Case Report

Interstitial lung disease as a late complication of pulmonary alveolar proteinosis

Alexandre Semionov, MD, PhD*, John Kosiuk, MD

McGill University Health Centre, Department of Diagnostic Radiology, Montreal General Hospital, 1650 Cedar Avenue, Montreal QC H3G 1A4, Canada

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Pulmonary alveolar proteinosis is a rare condition characterized by accumulation of intra-alveolar surfactant. Here, we report a case of interstitial lung disease which developed over the years in a patient with pulmonary alveolar proteinosis.

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Case presentation

A 42-year-old man was diagnosed with pulmonary alveolar proteinosis (PAP) following investigation of slowly progressive mild dyspnea. The patient had no history of exposure to industrial dusts or gases, neoplasia, or immunodeficiency. His original chest radiograph demonstrated patchy airspace disease, which, on follow-up chest computed tomography (CT), corresponded to areas of ground-glass opacity intermixed with interlobular septal thickening, a crazy-paving pattern (Fig. 1). Analysis of bronchoalveolar lavage fluid confirmed diagnosis of PAP. Later on the patient underwent whole lung therapeutic lavage. The chest radiograph and CT scan following the lavage showed marked regression of the ground glass opacities with mild residual interlobular septal thickening at the lung bases (Fig. 2).

Over the next 17 years, the patient continued to have gradually worsening mild dyspnea. CT chest performed 12 years after the original CT showed bilateral subpleural reticulonodular densities with traction bronchiolectasis and architectural distortion, suggestive of nonspecific interstitial pneumonitis (Fig. 3). At that time patient’s pulmonary function test was within normal limits. Five years later, his follow-up patient’s pulmonary function test showed decrease in forced vital capacity form 3.43 L to 2.9 L. A CT performed at the same time showed progression of the interstitial lung disease, with increased irregular subpleural reticulations, associated with increased bronchiolectasis and architectural distortion, consistent with nonspecific interstitial pneumonitis (Fig. 4).

Discussion

PAP is a rare condition thought to result from impaired pulmonary surfactant homeostasis [1,2]. The primary physiological role of surfactant is to decrease alveolar surface tension.

* Corresponding author.
E-mail address: alexandre.semionov@mail.mcgill.ca (A. Semionov).
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and prevent alveolar collapse during expiration. Surfactant is produced by type II pneumocytes and subsequently removed from alveoli by pneumocytes and alveolar macrophages [1,2]. Surfactant homeostasis is altered in cases of PAP with resultant intra-alveolar accumulation of surfactant lipoproteins, which interferes with normal gas exchange [2].

Three types of PAP are recognized: autoimmune, secondary, and congenital [2]. Autoimmune PAP, which is also referred to as “idiopathic,” “acquired,” or “adult-type,” is the most common, accounting for 90% of PAP cases. Most cases of idiopathic PAP are thought to be secondary to anti-bodies against granulocyte macrophage colony stimulating factor (GM-CSF). The latter is crucial for normal functioning of macrophages, and GM-CSF inhibition by auto-antibodies leads to impaired clearing of the surfactant by alveolar macrophages [2]. Secondary PAP can be seen in some patients with inhalational exposure to inorganic dusts and nitrogen dioxide, in patients with hematologic malignancies, and in immunocompromized patients. All these conditions are believed to ultimately result in alveolar macrophages depletion or impaired surfactant clearing function [2]. Congenital PAP is rare, accounting for about 2% of cases, and manifests in neonatal period [2]. It could be secondary to mutations of surfactant protein genes (SFTP-A, -B, -C, and -D) resulting in altered properties of the surfactant, which impair both its normal secretion and clearing [2]. Congenital PAP could also result from mutations of the GM-CSF receptor genes [2].

Clinical manifestation of PAP is variable, ranging from mild dyspnea to respiratory failure. The predominant CT feature of PAP is a “crazy-paving” pattern—smoothly thickened interlobular septa with intervening ground-glass opacities, often with geographic sparing [3]. Extent and degree of pulmonary parenchymal abnormality on CT tends to correlate with clinical severity of the disease [3].

Definitive diagnosis is made with lung biopsy or bronchoalveolar lavage specimens that reveal intra-alveolar deposits of proteinaceous material, dissolved cholesterol, and eosinophilic globules. Treatment includes whole lung lavage. Post-therapeutic lavage CT may reveal persistent septal lines despite interval resolution of ground-glass opacity [3].

Pulmonary fibrosis has been reported in a small number of PAP cases [1–5]. Currently, it is not known whether pulmonary fibrosis in patients with PAP is coincidental or results as a consequence of long standing PAP. In either case, fibrosis develops in a minority of PAP patients, usually many years following initial diagnosis. It seems that GM-CSF plays a protective role in bleomycin-induced lung fibrosis [5,6]. It is therefore plausible that pathogenesis of pulmonary fibrosis in PAP, which is presently unknown, could be related to GM-CSF receptor impairment by auto-antibodies.
Fig. 2 – Chest radiograph and selected images of CT chest in the same patient following whole lung lavage, demonstrate near-resolution of the ground-glass opacities. There remain scattered areas of septal thickening, predominantly at the lung bases.

Fig. 3 – Chest radiograph and selected images of CT chest in the same patient, obtained in March 2012, demonstrate progression of the basilar-predominant interlobular septal thickening, which is now nodular, and associated with mild bronchiolectasis and architectural distortion - pattern suggestive of NSIP-type interstitial lung disease. NSIP, nonspecific interstitial pneumonitis.
Fig. 4 – Coronal and axial CT chest images in the same patient, obtained in February 2017, demonstrate mild progression of the basilar-predominant interlobular septal thickening and subpleural reticular densities, associated with increased bronchiolectasis and architectural distortion, compatible with NSIP. NSIP, nonspecific interstitial pneumonitis.

Declaration of interest

None.

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