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Pleuroparenchymal fibroelastosis presenting with pneumothorax

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Abstract

A 47-year-old woman presented with spontaneous right side pneumothorax. Image studies showed consolidations and reticular opacities involving the pleural and subpleural regions of bilateral lungs. Wedge biopsy specimens of right upper, middle and lower lobes showed fibrosis of the visceral pleura and subpleural area in all three lobes, more significant in the upper lobe. Elastic Van Gieson stain showed a pattern of alveolar septal elastosis with intra-alveolar fibrosis. The clinical presentation and pathological findings are compatible with pleuroparenchymal fibroelastosis, a rare and distinct type of interstitial lung disease. This entity is different from usual interstitial pneumonia by its relationship to pleura, upper lobe predominance and temporal homogeneity. It is different from non-specific interstitial pneumonia by its pleural involvement and scanty inflammatory cell infiltration. Pleuroparenchymal fibroelastosis is a slowly progressive disease; about half of the patients die in 10 years. No curative treatment is available at present time.

Keywords

Interstitial lung disease, pleura, pneumothorax

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Introduction

Pleuroparenchymal fibroelastosis (PPFE) is a rare interstitial lung disease characterized by pleural and subpleural fibrosis with a high density of elastin fiber. To date, about 120 cases have been reported worldwide.[1] Here we describe the first case of PPFE diagnosed in Taiwan with a brief discussion of current understanding of the disease.

Case

A 47-year-old woman presented to the emergency department with sudden-onset right side chest pain. Physical examination revealed diminished breathing sound in the right chest. Chest radiograph showed a small amount of right side pneumothorax (Figure 1(a)). Her vital signs were stable, and no respiratory distress was noted. Five months before this event, she visited our outpatient clinic for bilateral heel pain; ankylosing spondylitis was suspected at that time, but examinations showed no sacroiliitis or other evidence of the disease, and she received symptomatic treatment only. For the pneumothorax, the patient was discharged from the emergency department after conservative oxygen therapy. However, the symptoms did not resolve. Chest computed tomography performed 5 days after symptom onset showed persistent right side pneumothorax. In addition, consolidations and reticular opacities involving the pleural and subpleural regions indicating fibrosis at bilateral upper and middle lung zones were noted (Figure 1(b) and (c)). She was admitted to our hospital for surgical intervention. Eleven days after

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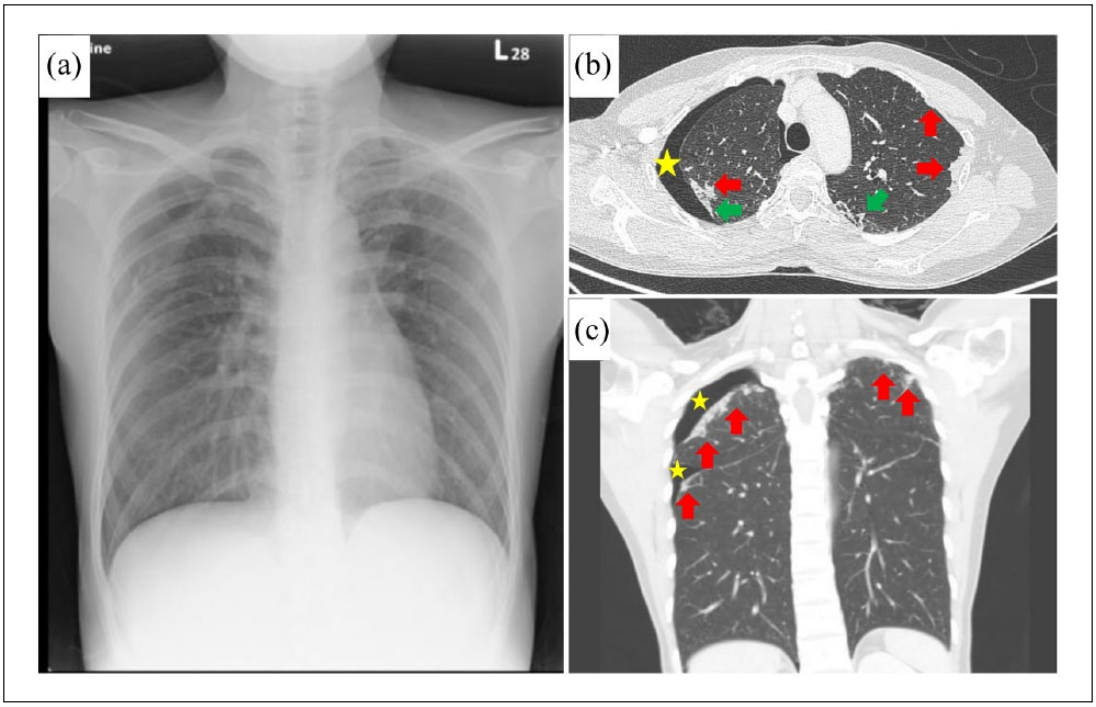

Figure 1. Image of the patient showed right side pneumothorax in a supine chest X-ray (a). Computed tomography of the chest (b) and (c) showed consolidations (red arrow) and reticular opacities (green arrow) involving bilateral pleural and subpleural regions indicating fibrosis at upper and middle lung zones, in addition to the right pneumothorax (yellow star).

symptom onset, she received video-assisted thoracoscopic surgery (VATS). During the surgery, multiple blebs and consolidated areas in right upper, middle and lower lobes were noted. The lesions were wedge-biopsied, and mechanical pleurodesis was performed. The patient recovered well after the surgery.

Three lung wedge biopsies were received for examination. No obvious blebs were seen on the pleura surface, but the pleura appeared thickened, and the parenchyma immediately below the pleura was consolidated. Microscopically, small blebs and foci of intrapleural hemorrhage were seen in all three wedges. Fibrosis of the visceral pleura was noted in the specimens from all three lobes, more significant in the upper lobe (Figure 2(a)–(c)). Prominent, homogenous subpleural fibrosis was also noted, while the alveolar parenchyma away from the pleura appeared relatively normal. There were a few lymphocytic aggregates in the fibrotic zone, while no fibroblastic focus was observed. Elastic Van Gieson (EVG) stain was performed and showed a pattern of alveolar septal elastosis with intra-alveolar fibrosis (Figure 2(d)). These findings established the diagnosis of PPFE.

Discussion

PPFE is a unique pattern of pulmonary fibrosis that is distinctive from other types of interstitial lung disease. Amitani et al. first described patients with pulmonary fibrosis that focused in the upper lobes in 1992,[2] while Frankel et al. coined the term PPFE in 2004.[3] There is a wide range of age at onset of the disease, affecting young adults as well as elderly patients. The male-to-female ratio is close to 1:1. No association with cigarette smoking has been identified.[4] These patients usually present with respiratory symptoms such as shortness of breath and cough.[4] Pneumothorax is a common complication, occurring in 33 of 44 patients in a recent retrospective multicenter study.[5] In chest imaging, pleural thickening, subpleural nodular or reticular densities are often observed, frequently involving bilateral lungs, with the upper lobes affected more significantly than the middle or lower lobes.[4] Pathological examination of the lung shows pleural and subpleural parenchymal fibrosis with characteristic sparing of parenchyma distant from the visceral pleura.[6] The transition between affected and spared lung parenchyma is often abrupt. EVG stain demonstrates heavy elastin deposition in the affected area, which may show a pattern of septal elastosis with intra-alveolar fibrosis. These observations are usually made on surgical lung biopsies, but when peribronchial distribution of the lesion also exists, diagnosis may also be made with transbronchial lung biopsy.[7] Comparing to usual interstitial pneumonia (UIP), the lesions seen in PPFE are more significant in the pleural and subpleural area and in the upper lobes, do not show temporal heterogeneity, contain few or no fibroblastic foci and show little inflammatory cell infiltration. Comparing to non-specific interstitial pneumonia (NSIP),

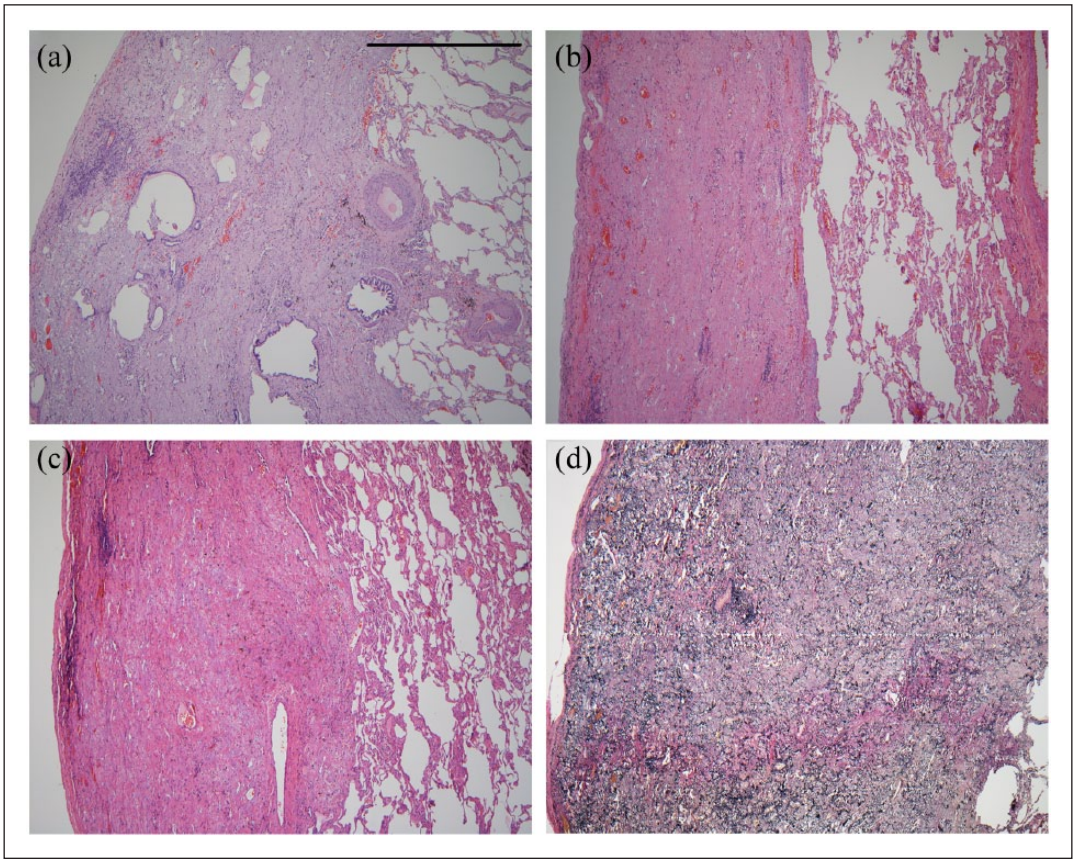

Figure 2. Microscopic examination of H&E stains of the patient's right upper lobe (a), right middle lobe (b) and right lower lobe (c) all showed thickening of the visceral pleura and subpleural parenchymal fibrosis, with abrupt transition to normal parenchyma distant from pleura. A small amount of lymphoplasmacytic infiltration was present. EVG stain (d) showed heavy deposition of elastin fibers, some showing preserved alveolar septal pattern. All photos taken at 40× magnification. Scale bar: 1 mm.

the parenchyma fibrosis is usually diffuse in NSIP with little pleura involvement, and there is usually prominent inflammatory infiltrate in the interstitium. Therefore, PPFE appears to be a distinct pattern of its own. Although the histological picture is similar to so-called "apical cap" of the lung, the frequent involvement of the middle and lower lobes in PPFE, albeit to a lesser extent, distinguishes these two entities.

The pattern of PPFE has been reported in patients without underlying medical conditions (primary or idiopathic), as well as in patients with a variety of preexisting conditions (secondary). The most often reported conditions are bone marrow/hematopoietic stem cell transplantation and lung transplantation. In addition, prior chemotherapy, asbestos exposure, rheumatoid arthritis, ulcerative colitis, psoriasis and ankylosing spondylitis have all been reported to be associated with PPFE.[4] Some authors proposed that PPFE may not be a distinct disease but is a pattern of response to long-standing lung injury.[8] Tracing back her history, our patient came to our outpatient clinic 5 months before the pneumothorax episode because of bilateral heel pain. Enthesitis of the Achilles tendons was suspected. Serial work up showed no evidence of rheumatic disease; tests for serum anti-nuclear antibody, rheumatic factor and HLA-B27 typing were negative, and lumbar spine X-ray showed no sacroiliitis. Therefore, the patient received symptomatic treatment only. Although her presentation did not fulfill the criteria of ankylosing spondylitis, the patient's pulmonary manifestation could possibly signal an underlying autoimmune process, and clinical follow-up will be necessary.

PPFE has a slowly progressive clinical course. In previous studies, about half of the patients died within 10 years.[4] In the late stage, the disease affects all lobes of lung, and fibroelastosis of the parenchyma also becomes diffuse and no longer limited to the subpleural area, with the symptoms progressing to respiratory failure. No specific treatment is available. Patients with respiratory failure may be treated with lung transplantation,[9] but there is limited research about whether the disease can recur in the donor organ. Animal studies have shown a pathogenic role of transforming growth factor alpha (TGF-alpha) in pulmonary fibrosis of a similar pattern.[10] Whether specific targeted therapy can benefit the patients with PPFE remains to be elucidated.

Conclusion

It is important to consider the diagnosis of PPFE in patients presenting with bilateral upper lobe-predominant interstitial lung disease. The combination of pleural and subpleural distribution of lesions with the findings of septal elastosis and intra-alveolar fibrosis is the most important for establishing a pathological diagnosis.

Declaration of conflicting interests

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Ethics approval

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Informed consent

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