



CASE REPORT

# A Case of Pulmonary Alveolar Microlithiasis Diagnosed by Transbronchial Biopsy

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## Abstract

Pulmonary alveolar microlithiasis is a rare infiltrative pulmonary disease, in which intraalveolar accumulation of small stones (microliths) consisting of calcium phosphatite occurs. It is an autosomal recessive disorder. The disease occurs as a result of the disruption of type IIb sodium phosphate cotransporter in type II alveolar cells after the mutation of *SLC34A2*. Majority of patients are diagnosed between age 20 and 40. Here, we present a case of alveolar microlithiasis that was diagnosed with transbronchial biopsy.

**KEYWORDS:** Microliths, pulmonary alveolar microlithiasis, transbronchial biopsy

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## INTRODUCTION

Pulmonary alveolar microlithiasis (PAM) is an extremely rare interstitial lung disease, which is characterized by intraalveolar accumulation of microliths. It is an autosomal recessive disorder [1]. Clinical presentation varies from asymptomatic to life-threatening respiratory failure [2]. The typical radiological image is a bilaterally dense diffuse micronodular view called snowstorm. White lung pattern may be seen in advanced disease [3]. Clinicoradiologic findings, genetic studies, and histopathological confirmation are used to diagnose PAM. The definitive treatment of PAM is only lung transplantation [4]. Here we present a case of PAM that was diagnosed with transbronchial biopsy.

## CASE PRESENTATION

A 31-year-old non-smoker female was admitted to our clinic with non-productive cough, chest pain, and dyspnea symptoms. She had no remarkable diseases in her past history. End-inspiratory fine crackles were detected on thorax auscultation. Posteroanterior chest X-ray showed intense reticulonodular pattern in bilateral lung fields. Thorax computed tomography revealed a bilateral diffuse dense reticulonodular appearance with no mediastinal lymphadenopathy (Figure 1). There was restrictive pattern on pulmonary function testing (forced vital capacity: 71%, forced expiratory volume: 72%; Tiffeneau index: 88%) and mild hypoxia on arterial blood gas analysis. Hemogram, biochemistry, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) tests were normal. After the patient and her relatives signed informed consent forms, diagnostic fiberoptic bronchoscopy was performed and endobronchial lesion was not observed. Transbronchial biopsy and bronchoalveolar lavage were performed. Results of AFB tests and tuberculosis culture (Löwenstein-Jensen medium) from bronchial lavage samples were negative. Transbronchial pathology was reported as alveolar lamellar calcification (Figure 2). Increased uptake of Tc-99m was observed in the middle and lower parts of the bilateral lungs on whole body bone scan and patient diagnosed as alveolar microlithiasis (Figure 3). Family screening was performed with chest X-ray, and no abnormality was found in other family members and it was considered sporadic PAM.

## DISCUSSION

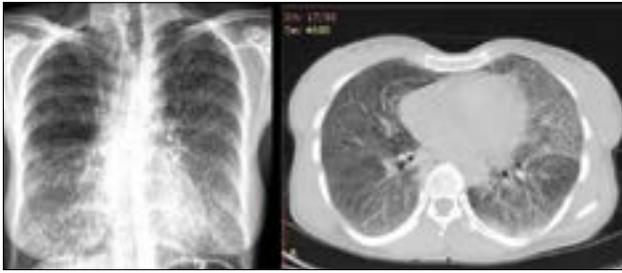
Pulmonary alveolar microlithiasis is an autosomal recessive disease characterized by the deposition of stones called microliths in the intraalveolar space. *SLC34A2* mutation results in a disruption in the sodium phosphate transport in type II alveolar cells and calcium phosphate stones called microliths begin to accumulate in the interstitium [5,6].

Until now, a total of 1022 cases of PAM have been reported worldwide, with the most number of reports being from Turkey with 139 patients. While sex differences varies with region, male sex has been reported more frequently in Turkey (67% male and 33% female). Although it can be seen in almost all age groups, it is often diagnosed in the second and third decades [1].

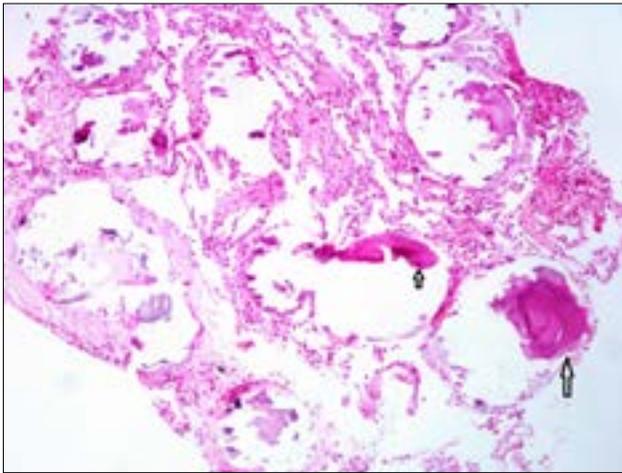
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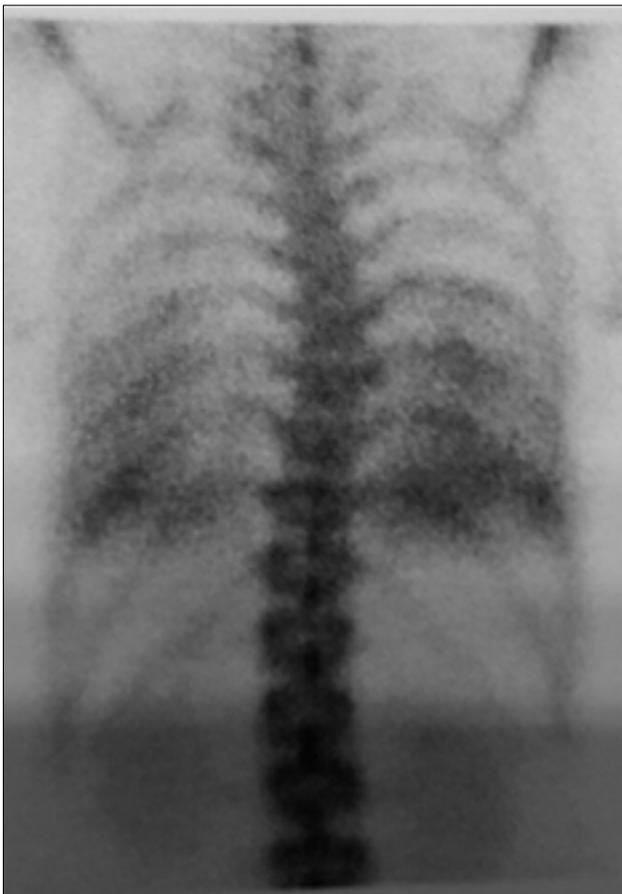




**Figure 1.** Bilaterally diffuse dense multiple micronodules



**Figure 2.** Calcified lamellar bodies (arrows) are viewed in the alveolar lumens  
(Hematoxylin & Eosin, 100× magnification)



**Figure 3.** Increased uptake of Tc-99m is observed in the bilateral lungs field

We reached the following conclusions when we examined previous articles on the Turkish population. Ucan et al.[7] published a review article that included 52 cases of PAM, and they stated that the female/male ratio was approximately 1/2, mean age was 27.3, and the most common symptoms were cough and dyspnea. Usually restrictive pattern was detected on pulmonary function test, and family history was reported in almost half of the cases. Tanrikulu et al.[8] said that in a case series of eight patients with PAM in Turkey, PAM was more common in males. Although the majority of patients were asymptomatic, the most common symptoms were cough and shortness of breath. Restrictive pattern was determined in pulmonary function test of patients. The incidence of PAM per million of population was 1.85 for Turkey and male predominance was reported by Castellena et al.[9].

Clinical presentation varies from asymptomatic to pneumothorax, even life-threatening respiratory failure [2]. Our patient had exertional dyspnea, non-productive cough, and chest pain complaints. The characteristic radiological finding is a bilaterally dense diffuse micronodular changes called sandy or snowstorm. White lung phenomenon can be seen in advanced cases [3]. There was a snowstorm view in radiologic images of our patient, and increased uptake of radiopharmaceutical substance was observed in the bilateral lungs area on bone scan. Similar radiological appearances can also be seen in pneumoconiosis, sarcoidosis, tuberculosis, hemosiderosis, and amyloidosis.

Diagnosis and differential diagnosis are made by bronchoalveolar lavage, transbronchial biopsy, and open lung biopsy [9,10]. Our patient was diagnosed with bronchoscopy and transbronchial biopsy. Genetically autosomal recessive transition and mutation in *SLC34A2* gene are defined in this entity [5]. We could not perform genetic studies on our patient. Approximately 32% of cases are familial [1]. Our case was considered a sporadic PAM as there was no familial feature.

Histopathologically PAM characterized by intraalveolar microliths accumulation which staining with periodic acid-Schiff and microliths consist of calcareous concentric lamellae around a central nucleus with an amorphous or granular aspect. Calcifications are located in interstitial or vascular compartments [3,6]. Histopathologic examination of our case revealed that calcified lamellar bodies exist in the alveolar lumens.

Therapeutic options are limited and the only definitive treatment is lung transplantation. Calcium sequestrants, serial bronchoalveolar lavage, and corticosteroid treatment have been shown to be effective in preventing disease progression and are thought to have a palliative role. Although bisphosphonates are recommended in the treatment of PAM, efficacy data are limited. Therefore, although there is no prognostic data to identify the same indications, lung transplantation remains the only current treatment option [1-4].

Pulmonary alveolar microlithiasis is a rare interstitial lung disease that can persist with mild symptoms, and it should be kept in mind in the differential diagnosis of interstitial lung

disease, and transbronchial biopsy can be used for diagnosis at centers where genetic mutations cannot be studied.

**Informed Consent:** Written informed consent was obtained from patient who participated in this case.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - H.A., M.S., N.A., F.B., A.Y.B., H.K., M.T.; Design - H.A., M.S., M.A., F.B., A.Y.B., H.K., M.T.; Supervision - H.A., M.S., M.A., F.B., A.Y.B., H.K., M.T.; Resources - H.A., M.S., N.A.; Materials - H.A., M.S., F.B.; Data Collection and/or Processing - H.A., M.S., H.K.; Analysis and/or Interpretation - H.A., M.S., M.T.; Literature Search - H.A., M.S., M.T.; Writing Manuscript - H.A., M.S., A.Y.B.; Critical Review - H.A., M.S., N.A.; Other - H.A., M.S., M.T.

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