 was 105 g (body surface, 1.5 m²).

The MRI showed normal pericardial thickness with mild pericardial effusion, dilatation of the atria and the venae cavae, normal biventricular cavity size, and mildly thickened ventricular walls suggestive of restrictive cardiomyopathy. There was no alteration of signal intensity suggesting myocardial infiltration was documented by MRI.

At this point, cardiac catheterization with coronary angiography and right ventricular endomyocardial biopsy was performed. Cardiac catheterization showed elevation, with equalization, of mean right atrial, left and right ventricular end-diastolic and wedge pressures (measuring on all sides 25 mm Hg) and a dip-and-plateau pattern suggestive of constrictive pericarditis.

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**Idiopathic Myocardial Vasculitis Presenting as Restrictive Cardiomyopathy**

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A previously unreported case of small-vessel myocardial vasculitis presenting as restrictive cardiomyopathy and congestive heart failure is described. The hemodynamic study, showing severely increased and equalized diastolic pressures in atrial and ventricular chambers, and cardiac MRI, showing normal pericardium and ventricular endomyocardial biopsy, not including myocardial vascular component, were insufficient to make a diagnosis. This made a thoracotomy and surgical cardiac biopsy necessary. Steroids and cyclophosphamide, introduced after histologic evidence of necrotizing vasculitis, unassociated with a systemic disease, became available and improved the clinical profile and the diastolic dysfunction at two-dimensional echocardiographic Doppler analysis.

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**Key words:** heart failure; myocardial vasculitis; restrictive cardiomyopathy

**Abbreviations:** LV=left ventricular; RV=right ventricular

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