Case Report

Idiopathic pleuroparenchymal fibroelastosis: The first case to be managed with a successful lung transplant at King Faisal Specialist Hospital and Research Center, Riyadh

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Abstract:

Idiopathic Pleuro-Parenchymal Fibroelsatosis (PPFE) is a rare, progressive and recently recognized subtype of idiopathic interstitial lung disease with no recorded successful treatment other than lung transplant. We report a case of idiopathic pleuroparenchymal fibroelastosis from the Middle East, managed successfully by bilateral lung transplant performed on a 26 year old Saudi male.

Keywords:

Interstitial lung disease, lung transplant, pleuroparenchymal fibroelastosis

Idiopathic pleuroparenchymal fibroelastosis (PPFE) is a rare, progressive, and recently recognized subtype of idiopathic interstitial lung disease (ILD) with no recorded successful treatment other than lung transplant. We report a case of idiopathic PPFE from the Middle East, managed successfully by bilateral lung transplant performed on a 26-year-old Saudi male.

Case Report

A 27-year-old Saudi male presented to our pulmonology outpatient clinic with an 18-month history of progressive dyspnea and nonproductive cough. He was previously fit and healthy, not known to have any medical illnesses, and not on any regular medications. The patient denied any smoking history, recreational drug use, or relevant occupational exposure. His family medical history was unremarkable.

At his initial presentation, he was in mild respiratory distress; his oxygen saturation was 97% at rest breathing room air and dropped to 86% with mild exertion. He was mildly tachypneic at 24/min. His chest auscultation revealed diminished vesicular breathing and mild bilateral inspiratory crackles. Digital clubbing was present. Cardiovascular, abdominal, and rheumatologic examinations were all normal.

His arterial blood gases on room air revealed hypoxemia, pH: 7.41, paO_2 9.0 kPa, $paCO_2$ 6.0 kPa, HCO_3: 24.5 mmol/l. Other blood workup was unremarkable. Collagen vascular workup was negative. His pulmonary function test was consistent with a severe restrictive pattern.

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His X-ray at presentation showed extensive interstitial thickening with patchy areas of parenchymal densities bilaterally and suspected cardiomegaly [Figure 1]. He underwent a high-resolution computed tomography chest which showed pleuroparenchymal fibrotic changes and bronchiectasis in both lungs, with upper lobe predominance in keeping with ILD [Figure 2]. There was no suspicion of pulmonary masses or consolidation.

The workup was indicative of ILD and the likely diagnosis of PPFE. The case was discussed in our pulmonary/ILD multidisciplinary team, and a surgical lung biopsy to confirm the diagnosis was recommended; however, this was deemed to be a high-risk procedure due to his poor pulmonary function test; therefore, the patient underwent all the necessary workup for lung transplant after he was formally accepted by the lung transplant team.

His condition progressed; throughout the year we followed him up, in terms of O_2 requirement and exercise capacity. He was also admitted on a few occasions with mild infective exacerbations.

He was admitted electively and underwent bilateral lung transplant surgery. The histopathological examination of the resected lungs was consistent with the diagnosis of PPFE [Figures 3 and 4]. Postsurgery, he was commenced on mycophenolate, tacrolimus, and Prednisolone. Postoperatively, the patient developed bilateral vocal cord paralysis and severe respiratory distress secondary to aspiration pneumonia which necessitated tracheostomy.

The transplant was also complicated by bilateral bronchomalacia at the site of the anastomosis, more pronounced on the right side. Stenting was successfully performed on the right side.

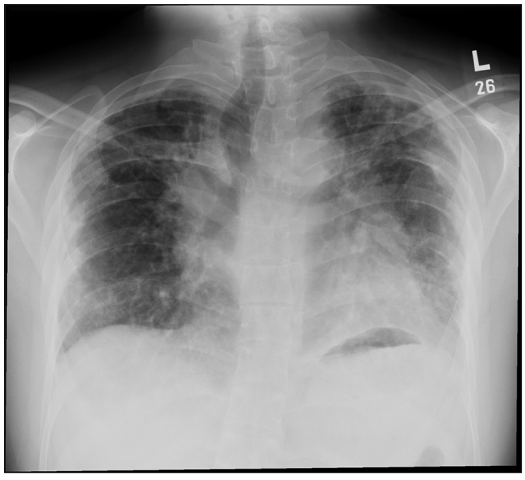

Figure 1: Extensive diffuse bilateral interstitial and patchy areas of parenchymal density. Pleural thickening suspected bilaterally

The patient improved significantly under regular evaluation by tracheostomy care team and speech therapists. Later, during the same admission, his nasogastric and tracheostomy tubes were removed and he started to mobilize and feed orally. He was discharged 45 days after his admission in a stable condition maintaining oxygen saturation of 96% on air [Figure 5].

Discussion

PPFE is a rare, newly described ILD.[1] A report of pulmonary upper lobe fibrosis was initially described in 1992 by Amitani *et al.* but lacked detailed histologic description.[2] In 2004, Frankel *et al*. reported a similar entity with detailed histologic description and it was termed "PPFE."[3] Since then, many cases have been reported from around the world but we have found no reports from the Middle East. This is the first report of PPFE in the region. In 2013, the disease was classified by the American Thoracic Society/European Respiratory Society classification of ILD as a subtype of rare ILDs[4] [Table 1].

Clinically, PPFE patients are usually slim with a flattened rib cage. Our patient had a normal body

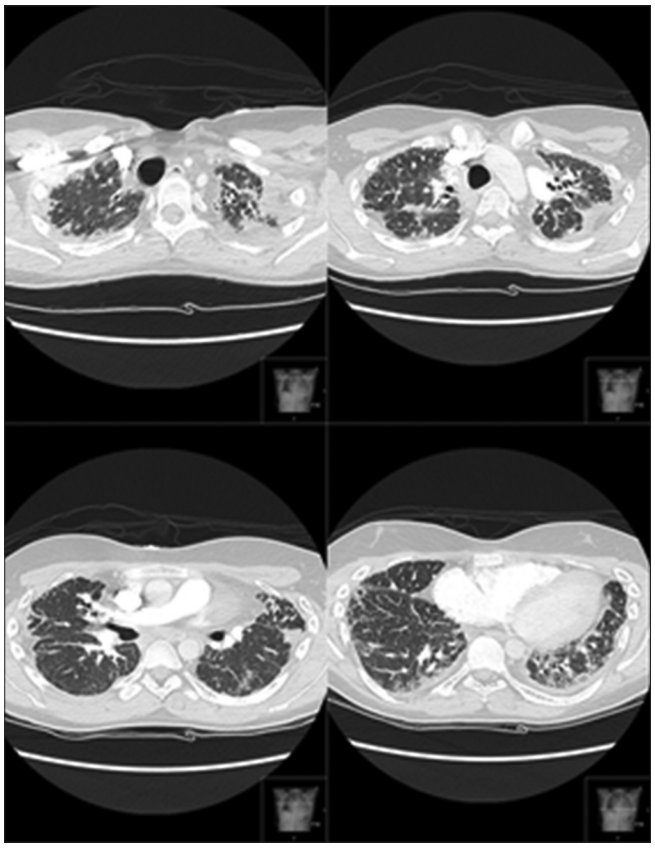

Figure 2: Fibrotic changes and traction bronchiectasis are seen at both lungs with upper lobes predominance in keeping with interstitial lung disease

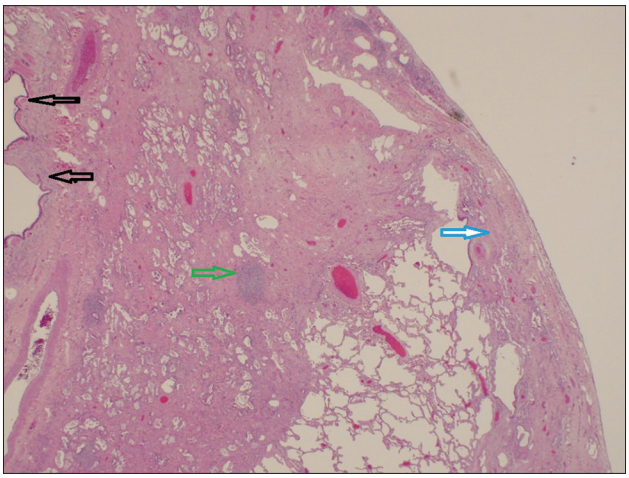

Figure 3: A section from the upper lobes showing elastic fibrosis in the sub pleural location extending into the parenchyma (blue arrow). Rare lymphoid aggregations are noted (green arrow). Minimal traction bronchiectasis (black arrow)

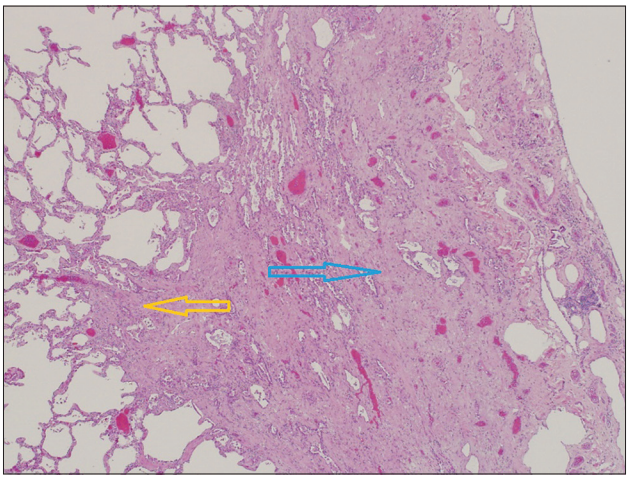

Figure 4: Sections from the upper lobes showing elastic fibrosis in the sub pleural location extending into the parenchyma (blue arrows). Margins between the normal lung and affected fibrotic areas are sharply defined (orange arrow)

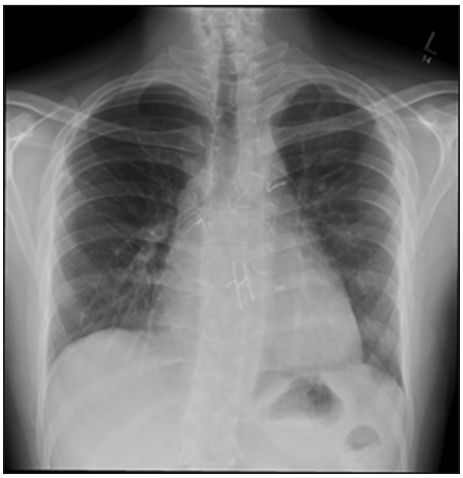

Figure 5: Posttransplant chest X-ray

build with a body mass index of 19 and a small ribcage that necessitated pediatric lungs for transplant. In contrast to idiopathic pulmonary fibrosis, reports show that patients with PPFE are less likely to have finger clubbing and crackles on examination.[1,5] Nonetheless, both features were present in our patient. They characteristically present with exertional dyspnea, chronic nonproductive cough, and frequent respiratory tract infections. With a wide age range, PPFE affects patients aged 13–87 years with a mean of 53 and has no gender predilection.

There has been no association with smoking; however, reported associations include bone marrow transplantation, chronic hypersensitivity pneumonia, autoimmune disease, collagen vascular disease, infections, drugs, and occupational exposure.[6]

Radiologically, PPFE manifests initially by apical plueroparenchymal thickening with otherwise normal lungs. With progression of the disease, imaging shows apical reticular and nodular opacities and occasional coexistent ILD in other parts of the lungs.[7]

Histologically, PPFE is characterized by (1) intense fibrosis of the visceral pleura; (2) prominent, homogenous, subpleural fibroelastosis; (3) sparing of the parenchyma distant from the pleura; (4) mild, patchy lymphoplasmacytic infiltrates; and (5) small numbers of fibroblastic foci.[8]

Laboratory workup in patients with PPFE tends to be unhelpful in confirming the diagnosis;[9] the results are usually nonspecific as in our case.

The restrictive histological changes result in a restrictive pattern of pulmonary function test with decreased forced vital capacity (FVC) and total lung capacity and an increased ratio of forced expiratory volume in 1 s/FVC. Gas exchange impairment and decreased

Table 1: Revised American Thoracic Society/European Respiratory Society classification of idiopathic interstitial pneumonias[4]

Major idiopathic interstitial pneumonias
Idiopathic pulmonary fibrosis
Idiopathic nonspecific interstitial pneumonia
Respiratory bronchiolitis-interstitial lung disease
Desquamative interstitial pneumonia
Cryptogenic organizing pneumonia
Acute interstitial pneumonia
Rare idiopathic interstitial pneumonias
Idiopathic lymphoid interstitial pneumonia
Idiopathic pleuroparenchymal fibroelastosis
Unclassifiable idiopathic interstitial pneumonias

diffusion capacity of carbon monoxide are also observed in PPFE.

Based on the findings of case series and recent publications on PPFE, Rosenbaum *et al*. proposed a diagnostic criteria for PPFE, which includes (1) fibrous interstitial pneumonia with >80% fibroelastic changes in nonatelectatic lung; (2) subpleural and/or centrilobular distribution; (3) overall inflammation absent to mild; and (4) rare or no granulomas.[10,11]

There is no definitive treatment other than lung transplant. The disease has been consistently shown to be refractory to steroids. Pirfenidone use has been reported recently in a single case to prevent lung function decline.[12] A recent case series by Nasser *et al*. found that nintedanib may reduce FVC decline in patients with idiopathic and secondary PPFE.[13] Conservative treatment with home oxygenation and infection prophylaxis is usually given to patients with progressive course of disease. Our patient is the first to be successfully treated by bilateral lung transplant in the region.

According to Amitani *et al*., PPFE has an indolent and progressive course of 10–20 years.[2] The Kaplan–Meier survival curve showed a mean survival rate of 11 years in PPFE[14] [Figure 6]. Poorer prognosis was found in transplant-associated disease.[14]

Prognosis is mainly dependent on the onset of and the expression of disease. According to Watanabe, early onset of disease, longer subclinical stage, and extensive disease extending to adjacent or lower lobes are associated with poorer prognosis.[14]

Conclusion

PPFE has been recently included as a rare idiopathic interstitial pneumonia. Diagnosis is confirmed by characteristic histological and radiological signs. The presentation can be misleading; therefore, a high index of clinical suspicion is required to recognize PPFE and start appropriate multidisciplinary management. So far, lung transplant is the only reported successful management for PPFE. In our case, a multidisciplinary approach has led to the first reported case of PPFE managed with a successful bilateral lung transplant in the Middle East.

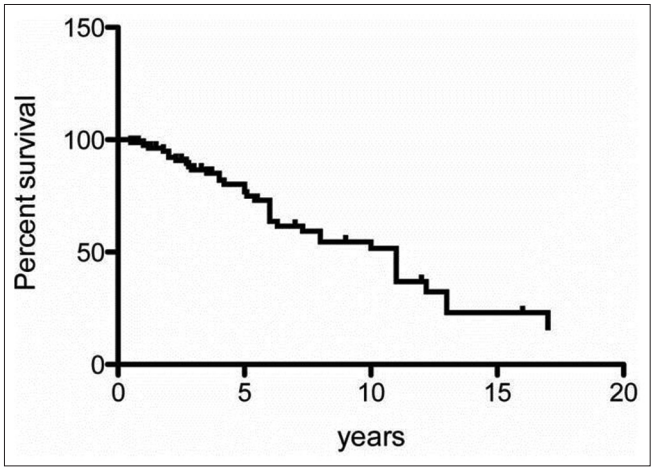

Figure 6: A Kaplan–Meier survival figure using 85 patients from previous studies[14]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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