Case Report

Pleuroparenchymal Fibroelastosis: A Rare Entity

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Abstract

Pleuroparenchymal fibroelastosis (PPFE) is a rare variant of interstitial lung disease (ILD). PPFE is characterizsed by peculiar clinical, radiological and histological features. Initially considered an idiopathic entity, this disease is now classified in the rare category of the recent classification of idiopathic interstitial pneumonias (IIPs). However, it largely continues to be underdiagnosed owing to the lack of awareness about this condition. PPFE may be misdiagnosed as the other commonly diagnosed ILDs, especially IIP. The diagnosis is clinched with lung biopsy. We report a case of PPFE diagnosed by transbronchial lung biopsy.
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Key words: PPFE, Fibrosis, Pneumothorax, TBLB.

Introduction

Pleuroparenchymal fibroelastosis (PPFE) is an uncommon distinct idiopathic interstitial pneumonia (IIP) characterised by its peculiar clinical, radiological and histopathological features.[1] It was first elucidated in the Japanese literature by Amitani *et al*.[1] In 2004, Frankel *et al*.[2] reported five cases with upper-lobe-dominant pulmonary fibrosis that progressed gradually to respiratory insufficiency. As the histology comprised of sub-pleural elastosis, intra-alveolar collagenous fibrosis with septal elastosis and collagenous thickening of the visceral pleura, they named this unique disorder as "pleuroparenchymal fibroelastosis". In 2013, PPFE was included in the rare IIP category of the international classification of IIPs.[3] The aetiology of the disease continues to remain enigmatic and can be postulated to be a complex interplay of various genetic, immunological and environmental factors.

Case Report

A 55-year-old lady, with no history of any addiction presented with dry cough and progressive dyspnoea for six months; which had further worsened in the last 15 days prior to admission. The patient had received therapeutic anti-tuberculosis therapy trial with no relief. On examination, patient had a flattened rib cage with the antero-posterior (AP) to transverse diameter being less than 0.5. The patient was afebrile with pulse of 92 beats per minute, blood pressure of 110/70 mmHg, respiratory rate of 28 breaths per minute and pulse oximetry showed a saturation of 88% on room air. Grade 3 clubbing and mild pallor were the other significant findings on general physical examination. The respiratory system examination revealed reduced breath sounds in the bilateral upper lobe areas with bilateral basal velcro crackles. The pulmonary component of second heart sound was loud.

Baseline haematological and biochemical investigations were within normal limits. Chest radiograph showed bilateral apical pneumothorax along with fibrocystic opacities. High resolution computed tomography (HRCT) of the chest showed fibrosing interstitial lung disease with upper lobe predominance and bilateral apical pneumothorax (Figure 1).

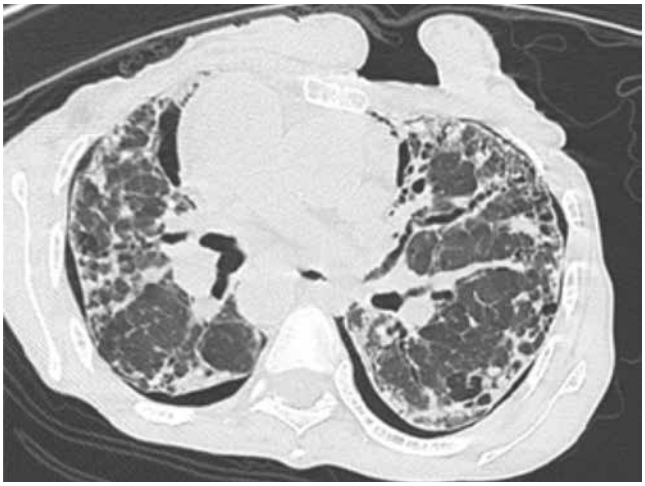

Figure 1. High resolution computed tomography of the chest showing ill-defined areas of intralobular, interstitial and septal thickening without subpleural sparing. There is honeycombing with bilateral apical pneumothorax.

Spirometry showed a restrictive abnormality with the ratio of forced expiratory volume in first second (FEV_1) to forced vital capacity (FVC) of 100 with FVC of 0.37 liters, *i.e.* 23% of the predicted value. Electrocardiogram was normal and two dimensional echocardiography showed severe pulmonary hypertension with pulmonary artery pressure of 60mmHg. The patient underwent a transbronchial lung biopsy (TBLB). Histopathological analysis confirmed the diagnosis of pleuroparenchymal fibroelastosis (PPFE) (Figure 2). The patient was managed with oxygen therapy and pulmonary rehabilitation.

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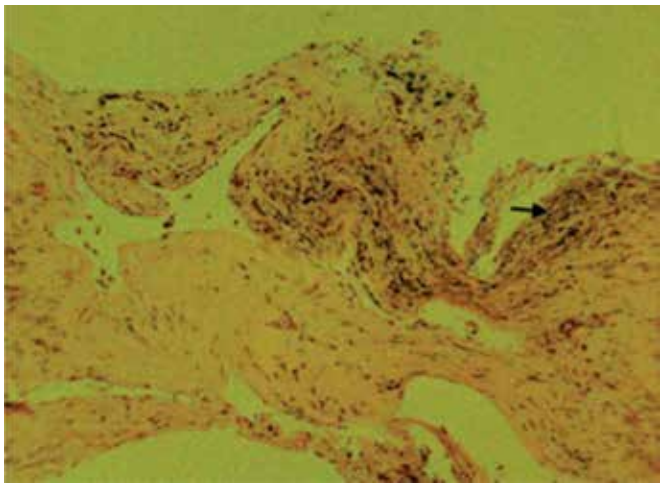

Figure 2. Photomicrograph of transbronchial lung biopsy histopathology showing fragment of fibrosed and hyalinised pleura with sparse lymphocytic and eosinophilic infilterate with Vas Gieson elastic stain showing increased elastic fibres within the thickened pleura. (Magnification 40×).

Discussion

Interstitial lung diseases are a group of disorders primarily affecting the interstitium of the lung and the alveolar capillary membrane. IIP is a rare subset of ILDs in which the aetiology remains obscure even after a meticulous evaluation for the identifiable causes. Over the years, the classification of IIP has been revised and the recent classification has now incorporated a group of rare IIPs to include ILDs, like PPFE. PPFE is a fibrosing ILD. Although there is ambiguity pertaining to its aetiology, several predisposing factors have been postulated including genetic predisposition, recurrent respiratory infections, collagen vascular diseases, bone marrow transplant, lung transplant, and post chemotherapy or post radiotherapy.[4] It generally presents in the fifth and sixth decades of life and has no gender predilection. The common presenting symptoms are exertional dyspnoea, dry cough and chest pain. Clubbing and crackles are the typical examination findings shared with other ILDs.[5] However, a flattened thoracic cage is a characteristic feature of this entity which can be attributed to the significant underlying fibrosis and volume loss. This clinical picture was seen in our case too. Some patients may present with additional symptoms or examination findings attributable to associated complications, like pneumothorax or infections with *Mycobacterium avium* complex and *Aspergillus* species.[6] Our patient presented with a complication in the form of bilateral apical pneumothoraces manifesting as reduced breath sounds in bilateral upper chest areas. The chest radiograph could be normal or could show apical fibrosis, pleural thickening or pneumothorax with or without bilateral reticulo-nodular opacities. This upper lobe predominant pattern of fibrosis can be seen in other conditions, like sarcoidosis, silicosis, berylliosis, ILDs associated with ankylosing spondylitis, ulcerative colitis, rheumatoid arthritis, hypersensitivity pneumonitis and Langerhans cell histiocytosis.[7] HRCT of the chest is the next step towards the diagnosis and may reveal intra-lobular and inter-lobular septal thickening with upper lobe predominance and a clear demarcation between the affected and the unaffected areas. Other findings, like consolidation, cysts, bullae may also be observed. The pulmonary function tests reveal restrictive abnormality with a disproportionate reduction in the FVC as compared to diffusion capacity of carbon monoxide (DLCO). This paradox is due to counter regulatory physiology between the extra-pulmonary resistance of the thoracic cage involvement and the simultaneous impairment of the pleural elasticity.[8]

The clinico-radiological suspicion, however, warrants a histopathological confirmation. The classical histopathology is that of dense sub-pleural fibrosis with significant elastosis as compared to usual interstitial pneumonia (UIP), prominent pleural fibrosis with alveolar wall elastin deposition.[9] There is an abrupt transition between normal to abnormal architecture on histopathology as observed on HRCT.[10] However obtaining a specimen for histopathology can be a major challenge. Surgical lung biopsy has been the modality of choice since decades. However, it is an invasive procedure associated with significant morbidity. Therefore, lesser invasive modalities for obtaining tissue material have become the mainstay of the diagnosis. Transbronchial lung biopsy results in a good yield in certain bronchocentric ILDs, like sarcoidosis and hypersensitivity pneumonitis. In PPFE, the intra-alveolar fibrosis shows a peribronchovascular distribution, and hence, TBLB has considerable chances of giving a positive yield.

In our patient, we could obtain a definite diagnosis on the basis of TBLB alone and a surgical lung biopsy was not needed. Though PPFE and IPF share some histopathological features; there are important differences between these two entities. Upper lobe predominant fibrosis, histology of fibroelastosis in sub-pleural areas, flattened thoracic cage and a restrictive ventilatory defect associated with increases residual volume to total lung capacity ratio are typical features of PPFE that are not encountered in IPF.

The clinical course of the disease is variably progressive with a suboptimal response to the treatment with steroids or immunosuppressive agents.[12] Long-term oxygen therapy and pulmonary rehabilitation are the mainstay of therapy to improve the quality of life.

In conclusion, PPFE is a rare IIP which remains largely underdiagnosed. This can be attributed to a great degree of overlap with other familiar ILDs. A high index of suspicion is required to establish the diagnosis of this rather unusual IIP.

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