Idiopathic pleuroparenchymal fibroelastosis confirmed by pathology: a case report

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Abstract
The case of a patient with cough and asthma after activity that each had a 1-month duration is reported. Chest high-resolution computed tomography (HRCT) showed visceral pleural thickening in both upper lungs (especially the right lung), which was accompanied by fibrous strips and patches near the pleura, and these were accompanied by distraction bronchiectasis. Idiopathic pleuropulmonary elastosis was confirmed by thoracoscopic lung biopsy. The patient was treated with acetylcysteine, but their asthma worsened after activity and their lung function decreased significantly after 10 months. Idiopathic pleuroparenchymal fibroelastosis is a rare new type of idiopathic interstitial pneumonia, which has no effective treatment except for lung transplantation.

Keywords
Pleuropulmonary elastosis, thoracoscopic lung biopsy, diagnosis, pleural thickening, distraction bronchiectasis, idiopathic, acetylcysteine, lung transplantation

Introduction
Idiopathic pleuroparenchymal fibroelastosis (PPFE) has been defined as a specific clinicopathologic entity in the updated 2013 American Thoracic Society/European Respiratory Society (ATS/ERS) classification of idiopathic interstitial pneumonias (IIPs). The clinical symptoms of PPFE were similar to other types of interstitial pneumonia, but its imaging and...
pathological findings had their own characteristics; the upper lobes were involved most often and, on microscopy, there was predominantly subpleural intra-alveolar fibrosis and elastosis (IAFE) and visceral pleural fibrosis. PPFE is a new type of IIP that was first proposed by Frankel et al.\(^2\) in 2004. Huang et al.\(^3\) reported the first case of PPFE in China, but the pathogenesis of the disease was not clear. However, repeated pulmonary infection, autoimmune disease processes, drugs, bone marrow transplantation, genetic susceptibility, and other factors may be involved in the disease occurrence.\(^4\) The median age of patients with PPFE is about 52 years.\(^5\)

There is currently no effective treatment for PPFE except for lung transplantation.\(^6\) Therefore, early diagnosis is significant for patients. The case of a newly diagnosed patient with PPFE, whose diagnosis was confirmed at our hospital on the basis of pathology results, is reported below to improve our understanding of this disease.

**Case report**

**General patient characteristics**

This patient was a 54-year-old woman who had no obvious cause of cough and expectoration, which had been ongoing for 1 month. She had a history of activity-induced asthma. The asthma symptoms occurred after climbing four floors. She also had dry mouth and dry eyes. She had no fear of cold and fever, chest pain and hemoptysis, joint pain, rash, or Raynaud’s phenomenon. Chest computed tomography (CT) examination at the local hospital showed “interstitial inflammation of both lungs and two lesions of upper pulmonary fibrosis”. She was then admitted to our department on 17 December 2018 for further diagnosis and treatment. Physical examination results were as follows: breathing sounds in both lungs were thick; and twist pronunciation could be heard in both lungs. She did not have pestle finger.

After admission, routine blood examination was performed, and the results were as follows: white blood cells (WBCs), \(6.6 \times 10^9/L\); neutrophils, 55.4%; eosinophil ratio, 13.1%; eosinophil count, \(0.86 \times 10^9/L\); hemoglobin, 123 g/L; and platelets, \(207 \times 10^9/L\). Liver and kidney function was normal. Autoantibody test results were as follows: anti-CENP-B antibodies were weakly positive (±); and other antibody test results were negative. Anti-neutrophil cytoplasmic antibody was negative (−). Routine immune response test results were normal. The erythrocyte sedimentation rate (ESR) was 4 mm/hour and C-reactive protein was 2.8 mg/L. Sputum acid-fast bacillus smear, sputum culture, and sputum fungal culture test results were all negative.

Chest high-resolution computed tomography (HRCT) showed that the visceral pleura in both upper lungs (especially the right lung) had thickened, which was accompanied by fibrous strips and patches near the diseased pleura, and there was tractive bronchiectasis as well as a small amount of pneumothorax on the right side. Pulmonary function test results were as follows: mild obstructive mixed ventilation function decreased, diffusion function decreased to mild-to-moderate (forced vital capacity [FVC], 89.7%; forced expiratory volume in the first second [FEV1], 87.5%; FEV1/FVC, 77.3%; total lung capacity in a single breath [TLC-SB], 82.1%; and diffusion capacity for carbon monoxide of lung [DLCOSB], 68.2%). Echocardiography results showed mild mitral and tricuspid regurgitation and normal pulmonary artery pressure.

**Treatment outcomes**

Thoracoscopic wedge resection in the right lung was performed on 24 December 2018.
Postoperative pathology indicated that the right upper lung apical segment showed pleural thickening, subpleural lung parenchyma loss, fibrous tissue hyperplasia, elastic fiber increase, chronic inflammatory cell infiltration, and bronchial mucosal metaplasia. Lung tissue from the posterior segment of the right upper lung showed proliferation and collagenization of pleural fibrous tissue on the surface of most areas, atrophy of subpleural pulmonary parenchyma, and an increase in elastic fibers with elastic scar formation (Figure 1a, b). The diagnosis of idiopathic pleuropulmonary elastosis was confirmed on the basis of the distribution in the upper and middle lungs on chest CT and pleural thickening combined with pathology. The patient was discharged with oral acetylcysteine.

**Clinical follow-up**

The patient was treated with acetylcysteine after discharge, but her asthma worsened gradually after activity. After 10 months, her pulmonary function had decreased significantly, showing a moderate-to-severe decrease in restrictive ventilation function and a mild-to-moderate decrease in diffusion function (FVC, 62.4%; FEV1, 58.0%; FEV1/FVC, 78.30%; TLC-SB, 68.6%; and DLCOSB, 64.6%). Another chest HRCT was performed, but the results showed little change. It was suggested that the patient’s prognosis was poor.

**Discussion**

The main clinical manifestations of PPFE were dry cough and shortness of breath after activity, which was similar to that of other interstitial lung diseases. Most pulmonary function damage showed restrictive ventilation dysfunction, some of which were associated with the concomitant complication of diffusion dysfunction, and there were a few cases with normal pulmonary ventilation function or obstructive ventilation dysfunction. The patient whose case is reported here also showed these symptoms. However, further information for a diagnosis was needed including imaging and pathological manifestations because her clinical manifestations were not specific.

PPFE differs from other interstitial lung diseases because of its imaging and pathological findings. The imaging features showed that the lesions were mainly distributed in the apical and upper lungs, and the lesions were symmetrically distributed bilaterally. The main manifestations are pleural thickening of the apical or upper lung layer,
a few localized calcifications, grid and honeycomb shadow in the subpleural lung tissue, nodular shadow, patchy shadow, and distraction bronchiectasis at the center of the lobule in some patients. Some patients may have interstitial lung disease in the middle and lower lungs (especially in the lower lungs). For our patient, chest HRCT showed thickening of the visceral pleura in both upper lungs (especially in the right lung), which was accompanied by fibrous strips, patches near the diseased pleura, and distraction bronchiectasis, which was consistent with a previous report.

The pathological features of PPFE can be summarized as follows: (1) significant thickening of the visceral pleura; (2) significant proliferation of elastic and collagen fibers in the pleura and its lower interstitium; (3) the lesion site was clearly demarcated from the normal lung tissue; (4) mild focal lymphocyte and plasma cell infiltration; and (5) a small number of fibroblasts on the periphery of the fibrosis.

When making a differential diagnosis of PPFE, interstitial lung disease with accompanying fibrosis may be confused with PPFE. Because of the predominant pleural and subpleural fibrosis in PPFE, the main histologic differential diagnosis would be an usual interstitial pneumonia (UIP) pattern. Generally, a UIP pattern is associated with extensive remodeling of the lung parenchyma with eventual end-stage fibrosis and honeycomb changes, which result in effacement of the original parenchymal architecture. This feature is not characteristic of PPFE because in PPFE, there is homogeneous intra-alveolar fibrosis with a generally preserved alveolar structure and even thickening of the alveolar structures through the process of elastic fiber deposition. In contrast to a UIP pattern, fibroblastic foci in PPFE should be sparse. In the idiopathic form of UIP or idiopathic pulmonary fibrosis, the disease characteristically involves the lower lobes of the lung in the initial stages, whereas classical PPFE typically affects the upper lobes. In problematic cases, a performance elastic fiber stain, such as elastic Van Gieson stain, would be useful because the stain demonstrates a more sparse, fragmented, and disorganized elastic fiber distribution in the areas of fibrosis in UIP compared with more marked and established elastic fiber deposition in relation to the alveolar walls in PPFE, which contains at least twice as much elastin compared with UIP. Although nonspecific interstitial pneumonia (NSIP) has been suggested as a differential diagnosis, NSIP shows more diffuse lung parenchymal involvement that is not associated with pleural fibrosis (except for in collagen vascular disease-related NSIP changes). Moreover, an interstitial process (which could be inflammation, fibrosis, or both) is characteristic of NSIP, whereas in PPFE, the process involves elastin deposition in relation to the alveolar walls with intervening collagen deposition. For both pleural and parenchymal fibrosis, possible differential diagnoses include asbestosis, advanced fibrosing sarcoidosis, or radiation/drug-induced lung disease. However, none of these differential diagnoses are associated with intra-alveolar fibrosis and septal elastosis as seen in PPFE.

This patient’s thoracoscopic lung biopsy revealed pleural thickening and collagen and elastic fiber hyperplasia in the pleura and lower pulmonary interstitium, which was mainly in a whirlpool and disorderly arrangement. The diagnosis of idiopathic pleuropulmonary elastosis was clear.

The prognosis for this disease is poor, and most of the patients with PPFE show disease progression after diagnosis. It was recently reported in the literature that the survival time of these patients ranges from 4 months to 7 years (median survival time, 2 years). There is no effective treatment for PPFE except for lung transplantation.
Conclusion
The case of a patient with PPFE that was confirmed by pathology is reported. The clinical symptoms were similar to those of other types of interstitial pneumonia, but the imaging and pathological findings had the characteristics of PPFE, including visceral pleural thickening that was mainly present in both the upper lungs (especially the right lung), pulmonary fibrous cord and patch shadow near the diseased pleura, and stretch bronchiectasis. The pathological manifestations were pleural thickening, fibrous tissue hyperplasia, and increased elastic fibers. Chronic inflammatory cell infiltration, bronchial mucosal metaplasia, and increased elastic fibers with elastic scar formation were also present. The information presented in this case report can help when making a diagnosis of PPFE.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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