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Pulmonary Alveolar Microlithiasis Diagnosed During Video-Assisted Thoracoscopic Surgery; A Case Report

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ABSTRACT

Pulmonary alveolar microlithiasis (PAM) is a rare inherited pulmonary disease characterized by the deposition of intra-alveolar calcium deposits. In most of the Asian and European countries, PAM is usually misdiagnosed as pulmonary tuberculosis and sarcoidosis. We presented a young case of PAM manifested as chronic progressive dyspnea unresponsive to corticosteroids for one year. The first diagnostic clues were made by high resolution computed tomography. Although Bronchoalveolar lavage and transbronchial lung biopsy examination were unremarkable, however, after performing a Video-assisted thoracoscopic surgery, the biopsy specimens confirmed the diagnosis of PAM.

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Introduction

Pulmonary alveolar microlithiasis (PAM) is an autosomal recessive disorder mostly remaining asymptomatic until adulthood (1). Although the insidious nature of the disease makes the establishment of the true prevalence of PAM more difficult, however, it has been reported that most of the patients with PAM are from Asian and European countries (2, 3). The first diagnostic clues of PAM are usually seen in classical imaging studies as numerous calcifications in the lungs (1). The most challenging issue regarding PAM is the late diagnosis and misdiagnosis of this rare pulmonary disease (1). Although there is not any definite treatment available for this rare disease; however, the earlier diagnosis could improve the outcome (1). The present report will discuss a case of PAM in a young male patient misdiagnosed as sarcoidosis.

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Case Presentation

A 30 years-old non-smoker male patient referred because of progressive dyspnea since a year ago. The patient did not have a history of fever, weight loss, or hemoptysis and the only remarkable medical condition was nephrolithiasis documented in a previous computed tomography scan. Moreover, the patient did not have any history of previous pulmonary diseases including tuberculosis, and none of his family members had similar clinical manifestations. Drug history was unremarkable and the dyspnea did not respond to corticosteroid therapy. On physical examination, the oxygen saturation was 97%, respiratory and pulse rates were 24 breaths/minute and 86 pulse/minute, respectively. The patient was afebrile and the systolic/diastolic blood pressure was 120/80 mmHg. The complete blood count and erythrocyte sedimentation rate were normal. The transthoracic echocardiography showed reduced left ventricular ejection fraction (40%) without any signs of left ventricular hypertrophy and mildly elevated pulmonary artery pressure (38 mmHg). To assess the possible cardiomyopathy, the patient underwent cardiovascular MR. The only remarkable cardiac findings were a top normal left ventricular mass, left ventricular ejection fraction of 45%, and a right ventricular ejection fraction of 35%. The patient underwent lung high resolution computed tomography (HRCT). The noncontrast HRCT showed numerous centrilobular and ground-glass infiltrates through both lung fields (Figure 1). Multiple lymph nodes of variable size and normal internal integrity were noted at the mediastinal and perivascular areas with the largest measuring about 15 mm at the pericardial region. The pulmonary trunk (43mm in diameter) and central pulmonary arterial branches appeared prominent. Further laboratory evaluations including antinuclear antibody (ANA), Anti-neutrophil cytoplasmic antibody (ANCA) (P and C), Anti-cyclic citrullinated peptide (anti-CCP), and quantitative levels of rheumatoid factor were unremarkable. The plasma ACE level was elevated (189 U/Lit, normal range: 8-65 U/Lit) highlighting the possible diagnosis of sarcoidosis.

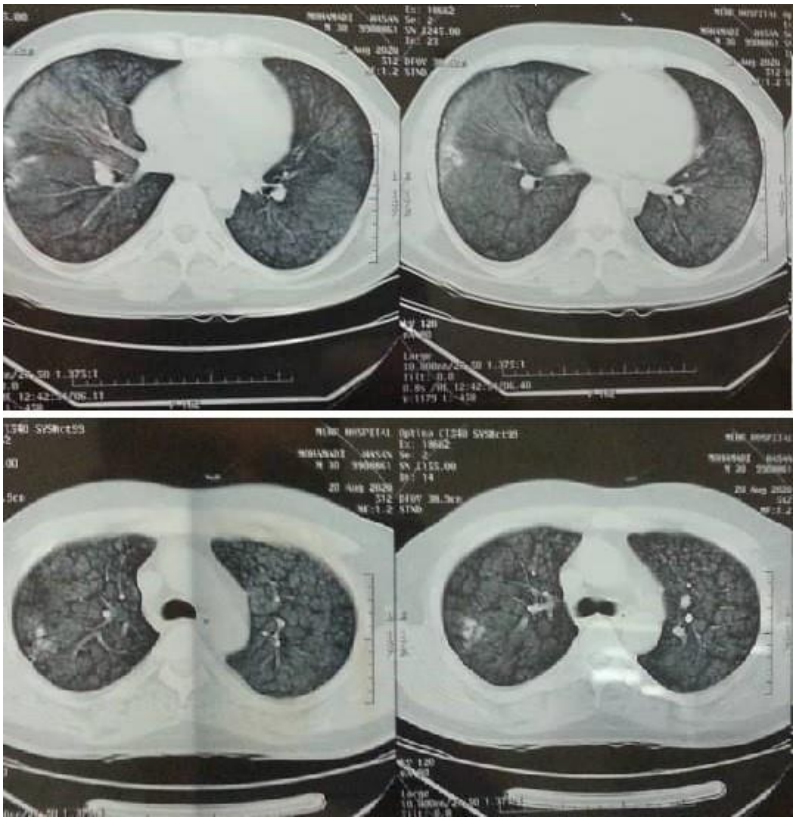

Figure 1. The high resolution computed tomography of chest revealed numerous centrilobular and ground-glass infiltrates in both lungs.

The patient then underwent a bronchoscopic evaluation (Figure 2). The bronchoscopic evaluation of the lungs revealed bilateral ill-defined nodular infiltration. The Bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) examination were negative for malignancy and there were not any acid-fast bacilli seen. After performing a Video-assisted thoracoscopic surgery (VATS), the pathologic evaluation of the upper and middle lobes of the lung segmentectomy was consistent with pulmonary alveolar microlithiasis indicating diffuse micro-calcification with lobular rounded calcospherites within the alveolar septa (Figure 3). The patient discharged on inhaled corticosteroids and remained asymptomatic during 6 mounths of follow up.

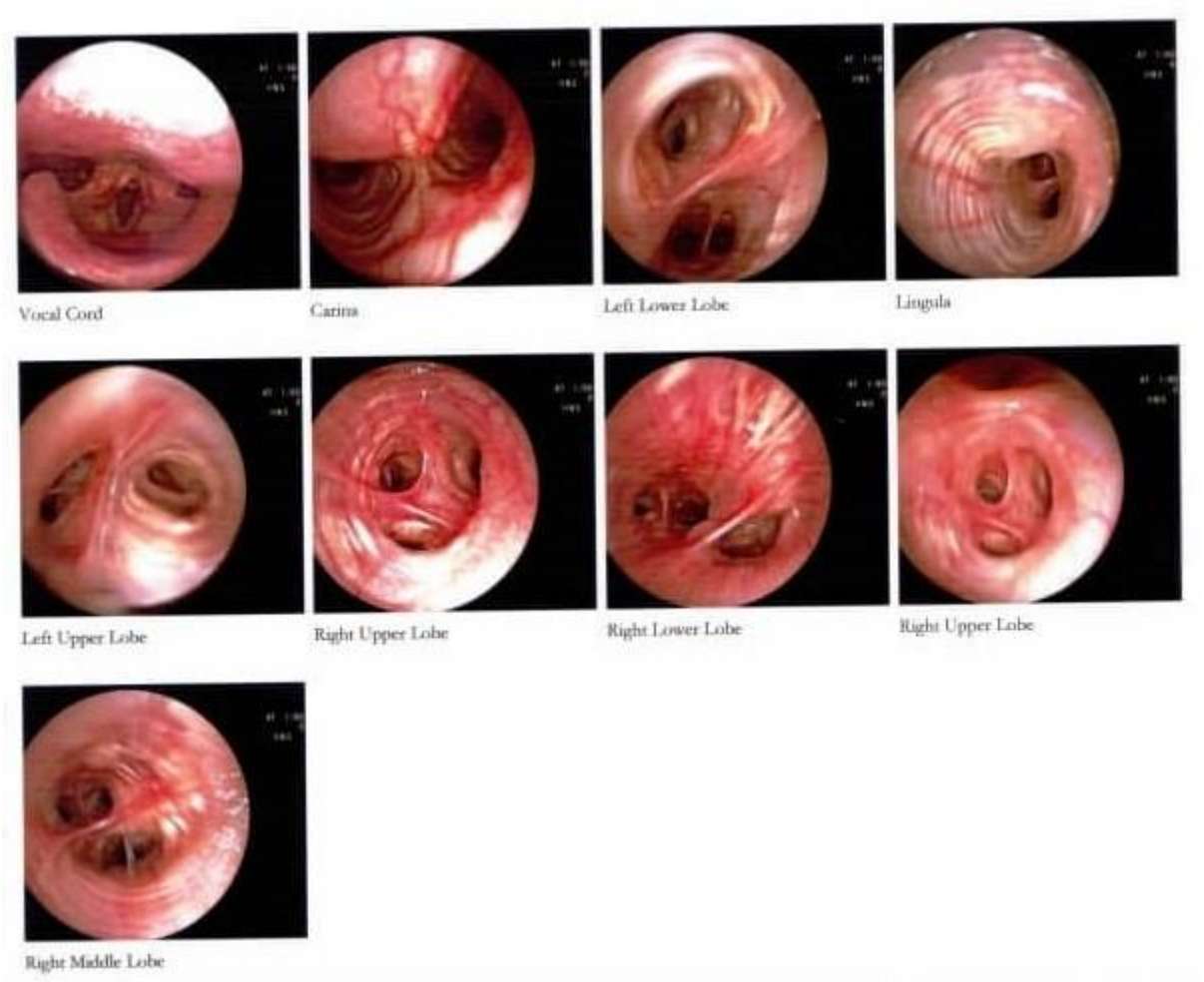

Figure 2. There was not remarkable finding during the bronchoscopic study.

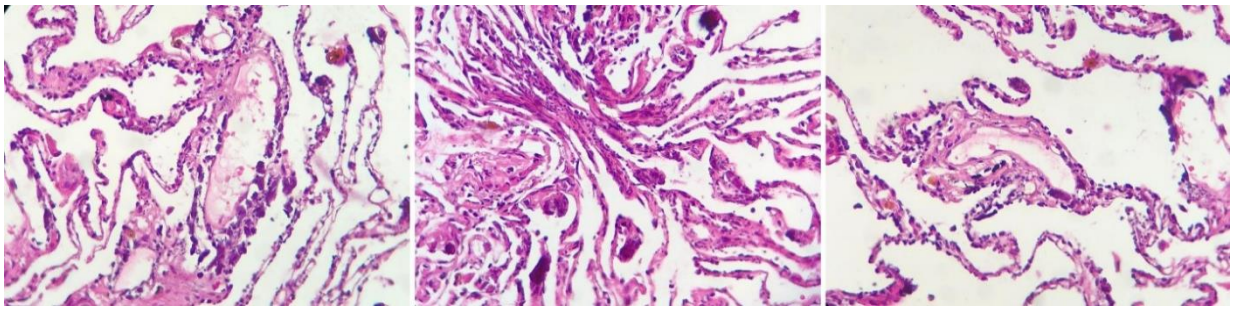

Figure 3. The Sections show alveolar walls filled with calcified materials and some giant cells Hematoxylin and eosin staining (x100).

Discussion

The present report discussed a case of PAM in a young male patient that was misdiagnosed and mismanaged as sarcoidosis. PAM is a rare autosomal recessive disorder where calcium phosphate microliths form gradually in intra-alveolar spaces. The former is a result of the inability of alveolar epithelial type II cells in clearing phosphorus ions leading to microlith formation. The solute carrier family 34 member 2 (SLC34A2) gene is responsible for coding a sodium phosphate-IIb transporter protein and mutations in SLC34A2 cause defective function of the transporter leading to calcium phosphate deposit .

It has been reported that approximately one-third of the PAM patients have a positive family history (2). Since PAM is a rare hereditary pulmonary disease with an insidious course, the diagnosis is usually delayed and misdiagnosis is probable. As the same as our patient, most of the PAM patients are diagnosed in their 3rd decade of life and the most common clinical manifestation is breathlessness (4). Although nephrolithiasis is rarely reported with PAM, however, our patient had nephrolithiasis on HRCT (4). It seems that the misdiagnosis of PAM mostly depends on the endemic pulmonary disease in each part of the world. While PAM is most prevalent in countries with a high prevalence of tuberculosis, a common differential diagnosis especially in the Mediterranean region could be miliary tuberculosis. Castellana et al. reviewed 1022 PAM cases from the literature and reported that more than 72 patients were incorrectly diagnosed as military tuberculosis (2). Similarly, a review of Indian literature on PAM revealed that misdiagnosed as pulmonary tuberculosis (4). Another review on 576 published studies also reported that tuberculosis and sarcoidosis are the 2 most likely differential diagnoses of PAM that is misdiagnosed in 88 cases (5). Therefore, considering the history of fever, cough, weight loss, and fatigue especially in a patient in an immunosuppressive state may facilitate the diagnosis of miliary tuberculosis and reduce the risk of misdiagnosis. Sarcoidosis is another differential diagnosis of PAM that could be misdiagnosed with pulmonary tuberculosis. Regarding the considerable number of differential diagnoses with similar imaging findings and because of the lack of diagnostic findings for PAM in imaging studies, performing invasive diagnostic techniques would be beneficial. Both bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) provide valuable diagnostic information and microliths might be seen by both techniques (6, 7). While the BAL and TBLB were unremarkable in our patient, it has been demonstrated that approximately one-third of BAL samples are suggestive for PAM and contain calcospherites (4). The most common biopsy findings in tissue samples are microliths in alveolar spaces as well as intra-alveolar spherical calcifications. It has been reported that most of the PAM cases are treated supportively (5). Although most of the PAM patients are treated with corticosteroids; however, the role corticosteroids are not studied in these patients (4, 5). Up to now, the only effective treatment for PAM is lung transplantation, which is mostly reserved for the end stage of the disease (4, 5).

Up to now, there is not any specific treatment available for PAM, and most of the patients are managed by both invasive and noninvasive palliative therapies. Lung transplantation is the only possible treatment for end-stage pulmonary diseases.

PAM is a rare genetic pulmonary disease that is mostly misdiagnosed by chronic pulmonary diseases including tuberculosis and sarcoidosis. Our present report demonstrated that PAM should be considered as a differential diagnosis of long-lasting dyspnea unresponsive to corticosteroids even if BAL and TBLB provided unremarkable findings.

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