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Case Report

Pulmonary alveolar microlithiasis with minimal symptoms and near-complete whiteout on chest imaging ☆

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ABSTRACT

Pulmonary alveolar microlithiasis (PAM) is a rare idiopathic disease characterized by accumulated calcium and phosphate crystals within the alveoli. Although PAM can be suspected in patients with clinical-radiological dissociation and characteristic imaging findings on chest computed tomography, definitive diagnosis requires a family history of PAM, identification of *SLC34A2* gene mutations, or lung biopsy to exclude differential diagnoses. We report a case of a 66-year-old female incidentally found to have diffuse pulmonary calcifications. The diagnosis was confirmed through typical imaging features, transbronchial lung biopsy, and a family history of PAM. This case highlights the hallmark imaging characteristics of PAM and the critical role of transbronchial lung biopsy in establishing a definitive diagnosis. As PAM is a rare disease with no established consensus on treatment, except for lung transplantation, symptomatic management remains a significant challenge.

Introduction

Pulmonary alveolar microlithiasis (PAM) is a very rare idiopathic disease characterized by accumulated calcium and phosphate crystals within the alveoli [1]. The condition primarily results from mutations in the *SLC34A2* gene, impairing phosphate transport out of alveoli [2]. PAM typically progresses slowly over many years, is often associated with familial predisposition, and presents with characteristic imaging findings on chest computed tomography, along with clinical-radiological dissociation [3,4]. However, a definitive

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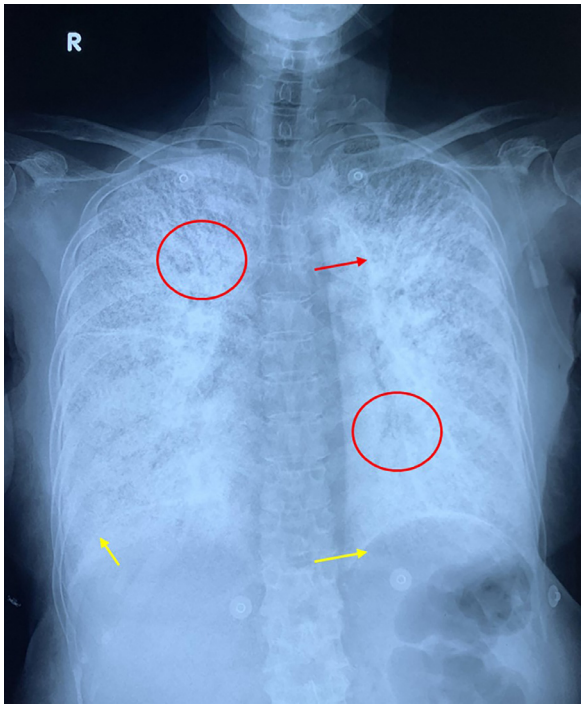

Fig. 1 – Chest X-ray reveals consolidation with air bronchograms (red circles) and high-density lesions, possibly indicative of calcification. A near-complete whiteout pattern is observed across both lung fields. Additionally, calcification of the mediastinal pleura (red arrow), diaphragmatic pleura, or diaphragm (yellow arrow) is recorded.

diagnosis requires histopathological evidence, confirmed *SLC34A2* gene mutations, or a family history of PAM [1]. Differential diagnoses, though rare, include metastatic calcification, dystrophic calcification, and pulmonary ossification.

We report a case of a 66-year-old female incidentally found to have diffuse pulmonary calcifications. The diagnosis was confirmed through typical imaging findings, transbronchial lung biopsy, and a family history of PAM. Despite near-complete bilateral pulmonary whiteout on imaging, the patient exhibited only mild hypoxemia at admission and minimal symptoms after discharge.

Case report

A 66-year-old female presented with upper respiratory tract infection symptoms, including sore throat, dry cough, and fever, lasting for 5 days. A chest X-ray revealed diffuse pulmonary lesions, prompting referral to the hospital for further diagnostic evaluation. The patient had a history of hypertension. No notable family history, including PAM, was reported.

At the Department of Pulmonary Medicine, the patient showed no significant respiratory symptoms except for a mild dry cough. Clinical examination revealed no abnormalities other than scattered crackles in both lung fields. Assessment of other organ systems was normal. Laboratory tests showed no abnormalities, including complete blood count, coagulation profile, antinuclear antibody (ANA), D-dimer, procalcitonin, anti-dsDNA, C3, C4 levels, liver enzymes, and renal function. The arterial blood gas analysis noted mild hypoxemic respiratory failure: pH 7.47, $PaCO_2$ 38.1 mmHg, PaO_2 51 mmHg (FiO_2 21%), and HCO_3- 28.2 mmol/L. Blood tests revealed hypocalcemia with a total calcium level of 2.0 mmol/L (normal range: 2.2–2.6 mmol/L) and hypophosphatemia with a phosphate level of 22.9 mg/L (normal range: 25-42 mg/L). Chest X-ray shows diffuse bilateral pulmonary consolidation, suspected calcification, and pleural or diaphragmatic calcifications (Fig. 1). Chest computed tomography reveals typical features of PAM, including extensive calcified lesions, interlobular septal thickening, and ground-glass opacities, resulting in near-complete lung whiteout. Lesions are more prominent in the lower lobes and peripheral lung regions (Fig. 2). The patient underwent a bronchoscopy to exclude differential diagnoses. Results revealed normal bronchial mucosa, with negative microbiological tests, including Acid-fast bacillus, fungal cultures, and bacterial cultures from bronchoalveolar lavage fluid (BALF). Liquid-based cytology of BALF showed no malignant cells. A transbronchial lung biopsy from the right lower lobe demonstrated numerous laminated calcified bodies scattered among macrophages, consistent with pulmonary microlithiasis. These findings confirmed the diagnosis of PAM (Fig. 3).

Following the confirmed diagnosis, the patient was counseled on the disease and advised to screen family members for PAM. The patient's biological sister was subsequently diagnosed with asymptomatic PAM. The patient is under monitoring, as lung transplantation is not feasible, and no proven effective treatment is currently available.

Discussion

Our case represents a rare instance of PAM, confirmed through histopathological evidence of pulmonary parenchyma. This report highlights the essential criteria for a definitive diagnosis of PAM. Differential diagnoses, although uncommon, include metastatic calcification, dystrophic calcification, and pulmonary ossification.

Several characteristic factors of PAM were observed in this case. Firstly, family history is important and should be screened before other investigations. According to Patrick et al.'s diagnostic algorithm, PAM can be definitively diagnosed without further testing if chest computed tomography imaging is consistent and there is a family history of a sibling or parent with confirmed PAM [1]. This approach saves time, reduces costs, and avoids the risks of lung biopsy. In our case, family screening after the patient's diagnosis revealed her sister also had PAM, eliminating the need for further diagnostic tests for her. Secondly, clinical–radiological dissociation is a key characteristic of PAM, where the extent of diffuse lung damage on imaging is disproportionate to the patient's clinical symptoms [2,5]. Despite nearly complete bilateral lung opacification in our case, the patient presented with only mild hypoxemia on admission and minimal exertional limitation postdischarge. Thirdly, the hallmark imaging finding in PAM on chest computed tomography is dif-

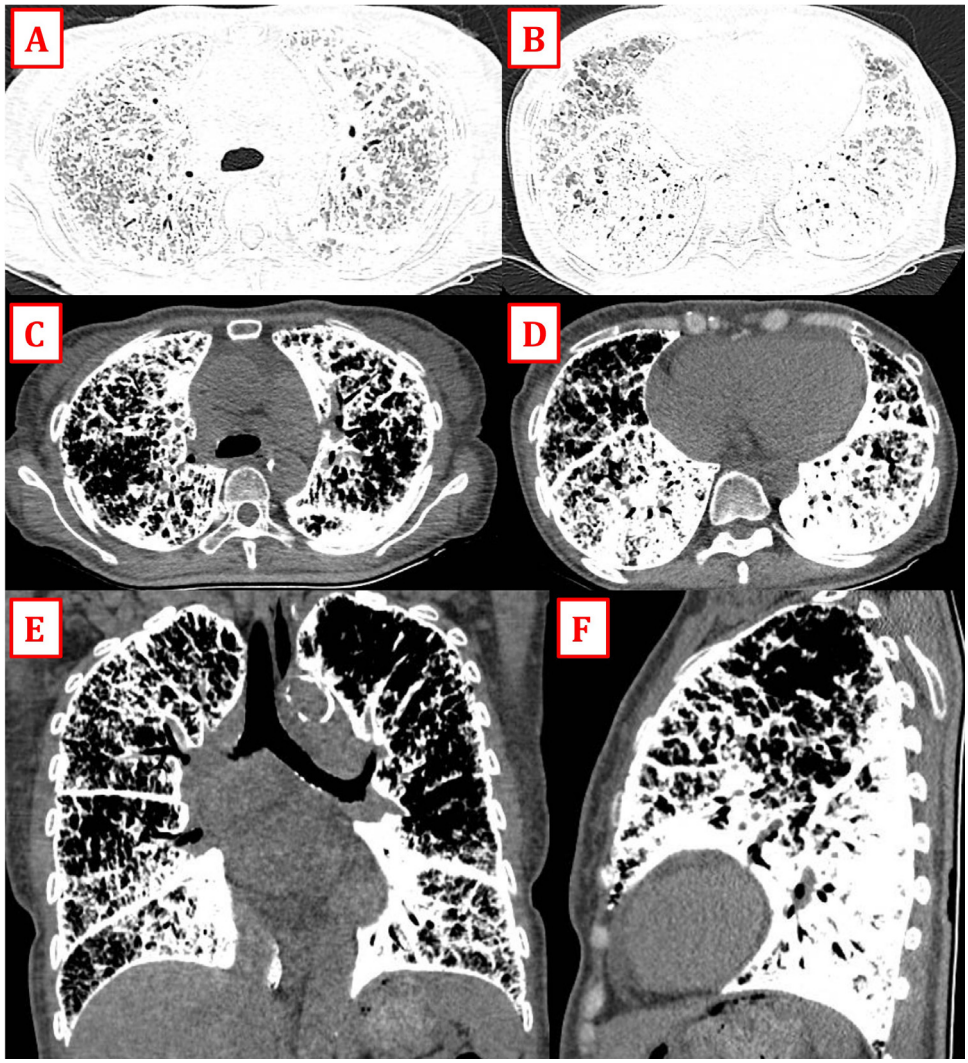

Fig. 2 – Chest computed tomography. (A and B) show extensive calcified lesions, interlobular septal thickening, and ground-glass opacities create a "crazy paving" pattern. (C and D) highlight calcifications predominantly in the lower lobes and peripheral regions, with thickened and calcified interlobar fissures. (E and F) provide detailed views of the lesions across different lung planes.

fuse bilateral pulmonary calcification, predominantly involving the lower lobes and subpleural regions, often with consolidation and air bronchograms [1,3,6]. This was consistent with our case report. Extrapulmonary calcifications, reported in organs such as the pleura, diaphragm, testes, breasts, small intestine, and kidneys, further suggest a systemic disorder like PAM [1].

PAM is a congenital disease caused by mutations in the *SLC34A2* gene. This gene inactivates the sodium-dependent phosphate cotransporter in alveolar type II cells, leading to excessive phosphate accumulation in the alveoli and the formation of calcium-phosphate complexes [1,4]. In our case, flexible bronchoscopy was performed to rule out possible differential diagnoses of PAM, including pulmonary tuberculosis, pneumoconiosis, autoimmune diseases, amyloidosis, sarcoidosis, dendriform pulmonary ossification, and metastatic calcification from hyperparathyroidism, end-stage renal disease, or malignancy. This was achieved through bronchoalveolar lavage cytology, microbiological tests, and histopathological examination of biopsy specimens. Patrick suggested a diagnostic algorithm to confirm a diagnosis of PAM [1]. If familial PAM screening is not feasible, genetic testing for *SLC34A2* mutations can aid in diagnosis. However, due to the rarity of PAM and the unavailability of *SLC34A2* genetic testing in many healthcare facilities, evidence of PAM from sputum, BALF, or lung tissue becomes essential for diagnosis [1]. In our case, the liquid-based cytology of BALF did not detect microliths or cells with suspicious malignancy. Ultimately, lung tissue biopsy—via transbronchial lung biopsy, cryobiopsy, or video-assisted thoracoscopic surgery—was necessary to confirm the diagnosis and exclude differential diagnoses such as metastatic calcification, dystrophic calcification, and pulmonary ossifica-

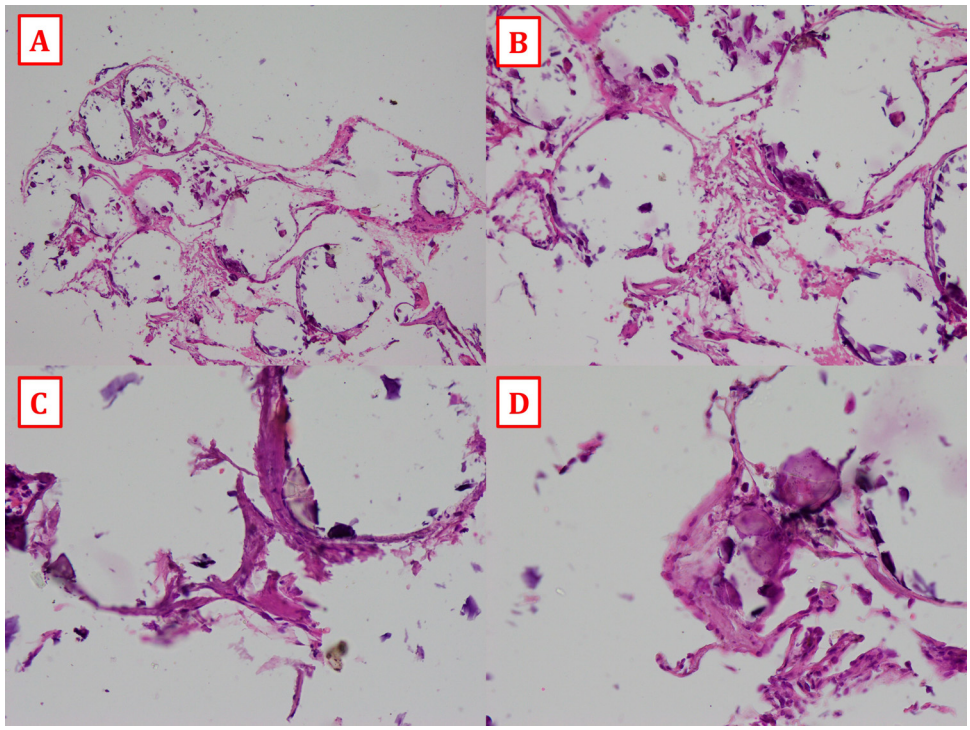

Fig. 3 – Histopathology of transbronchial lung biopsy from the right lower lobe stained with Hematoxylin-Eosin (HE). (A) (100x magnification) and 3B (200x magnification) show pulmonary calcification deposits. (C and D) reveal laminated calcified bodies with sheet-like structures.

tion. In this patient, a transbronchial lung biopsy revealed microliths confined to alveoli without interstitial involvement, supporting the diagnosis of PAM. This approach emphasizes the importance of histopathology in establishing a definitive diagnosis when noninvasive methods are inconclusive.

To date, lung transplantation remains the only effective treatment for PAM. Other approaches, such as disodium etidronate (a bisphosphonate) and dietary phosphate restriction, have not demonstrated efficacy in adult patients [1,4]. Therefore, in our clinical case, the decision was made to continue monitoring the patient without initiating specific treatments. This highlights the challenges in managing PAM and the need for further research to identify alternative therapeutic options.

Conclusion

Pulmonary alveolar microlithiasis is a rare idiopathic disease. A definitive diagnosis requires consistent imaging on chest computed tomography, a family history of pulmonary alveolar microlithiasis, identification of *SLC34A2* gene mutations, or lung tissue biopsy. The management remains challenging, as no treatments have been proven effective except for lung transplantation. This underscores the importance of early detection, family screening, and ongoing research into therapeutic strategies for this rare condition.

Patient consent

Written informed consent was obtained for the publication of this case report.

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