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Extensive pulmonary alveolar microlithiasis

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Keywords
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Abstract

Pulmonary alveolar microlithiasis is a rare pulmonary disorder that is caused by abnormal sodium-dependent phosphate co-transporter from the mutation of *SLC34A2* gene, leading to accumulation of microliths in the alveoli. We report the extensive pulmonary alveolar microlithiasis in an elderly woman who presented with progressive dyspnea for 2 months. Chest radiograph revealed diffuse pulmonary calcification. Tissue histopathology from open lung biopsy demonstrated widespread intra-alveolar laminated calcium deposits compatible with pulmonary alveolar microlithiasis.

Introduction

Pulmonary alveolar microlithiasis (PAM) is a rare pulmonary disorder characterized by intra-alveolar accumulation of microliths consisting of calcium phosphate [1]. PAM is found worldwide but it predominates in Italy, Turkey, and the USA, whereas the reported cases of PAM in Thailand are only 14 in the literature [2]. The hallmark of this disorder is clinical-radiological dissociation. Many patients have no symptoms and are detected by characteristic chest radiograph findings. The disease is usually slowly progressive and may worsen over time, progressing into pulmonary fibrosis, respiratory failure, and cor pulmonale. We report the case of an elderly woman who presented with progressive dyspnea on exertion and hypoxemia for 2 months. Her chest radiograph showed diffuse pulmonary calcification and PAM was diagnosed by tissue histopathology.

Case Report

A 70-year-old woman with underlying disease of hypertension and ischemic left hemiparesis for 20 years, but who could perform the basic activities of daily living, presented with progressive dyspnea on exertion for 2 months but no fever, cough, or weight loss. Physical examination revealed crackles at both lower lungs, and oxygen saturation from pulse oximetry was 80% at room air. She was a cooked food seller her whole life and had no history of working in an industrial company. Her chest radiograph demonstrated diffuse pulmonary calcification (Fig. 1A). She underwent computed tomography of the chest, which showed bilateral extensive calcification diffusely involving both pulmonary parenchyma and interstitium (Fig. 1B and C). Open lung biopsy was performed and tissue histopathology revealed a widespread intra-alveolar laminated, onion-like calcium deposits with occasional ossification compatible with PAM (Fig. 2). The spirometry was not performed because the patient could not cooperate. She received supportive treatment and long-term oxygen therapy via nasal cannula 3 L/min. The lung transplantation was not offered in this patient because of her age. After discharge from the hospital, her condition improved and oxygen saturation increased up to 93%.

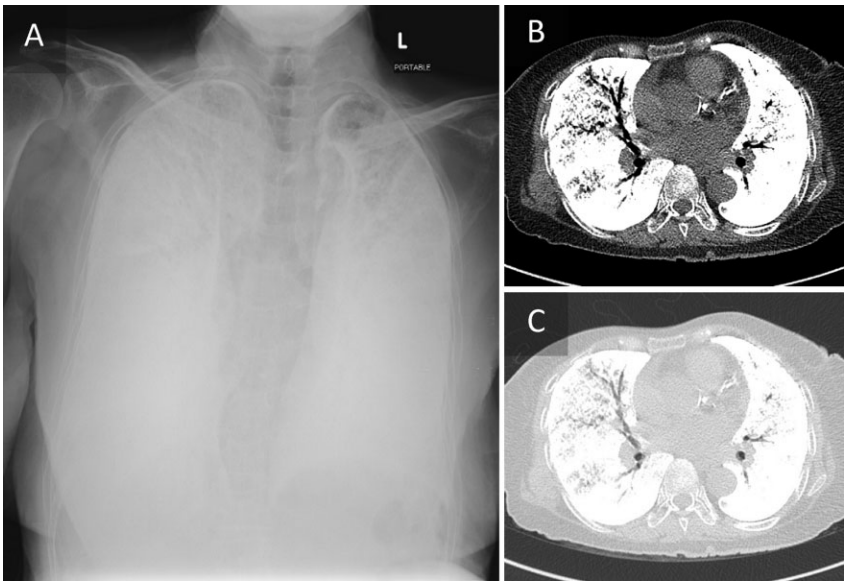

Figure 1. Chest radiograph (A) and high-resolution computed tomography of chest in mediastinal window (B) and lung window (C) demonstrated bilateral extensive calcification diffusely involving both lungs.

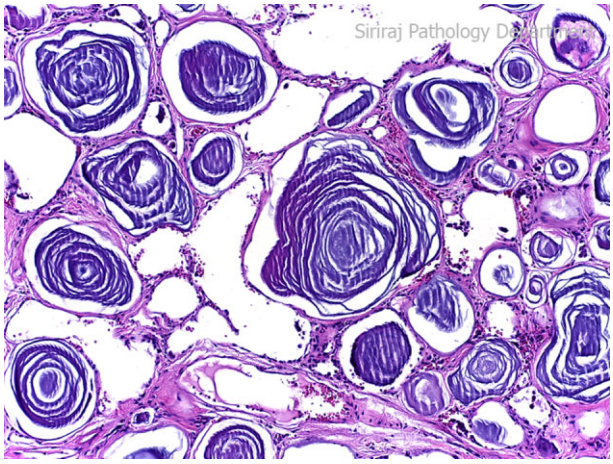

Figure 2. Tissue histopathology from lingula revealed a widespread intra-alveolar laminated calcium deposits.

Discussion

PAM is a rare pulmonary disease characterized by intra-alveolar accumulation of microliths consisting of calcium phosphate [1]. Mutation of *SLC34A2* gene, which encodes a type IIb sodium-dependent phosphate co-transporter, causes alveolar microlith deposit. The abnormal co-transporter cannot remove phosphorus ions from the alveolar spaces, leading to microliths formation in extra-cellular fluids [3]. PAM is found worldwide but it predominates in Italy, Turkey, and the USA, whereas the reported cases of PAM in Thailand are only 14 in the literature [2]. This disease is usually diagnosed from birth up to 40 years of age in both men and women. The hallmark of this disorder is clinical-radiological dissociation. Many patients have no symptoms and are detected by characteristic chest radiograph findings. In symptomatic patients, common presentation are dyspnea, non-productive cough, chest pain, and asthenia. The disease is usually slowly progressive and may worsen over time, progressing into pulmonary fibrosis, respiratory failure, and cor pulmonale. Blood chemistry testing, including serum calcium, phosphate, liver, renal, and parathyroid hormone, remains within normal range. However, some patients may develop extra-pulmonary calcifications, which are related to mutation in the *SLC34A2* gene, including medullary nephrocalcinosis, nephrolithiasis, gallstone, calcification of the lumbar sympathetic chain, and testicular involvement. Comorbidities associated with PAM include pectus excavatum, hypertrophic pulmonary osteoarthropathy, milk-alkali syndrome, diaphyseal aclasis, autosomal recessive Waardenburg anophthalmia syndrome, and lymphocytic interstitial pneumonitis [4].

Chest radiographic findings in PAM showed diffuse, sand-like micronodular infiltration particularly in lower lung zones, and other radiographic findings include dense consolidation and "black pleura" sign, which appears as an area of linear hyperlucency along the ribs or mediastinum caused by small, thin-walled subpleural cysts [1]. Common findings from high-resolution computed tomography (HRCT) are ground-glass opacities and subpleural

linear calcifications. Other HRCT findings are small parenchymal nodules, subpleural nodules, calcification along the interlobular septa, dense consolidation, and subpleural cysts [5].

Histopathology is sometimes required to confirm the diagnosis. Macroscopic lung examination reveals increased weight and consistency. Microscopic examination demonstrates numerous concentrically laminated with onion skin-like microliths within the alveolar spaces, which usually range from 50 to 1000 μm in diameter [4]. The microliths are mainly composed of calcium and phosphorus. In advanced cases, the microliths are deposited in the subpleural space, interlobular septa, and in bronchovascular bundles, where fibrosis and ossification are often observed.

Currently, the only effective therapy is lung transplantation. Another specific treatments such as systemic glucocorticoids, bronchoalveolar lavage, or disodium etidronate have not been proven to effectively prevent the progression of PAM [1]. Long-term oxygen therapy is necessary for the patients with hypoxemia and chronic respiratory failure; this can improve subjective daytime function and oxygenation.

In this reported case, the clinical presentation is not typical in that her symptoms developed in her old age and the lung parenchyma was extensively covered by microliths in the entire both lungs. However, the diagnosis of PAM was confirmed by open lung biopsy and characteristic histopathology. She received long-term oxygen therapy and supportive treatment. The lung transplantation was not offered in this case because of advanced age and comorbidities that indicate less optimal survival.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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