Secondary pleuroparenchymal fibro-elastosis with airway-centered fibro-elastosis and constrictive bronchiolitis associated with agriculture dust exposure

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ABSTRACT

Pleuroparenchymal fibro-elastosis (PPFE) is a rare idiopathic interstitial pneumonia. Secondary forms of PPFE may occur in patients following lung- or bone marrow transplantation. Here we report a middle-aged woman who presented with dyspnea and cough. She had been working as a cleaning woman in an agriculture company and logistic firm. Chest HRCT was highly suggestive for PPFE. Histopathological examination of a surgical biopsy showed a pattern of PPFE with airway-centered fibro-elastosis, constrictive bronchiolitis and birefringent particles in the pathological areas only. Using transmission electron microscopy with X-ray diffraction (TEM/EDX) these particles were identified as quartz and silicates, both components generally found in soil. The present case illustrates that secondary PPFE may result from agricultural dust exposure and stresses the need for a careful workup of the occupational history.

Key Words: Pleuroparenchymal fibro-elastosis, Constrictive bronchiolitis, Occupational disease

1. INTRODUCTION

Pleuroparenchymal fibro-elastosis (PPFE) is a rare disease initially reported by Frankel et al.1 With approximately one hundred published cases, PPFE is now considered as a rare idiopathic interstitial lung disease that recently was included as a new entity in the revised international multidisciplinary classification of idiopathic interstitial pneumonias.2 The main characteristics of the disease are upper-lobe-dominant fibro-elastotic changes in non-atelectatic collapsed lung tissue with subpleural and/or peribronchiolar distribution and absence of inflammation or honeycombing. The main symptoms are dyspnea, non-productive cough, chest pain associated with pneumothorax and weight loss. Patients generally have a slender stature with so-called flattened thoracic cage, probably related to long-lasting fibrosis with shrinkage of the upper lobes.

Next to the idiopathic forms of PPFE, chemotherapeutic agents and occupational exposure may induce fibro-elastosis.3,4 Secondary PPFE following lung- and allogeneic bone marrow transplantation is characterized by com-

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bined PPFE and bronchiolitis obliterans due to chronic lung allograft dysfunction and graft-versus-host disease, respectively.\[5, 6\] Here we present a case with the clinical-pathological features of PPFE following dust exposure.

## 2. Case Presentation

In 2015 a 48-year-old non-smoking Caucasian woman was admitted to our hospital because of dyspnea, chronic non-productive cough and decreased exercise tolerance. Potential causes, particularly pulmonary infections and past drug treatment, were denied. Except for a de Quervain’s thyroiditis with normal thyroid function on admission, she had no significant medical history. There were no risk factors (no birds, no humidifier) suggestive for hypersensitivity pneumonitis and no complaints indicative of an autoimmune disease. On admission, her medication consisted of prednisolone (10 mg/day), formoterol turbuhaler (2 × 6 mcg/day) and paracetamol 1,000 mg.

Her symptoms had started five years ago and gradually worsened. The patient had been working since 2001 as an employee in an agricultural company where she had cleaned plastic vegetable crates in a big hall. Since 2008, she had been working in the basement of a logistic firm where she had stucked labels on bottles. The patient described both working places as “very dusty”.

Physical examination revealed fine crackles and reduced breath sounds. Serology tests for autoimmune diseases were negative. Lung function tests demonstrated a severe restrictive pattern (FEV1 37%, FVC 39%, FEV1/FVC 80%, TLC 64% of predicted and decreased diffusion capacity (41% of predicted). Arterial blood gas analysis revealed a respiratory insufficiency (pH 7.39; pCO2 6.4 kPa; pO2 8.38 kPa; HCO3 27.8 mmol/l; BE 4.6 mmol/l) with desaturation from 97% to 88% during 6-minute walking test (distance 375 m). Chest computed tomography showed reticular subpleural opacities with upper lobe predominance, tree-in-bud changes and air-trapping (see Figure 1A-C) consistent with PPFE.

![Figure 1](https://example.com/figure1.png)

**Figure 1.** Coronal reconstruction showing pleural thickening of the apical parts and apical-accentuated pulmonary changes (A; arrows). Axial HRCT-slice illustrating irregular structure of the bronchial wall (B) and a mosaic pattern with air trapping during forced expiration (C; *) corresponding to constrictive bronchiolitis.

To obtain a definite diagnosis, an open lung biopsy was performed. Histopathological examination revealed marked subpleural thickening by dense fibro-elastotic tissue with an abrupt transition towards normal lung parenchyma, peribronchiolar fibro-elastosis and subepithelial collagen depositions in the bronchioli, compatible with PPFE, airway-centered fibro-elastosis and constrictive bronchiolitis (see Figure 2A-G). In addition, birefringent, partly needle-shaped foreign particles were found in the fibro-elastotic areas only (see Figure 2C, inset). Using transmission electron microscopy with
X-ray diffraction (TEM/EDX), particle analysis revealed a predominance of silicates (including feldspar and mica) and quartz (see Figure 2H). Subsequently, occupational hygienist investigated the working places and estimated the respirable dust and quartz load in the agriculture firm being 1 mg/m\(^3\) and 0.2 mg/m\(^3\) (MAC-value 0.15 mg/m\(^3\)), respectively. For the second occupation, no details could be found, because the logistic firm did not exist anymore at the time-point of our investigation.

During a multidisciplinary discussion, the clinical-radiological-pathological diagnosis of PPFE associated with dust exposure was made. Repeated treatment with high-dose of corticosteroids did not result in clinical improvement. Because of clinically significant lung, functional impairment the patient was listed for bilateral lung transplantation. During follow-up, her pulmonary condition showed no significant progression as judged by lung function tests and CT-scans.

3. DISCUSSION

Here we report a non-smoking middle-aged woman with PPFE and constrictive bronchiolitis, which mirrors the radiological-pathological picture seen in lungs of patients following allogenic bone marrow transplantation.[5] The co-localization of birefringent foreign particles in the pathological areas suggests a causal relationship between mineral dust deposits and the fibro-elastosis. Histological examination combined with particle analyses of lung autopsy samples obtained from 112 agricultural workers has provided substantial evidence for a causal relationship between inorganic dust exposure, predominantly quartz, and small airways disease resembling mixed-dust pneumoconiosis in the agriculture workplace. Similar to our case birefringent particles were observed in the pathological areas only.[7] Constrictive bronchiolitis without PPFE has been described in soldiers who had served in Iraq and Afghanistan[8] whereas PPFE without constrictive bronchiolitis was found in a patient following exposure to aluminosilicate dust.[9] These studies and case reports support the concept that occupational exposure can cause PPFE. Since soil is largely composed of silicates and quartz, we speculate that the PPFE and constrictive bronchiolitis diagnosed in our case is associated with agricultural dust exposure.

Figure 2. Histology (A: magnification 20×, B-G 200×) showing collapse of the parenchyma with excess of elastin and collagen in the subpleural regions resembling PPFE (Figures B-C; HE and EvG) with presence of birefringent material in the pathological areas only (Inset C). Airway-centered fibro-elastosis and subtotal occlusion of bronchioli due to subepithelial fibrosis compatible with constrictive bronchiolitis (Figures D-G; HE and EvG). Energy dispersive X-ray analysis showing that the birefringent material (Figure H) mainly consisting of silica (S and O) compatible with quartz (Figure I).
4. CONCLUSION
To our knowledge, this is the first case of secondary PPFE associated with occupational dust exposure. Since supportive care and eventually lung transplantation are the only therapeutic options for patients with PPFE and constrictive bronchiolitis, further studies beyond this case report are needed to expand our knowledge of the pathophysiological mechanisms of secondary PPFE etiologically related to dust exposure. It also stresses the need for carefully collecting occupational exposure history to identify potential work place triggers when confronted with interstitial lung diseases such as PPFE.

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