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Case Report

Pulmonary Alveolar Microlithiasis: An Incidental Case Report from Jordan with Literature Review

Basheer Radi Alakhras[1, *], Omar Habashneh[1], Ahmad Basim Yaghi[2], Abdallah Daseh[3], Adham Alkilani[4]

[1]Pathology Department, Albasheer Hospital, Amman, Jordan
[2]Radiology Department, Albasheer Hospital, Amman, Jordan
[3]Faculty of Medicine, Hashemite University, Zarqa, Jordan
[4]Department of General Surgery, Albasheer Hospital, Amman, Jordan

Abstract

Pulmonary alveolar microlithiasis (PAM) is one of the rare lung diseases, in which an otherwise healthy individual develops diffuse alveolar calcifications. It is reported to be caused by mutation of the SLC34A2 gene. Patients who are eventually diagnosed with PAM usually present late when progression to cor pulmonale has already developed, or for other reasons not related to the disease itself when their clinical work up results incidentally reveal much worse findings than the patient's actual state. Unlike the familiar information that no effective treatment other than lung transplant, cardiokinetics, diuretics, oxygen, and repeated bronchoalveolar lavage were reported with relatively satisfactory results and chest X-ray changes. In this report, we focus on the relation between clinical, radiologic and histologic findings, in which clinical scenario was first mistaken for interstitial fibrosis or suspected metastasis, and on literature review. Chest radiography, bronchoalveolar lavage and lung wedge biopsy were the main steps to reach the diagnosis of PAM. Gradual improvement after conservative treatment was noted prior to discharge. Then clinic appointment for follow up and family members surveillance was scheduled. A rare disease incidentally diagnosed by high awareness of the attending physician and simple methods that points to a question of disease prevalence in Jordan.

Keywords

Lung Calcification, Pulmonary Alveolar Microlithiasis, Stone Lung

1. Introduction

Pulmonary alveolar microlithiasis (PAM) is rarely diagnosed lung disease with less than 1500 reported cases around the world and 2 reported cases in Jordan including this case report [1]. PAM often has a late presentation due to slow progression and lack of symptoms which usually present in the form of hypoxia related signs and symptoms including shortness of breath and dry cough. A characteristic radiological finding on chest x-ray and high-resolution computed tomography scan help to tract physician's attention to this entity, findings including diffuse sand storm appearance and

*Corresponding author: basheerradi@yahoo.com (Basheer Radi Alakhras)

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black pleura sign. Lung biopsy is usually required for definite diagnosis with the characteristic concentric calcified concretions in alveolar spaces, especially where genetic study is unavailable given that SLC34A2 gene mutation is reported to be found in both hereditary and sporadic forms of this disease. A silent easily diagnosed disease, with rather devastating outcome could possibly be emerging in Jordan and middle east countries unnoticed. While no definite treatment is agreed on in literature other than conservative methods mentioned later on, lung transplant presents as a viable option for patients with severe disease and cardiac complications [2].

2. Clinical presentation

A 38 y/o female, a housewife who is otherwise medically free, nonsmoker, presented to emergency room complaining of worsening shortness of breath at rest and with minimal exertion, associated with dry cough for 10 months, her cough was not altered by environmental changes, she also complained of weight loss (15 kg in a year) and anorexia, without hemoptysis or fever, she also noted changes in her nail bed shape.

Her vitals were: afebrile (temperature 37c), with mild tachypnea and tachycardia (respiratory rate 21 and heart rate 100), her blood pressure reading was (108/61) and oxygen saturation was 71% in room air and reached 94% on simple face mask. On physical examination she had decreased air entry bilaterally without crackles, her heart sounds were normal, clubbing of her nails was noted, no chest or spine deformities were identified. No electrocardiogram changes, and venous blood gas results were as follows: PH: 7.42, HCO3: 22.2, PCO2 34.6, PO2 61.3

Chest X-ray showed diffuse tiny opacities scattered all over lung fields (Figure 1). High resolution chest CT scan revealed extensive sand like calcifications of the pulmonary parenchyma with relative sparing of the subpleural area forming the black pleura sign. The heart, great vessels and esophagus were normal in appearance. There is no lymphadenopathy. The pleural spaces are clear (Figure 2).

2 Dimension Echocardiogram was performed and showed quite normal left ventricular systolic function, ejection fraction of 60%, normal pressure gradient, normal aortic valve, trace mitral regurge, grade 1 tricuspid regurge, pulmonary arterial pressure of 25mmHg and no pericardial effusion.

Routine blood investigations revealed no significant abnormality. The patient was admitted as a case of lung fibrosis versus metastatic malignancy for investigation, was placed on oxygen and conservative therapy and was planned for lung biopsy given that bronchoalveolar lavage (BAL) cytology results were inconclusive.

Histopathologic examination of a lung wedge resection revealed extensive alveolar and interstitial basophilic, concentric, laminated calcified concretions (Figures 3, 4). Mild interstitial fibrosis with minimal inflammatory cells (Figure 5). Histologic findings along with radiologic appearance were conclusive to the diagnosis of pulmonary alveolar microlithiasis. Conservative treatment with oxygen were enough for gradual improvement in oxygen saturation and relieving symptoms. Appointment for clinic visit was scheduled for follow up and surveillance of other family members for any clinical or radiologic evidence of PAM.

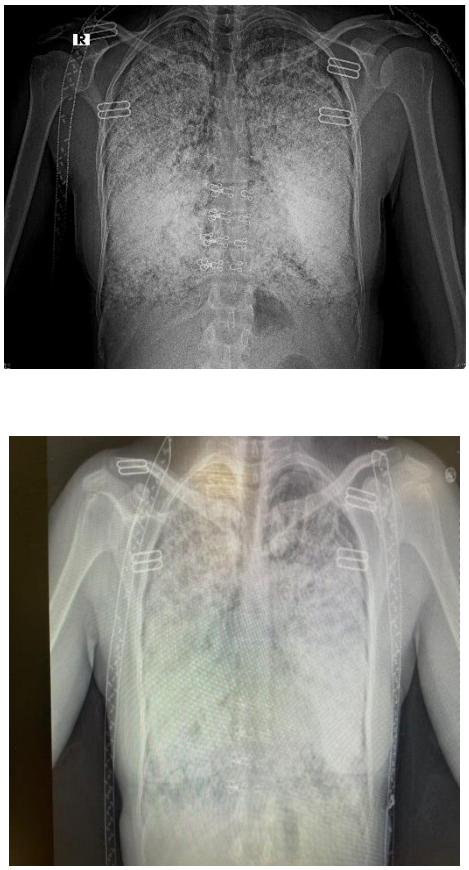
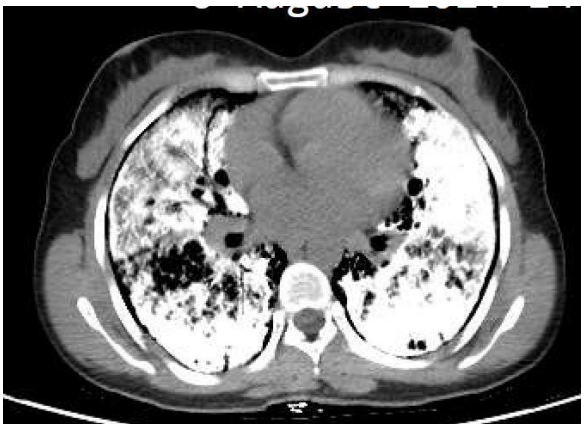


Figure 1. *Chest x-ray images showing sand storm appearance in both lung fields.*



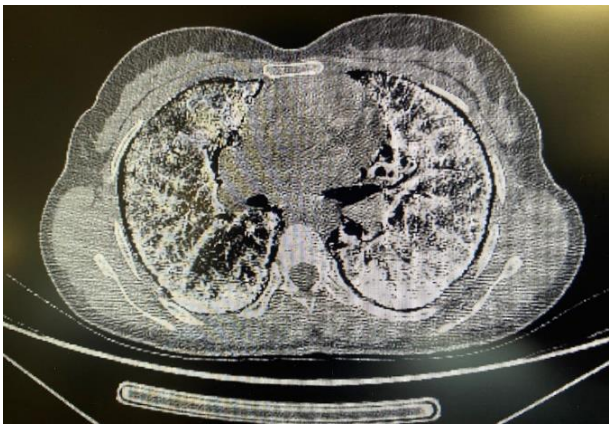


Figure 2. *HRCT showing extensive sand-like calcifications of the lung parenchyma with the black pleura sign.*

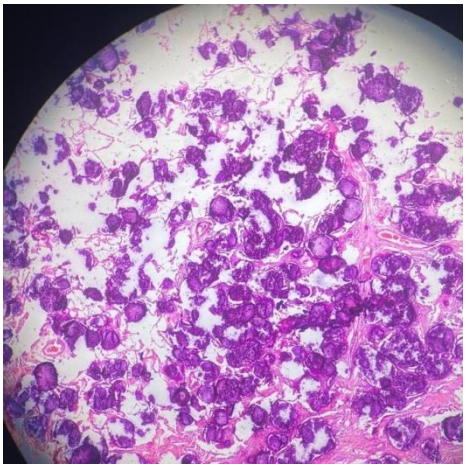


Figure 3. *40x magnification of lung tissue showing diffuse alveolar basophilic calcifications.*

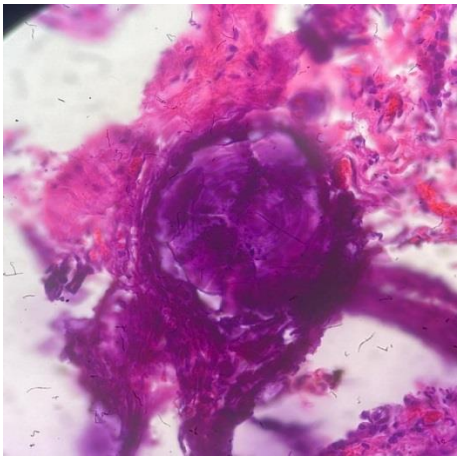


Figure 4. *400x magnification of the concentric laminated calcified concretions.*

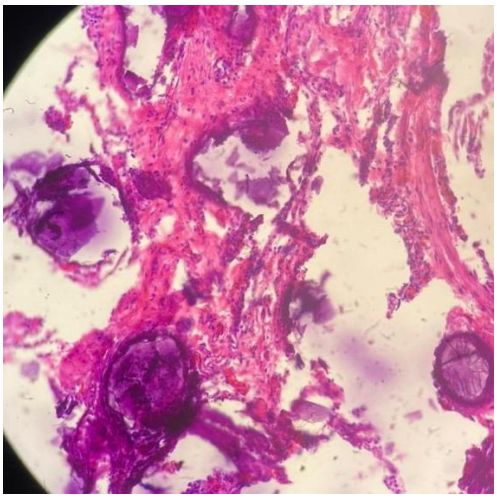


Figure 5. *100x magnification showing interstitial fibrosis and minimal inflammation with intra-alveolar calcifications.*

3. Discussion

PAM was first reported by Norwegian Harbitz in 1918 accordingly, it is also known as Harbitz′ syndrome. It was named as Pulmonary Alveolar Microlithiasis by Ludwig Puhr of Hungary in 1933 [3]. PAM is found worldwide, but an increased incidence is reported in Turkey, Japan and Italy [4]. Both sporadic and familial forms exist, the latter exhibiting an autosomal recessive pattern of inheritance. The sporadic form is more commonly seen in males, whereas the converse is found in familial cases [5]. Mutations of the SLC34A2 gene have recently been described in both familial and non-familial cases. The most common variants of the SLC34A2 gene are single nucleotide biallelic changes, but larger deletions are described [6, 7]. SLC34A2 mutation encodes for the type IIb sodium-dependent phosphate cotransporter (Npt2b). The loss of Npt2b transporter function from alveolar epithelial cells results in failure to export inorganic phosphate from the alveolar lining fluid, which then accumulates, binds to calcium, and forms hydroxyapatite microliths [8, 9]. Very rare sporadic cases have been reported following the inhalation of sand particles. Most patients are diagnosed in their second or third decade, though rare cases are seen in children and the elderly. In most patients, PAM is discovered incidentally on radiographs performed for other purposes, and the typical disease course is slow in progression ending with respiratory insufficiency over decades [10]. Difference between radiological findings and clinical scenario is a clue to this disorder. Signs and symptoms usually present late in the form of worsening shortness of breath and cough along with impaired lung function on spirometry, sometimes spontaneous pneumothorax can be the presenting sign. Some reports of pleural and renal involvement were encountered but rare [5]. The typical radiographic presentation would be the so called “sand storm” appearance on chest x-ray, which may be mistaken for fibrosis or even metastatic malignancy, that is far away from the overall clinical picture of PAM. High resolution computed

tomography typically reveals calcifications in the alveolar spaces, along bronchovascular bundles, in interlobular septa and in subpleural area [11, 12]. Interestingly, bone scintigraphy was reported as a reliable noninvasive diagnostic method [1]. Bronchoalveolar lavage (BAL) is not a specific test but may show calcified bodies on cytological examination, similar finding may be seen in patients with chronic obstructive pulmonary disease. A lung biopsy will typically be of firm gritty tissue, which is often difficult to slice. Microscopically, as the name states, laminated concentric calcifications composed mainly of calcium and phosphorus are seen in the alveoli and the interstitium. Reports and books state that frequently the subpleural space, interlobular septa and the bronchial mucosa are more frequently involved. Focal ossification of the alveolar calcifications may occur [13]. Most patients are stable, even though, prognosis is usually poor. In some cases, the disease progression is slow and eventual death from respiratory insufficiency is inevitable, albeit several decades after diagnosis. Rare reported cases showed rapid deterioration or spontaneous remission. Treatment options are limited usually to preventive and conservative therapy. Few treatment modalities were reported with satisfactory results and chest x-ray changes including cardiokinetics, diuretics, oxygen and repeated bronchoalveolar lavage [14], bone metabolism inhibitors had their share of trials but with controversial results making their use limited to research centers. Lung transplantation on the other hand reported to be useful with great benefit in selected groups of patients with severe respiratory failure and right heart failure who require supplemental oxygen therapy, most transplant reports come from India where bilateral lung transplant was conducted with promising outcomes. Logically, for a better chance of a successful outcome, patients should be operated before right side cardiac dysfunction takes place. Improvement in right ventricular ejection fraction and regression of right ventricular hypertrophy was reported however in patients undergone lung transplantation. Survival after lung transplant and the risk of PAM recurrence are unknown. Thorough search in literature didn't reveal a survival for a patient with PAM treated with lung transplantation more than 15 years without recurrence [15].

4. Conclusion

Although being rare to encounter in medical practice, PAM remains a challenging disease especially the familial form due to the silent nature and the fact that multiple family members may be affected simultaneously, similarity in presentation with interstitial lung disease and lack of reliable treatment options in many cases even though diagnosis can be made early with simple measures. The hallmark of this disorder is clinical-radiological dissociation, with typical imaging findings that correlate well with specific pathological findings. However, the long-term prognosis is unfortunately poor. Increasing numbers of reported cases in the past few years should raise awareness about this unfamiliar disease and provoke more research effort for better understanding its pathophysiology and treatment options.

Abbreviations

PAM	Pulmonary Alveolar Microlithiasis
CT	Computed Tomography
BAL	Bronchoalveolar Lavage
HRCT	High Resolution Computed Tomography

Author Contributions

Basheer Radi Alakhras: Project administration, Writing – original draft

Omar Habashneh: Supervision, Writing – review & editing

Ahmad Basim Yaghi: Investigation, Validation, Writing – review & editing

Abdallah Dasah: Resources, Writing – review & editing

Adham Alkilani: Investigation, Methodology, Writing – review & editing

Ethical Approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research Checklist

not applicable. Here, we report a rare case in medical practice as well as in histopathology specimens, as much interesting the case is as hard it is for the patient and the clinician. We tried to focus on the major details that showed universal agreement among different sources.

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Data Availability Statement

Not applicable.

Conflicts of Interest

The authors declare no conflicts of interest.

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