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Alveolar Microlithiasis in Clinical Practice: Case Report

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ABSTRACT

Pulmonary alveolar microlithiasis is a rare disease characterized by the deposition of microliths in the alveoli due to mutations in the SLC34A2 gene. The diagnosis is made more frequently between the second and fourth decade of life incidentally in chest images, it has a progressive course, with clinical-radiological dissociation, with no known effective treatment except for lung transplantation.

The case of a 37-year-old man with no personal history of exertional dyspnea is presented. Assessed by pulmonology with HRCT, which shows subpleural nodules and micronodules with diffuse pulmonary hyperdensity due to calcification, a pattern that suggests alveolar microlithiasis confirmed by histopathological study.

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Abbreviations

HRCT: High-resolution computed tomography
FEV1: Forced expiratory volume in one second
FVC: Forced vital capacity
DLCO: Diffusing capacity of the lungs for carbon monoxide
SP-A: Surfactant protein A
SP-D: Surfactant protein D

Introduction

Pulmonary alveolar microlithiasis is a rare autosomal recessive disease caused by mutations in the SLC34A2 gene, which encodes a sodium phosphate cotransporter, leading to difficulty in its elimination and consequent accumulation [1].

Their clinical presentation is highly variable; they can remain asymptomatic for many years before developing symptoms in their third or fourth decade of life. The most characteristic feature is clinical-radiological dissociation [2,3].

Confirming the diagnosis requires a lung biopsy. Currently, lung transplantation remains the effective treatment, although there is no prognostic data to determine the optimal time to refer a patient for lung transplantation [2].

A case of this condition is presented in a man whose presenting symptom was dyspnea.

Case Presentation

A 37-year-old Hispanic male patient, with no personal or family history. Clinical picture of several months' duration of exertional dyspnea. On physical examination, vital signs were normal, with blood pressure of 120/80 mm Hg, heart rate of 76 beats per minute, respiratory rate of 16 breaths per minute, temperature of 37°C, and oxygen saturation of 92% on room air. There were no signs of cyanosis or masses in the neck. Cardiac examination revealed a regular rhythm without murmurs, and breath sounds were diminished bilaterally. Abdominal examination revealed no masses, and pulses in the extremities were regular without edema. There was no evidence of clubbing of the nails.

Evaluated by the pulmonology service with pulmonary function tests, spirometry was normal with a forced expiratory volume in 1 second (FEV1) of 94%, forced vital capacity (FVC) of 103%, and FEV1/FVC ratio of 82%. There were no post-bronchodilator changes. Diffusing capacity of the lungs for carbon monoxide (DLCO) showed a mild decrease of 74%.

Imaging studies with chest X-ray revealed extensive reticulonodular interstitial opacities predominantly in the lower lobes. High-resolution computed tomography (HRCT) showed extensive alteration of pulmonary attenuation coefficients characterized by numerous subpleural peribronchovascular nodules and micronodules with thickening of interlobular septa and calcifications of some of these, ground-glass opacities with a disordered brickwork arrangement (Fig 1).

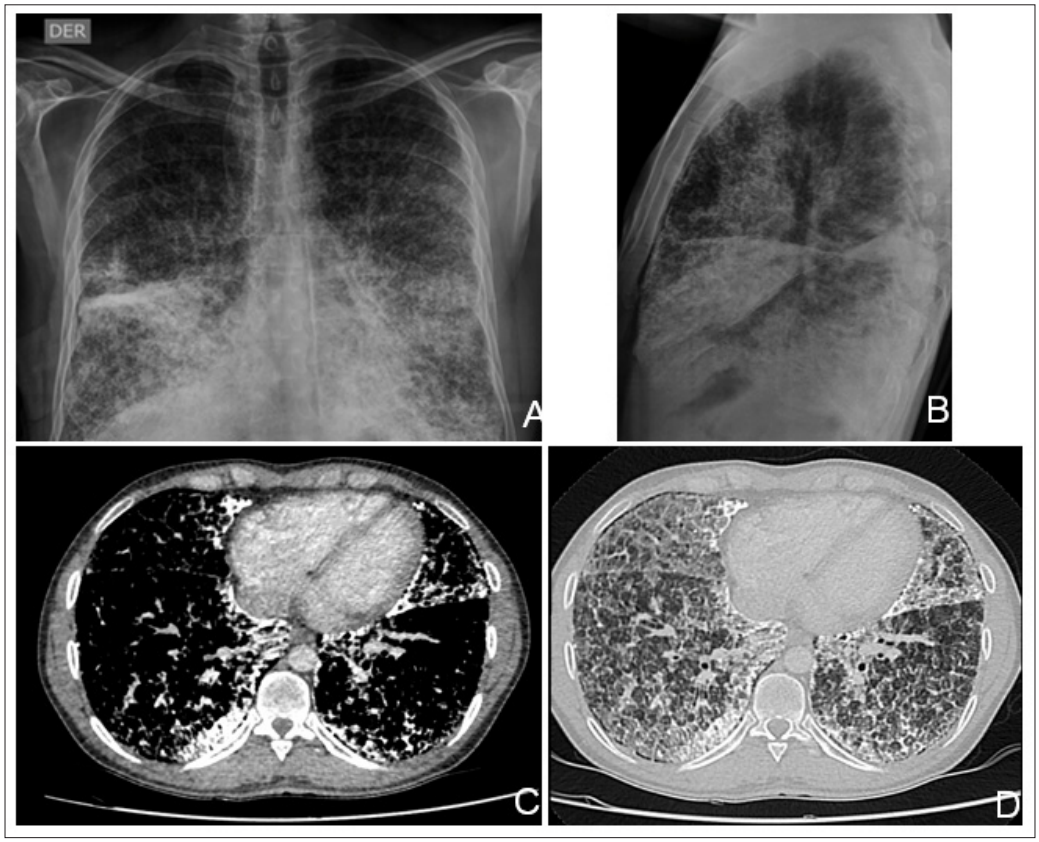

Figure 1A and B: Chest X-ray AP and lateral views, respectively showing multiple calcified nodular opacities bilaterally distributed, predominantly in the basal and hilar regions. C. High-resolution chest CT scan, mediastinal window, axial section, demonstrating calcified subpleural and peribronchovascular nodules. D. Pulmonary window, axial section, revealing thickening of interlobular septa associated with ground-glass opacities arranged in a disordered "crazy-paving" pattern.

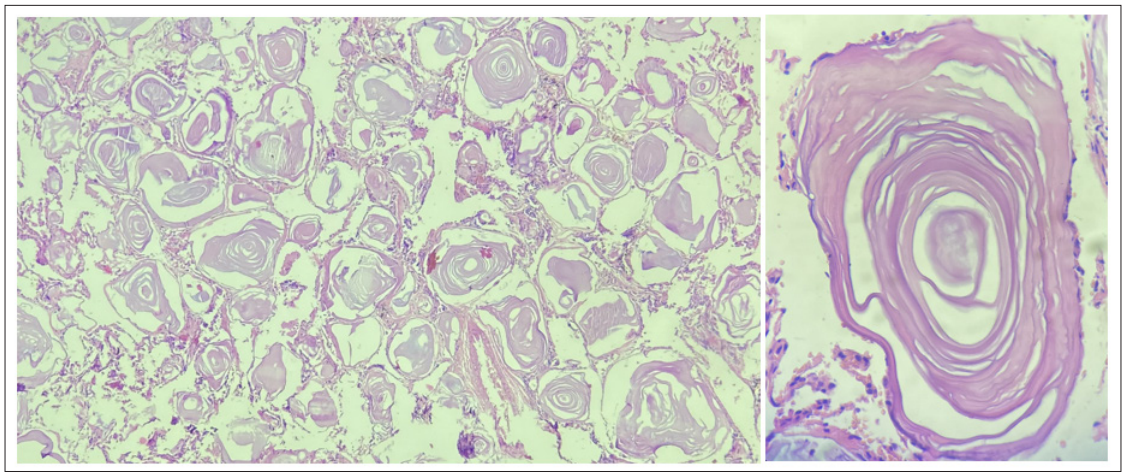

Figure 2: Hematoxylin and Eosin Staining. A. Multiple laminated calcospherites in the alveolar lumens and walls, and focal ossification (40x magnification). B. Laminated calcospherite (100x magnification).

Discussion

Pulmonary alveolar microlithiasis is an autosomal recessive disease caused by mutations in the SLC34A2 gene, which is mainly expressed in type II alveolar epithelial cells and is responsible for the absorption of phosphate released from phospholipids in surfactant [3]. Loss of function of this gene can lead to decreased phosphate absorption, which may result in the formation of intraalveolar microliths due to phosphate chelation by calcium in the extracellular fluid. The severity of the disease depends on the type of mutation (exon 12, exons 7 and 8) [4,5]. Currently, 1022 cases have been reported, with the majority in Asia (56.3%) and Europe (27.8%). The countries with the highest number of cases are Turkey (13.6%), China (13%), Italy (6.3%), and the USA (4.9%). The disease affects both sexes, with a slight male predominance (50.2%) and female (41.2%). Family history is present in 37.2% (381 out of 1022 patients), with females appearing to be predominant in familial cases [1].

Most of the described cases progress asymptomatically and are incidentally diagnosed between the third and fourth decades of life. Clinical features are heterogeneous and may include dyspnea, dry cough, chest pain, and fatigue. The disease can

progress slowly, remain stable, or over time progress to pulmonary fibrosis, respiratory failure, and cor pulmonale. Elevated serum concentrations of surfactant proteins SP-A and SP-D have been observed as the disease progresses, suggesting them as useful serum markers for monitoring disease activity and progression [4,6].

Pulmonary function tests are usually normal in the early stages of the disease but deteriorate over time. The main findings in spirometry include decreased forced vital capacity (FVC), normal or decreased forced expiratory volume in 1 second (FEV1), and a normal FEV1/FVC ratio, indicative of a restrictive pattern. Diffusion capacity of the lungs for carbon monoxide (DLCO) is decreased, and the 6-minute walk distance is reduced with desaturation as the disease progresses [2,4].

Chest X-ray is the initial study performed, where diffuse bilateral calcified micronodular infiltrates are documented, mainly in the middle and lower lung segments, resembling a "sandstorm" appearance. Four phases of radiographic evolution have been proposed. The first phase (precalcified) involves a small number of calcified microliths and ground-glass opacity, described in asymptomatic children. The second phase consists of scattered micronodules with diameters between 2 to 4 mm, with preserved cardiac and diaphragmatic borders. The third phase shows progressive opacification with interstitial thickening and blurring of cardiac and diaphragmatic borders. The fourth phase involves intense interstitial calcification with variable involvement of the pleural serosa, resulting in a lung "whitening" appearance [7-9].

High-resolution computed tomography (HRCT) identifies diffuse hyperdense micronodular opacities in the airspace, involving the posterior segments of the lower lobes and the anterior segments of the upper lobes. Microliths (calcified deposits) larger than 3 mm in diameter are also observed. Ground-glass opacities may be present, along with subpleural interstitial thickening, interlobular septal thickening, subtle cystic changes in the subpleural ventral region, and possible association with emphysema. The "black pleura" sign may also be observed, characterized by subtle subpleural cystic changes or a 1 to 2 mm wide layer of fat density between the ribs and the calcified parenchyma [2,9].

The histopathological examination reveals intra-alveolar deposits of spherical calcifications known as calcospherites, which can measure around 250 to 750 μm. Lamellated bodies with onion skin-like characteristics are also observed. Additionally, areas of interstitial fibrosis with minimal inflammatory reaction may be present [9].

There is no known effective treatment for the condition. Systemic corticosteroids, calcium chelating agents, and serial bronchoalveolar lavages have been demonstrated to be ineffective and are used as palliative treatments. Lung transplantation remains the only possible treatment for end-stage disease, with preference given to bilateral transplantation. However, there are no guidelines available for determining the optimal timing for this procedure. All patients should be referred for interdisciplinary management before they develop right ventricular dysfunction [4,10].

The present case corresponds to a patient in the fourth decade of life, where imaging and histopathological findings compatible with alveolar microlithiasis were documented. There is no history of comorbidities or family background. Clinical follow-up has remained unchanged to date. We consider the publication of this case relevant due to the scarcity of reported cases in Latin America.

Conclusions

Pulmonary alveolar microlithiasis is a rare disease, hence the need to increase suspicion based on imaging findings that allow for the classification of the disease's evolutionary stage. Multidisciplinary management involving pulmonologists, radiologists, and pathologists is considered relevant to avoid misdiagnosis and unnecessary treatments.

Authors' Contribution

All authors contributed equally to the review of the scientific literature, data analysis, and manuscript writing.

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Conflict of Interest

The authors declare no conflicts of interest. This manuscript has not been published and is not under consideration for publication elsewhere. Additionally, all authors have approved the content of this article and have accepted the journal's submission policies.

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