

Pulmonary Alveolar Microlithiasis: A Case Report

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Abstract

Pulmonary alveolar microlithiasis (PAM) is a rare disorder characterized by diffuse bilateral filling of the pulmonary alveoli by numerous calcific concentrations known as calcispherites. The radiological lesions in PAM closely resemble miliary tuberculosis. PAM should be suspected in cases when the radiological lesions do not correlate clinically. This may reduce the need for invasive procedures in a limited resource setting. A 40-year-old male agricultural laborer, never smoker presented with 10 months history of cough with expectoration and exertional breathlessness. He had completed 6 months of anti-tuberculosis treatment for the same complaints 4 months back. His general physical examination was unremarkable and he was not hypoxic at room air. On auscultation of the respiratory system, he had fine crackles in the left axillary region. Chest X-ray revealed bilateral diffuse nodular lesions with translucent band in bilateral upper zone (black pleura sign). Possibility of PAM was considered and it was confirmed with high resolution computed tomography of chest. Fiberoptic bronchoscopy was done. The bronchial brushings and washings revealed numerous calcific concretions of alveolar macrophages. Calcispherites were also demonstrated by percutaneous lung biopsy.

Key words: Biopsy, Calcispherites, High resolution computed tomography, Pulmonary alveolar microlithiasis

INTRODUCTION

Pulmonary alveolar microlithiasis (PAM) is a rare disease with unknown etiology. The disease is characterized by diffuse bilateral filling of the alveoli by calcific concentrations known as calcospherites. The radiological picture of PAM is often mistaken for miliary tuberculosis, and there are instances of being treated with a full course of anti-tubercular drugs.¹ We describe a patient with PAM who was misdiagnosed as miliary tuberculosis. The correct diagnosis was established by computed tomography (CT) of the thorax and by percutaneous lung biopsy.

CASE REPORT

A 40-year-old gentle man, agricultural laborer by occupation presented with 10 months history of cough with minimal expectoration and exertional breathlessness. The breathlessness was non-progressive and occurred on moderate to severe exertion. There was no restriction of his routine activities. He had consulted elsewhere 8 months back. A chest X-ray (CXR) and sputum examination were done and he was diagnosed as miliary tuberculosis and started on anti-tubercular drugs. He had completed 6 months of anti-tuberculosis treatment (ATT) for the same 4 months back. His symptoms continued to persist and hence he visited our hospital. On presentation, his general physical examination was unremarkable. He maintained saturation at room air. Respiratory examination showed a normal air entry and vesicular breath sounds bilaterally with fine crackles in the left axillary region. CXR was done which revealed bilateral diffuse nodular lesions with translucent band

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in bilateral upper zone? Black pleura sign (Figure 1). Possibility of PAM was considered and patient was subjected to a high resolution CT (HRCT) scan of the thorax. HRCT showed bilateral diffuse micronodular opacities which were distributed predominantly over the lower lobes and posterior regions with thickening of interlobar septa (Figure 2). A high suspicion of PAM was considered and a fiber optic bronchoscopy was done and bronchial brushings and washings were done. The bronchial washings showed calcific concretions of alveolar macrophages. Percutaneous lung biopsy was also done, which revealed numerous calcospherites, which confirmed our diagnosis (Figures 3 and 4). The patient's blood biochemistry including calcium and phosphorous levels were normal. His younger brother was also subjected to chest radiograph but was found to be normal. There was no similar illness in the patient's

family. His spirometry showed a mild restriction pattern and he had no evidence of pulmonary hypertension. He is currently managed symptomatically and has not worsened till the last contact.

DISCUSSION

PAM is a rare disease of unknown pathogenesis, characterized by the formation of widespread laminated microliths or calcospherites in the alveolar spaces with no underlying disorder of calcium metabolism. PAM was first reported by Harbitz in 1918² and was earlier known as Harbitz' syndrome. The name PAM was coined by Ludwig Puhin 1933. Though sporadic in occurrence, a familial autosomal recessive pattern of inheritance has been described particularly in Italy and Turkey.³⁻⁵ PAM occurs in both sexes with a slight predominance among males. Although, PAM is seen in all age groups, it is most frequently diagnosed from birth

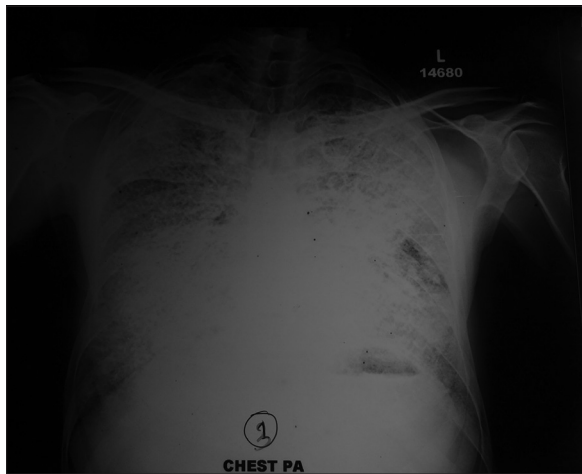


Figure 1: Chest X-ray showing bilateral diffuse nodular opacity involving all zones

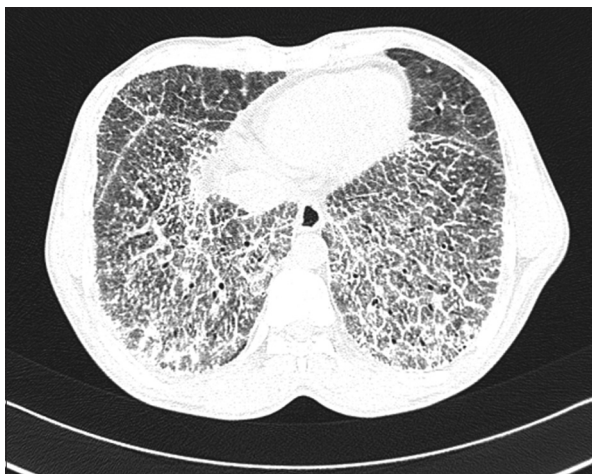


Figure 2: High resolution computed tomography thorax showing bilateral diffuse micronodular opacities with predominant lower lobes involvement and posterior regions with thickening of interlobar septa

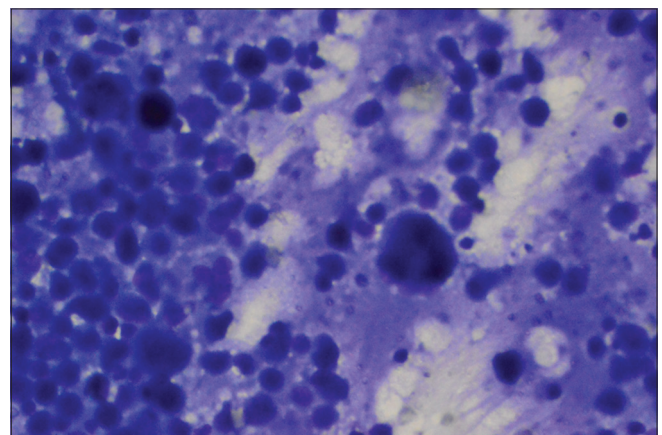


Figure 3: Smear showing sheets of macrophages and multinucleated giant cells in proteinaceous background, May-Grünwald-Giemsa stain, x200

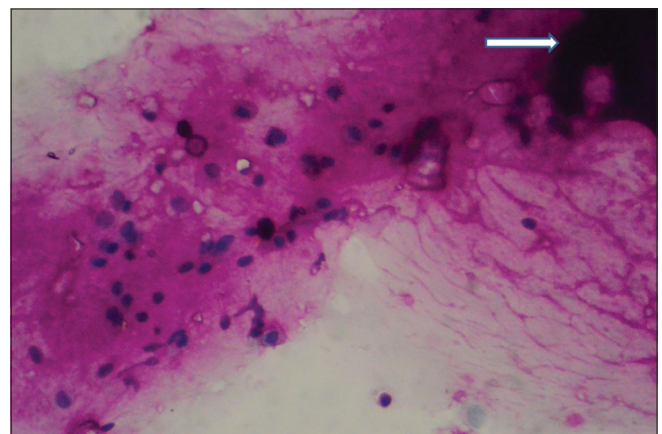


Figure 4: Smear showing numerous macrophages in a background of strong periodic acid-Schiff (PAS) positive proteinaceous material with calcified debris (arrow), PAS stain, x200

to 40 years of age. The first case in India was reported by Viswanathan *in*.⁶

The exact cause for this abnormal microlith formation has not been ascertained. Studies have shown the possible mutation of the of the solute carrier family 34 (sodium phosphate), member 2 gene (the SLC34A2 gene), which encodes a sodium/phosphate cotransporter as a possible cause of the disease.^{7,8} Defect in this cotransporter results in the inability of the alveolar type II cells to clean up the phosphorus ion from the alveolar space resulting in its accumulation and forming of microliths rich in calcium phosphate. Jönsson *et al.* have also identified possible variation in the gene mutation.⁹

The majority of the patients are asymptomatic despite extensive radiological lesions. Symptoms of dry cough and progressive dyspnea manifest in the third to fourth decade. A few cases of expectoration of microliths have been reported.¹⁰ The progressive disease leads to development respiratory fibrosis and cor pulmonale. Pulmonary function remains normal or only slightly impaired initially. As the disease process advances, the alveolar walls become fibrotic and a restrictive ventilator defect with a reduced diffusion capacity develops. Extrapulmonary calcifications have been reported including nephrolithiasis, testicular calcification and sympathetic chain calcification.¹¹⁻¹³

PAM is usually suspected radiologically. On CXR, there is bilateral diffusely distributed small intraparenchymal nodules predominantly in the lower zones and paracardiac zones. These nodules are smaller than 1 mm and well-defined (sandstorm appearance). HRCT is more sensitive than CXR for detecting the severity and extent of the disease. HRCT may show a wide variety of lesions like bilaterally distributed micronodules, subpleural nodules, nodular fissure, calcification along the interlobular septa, dense consolidations, paraseptal and centrilobular emphysema, subpleural cysts, black pleural lines, diffuse ground-glass attenuation areas, mosaic pattern and apical bullae. Diffuse interstitial involvement and mosaic pattern are usually seen in end stage disease.¹⁴

Histopathological diagnosis of PAM require an open lung biopsy, needle biopsy or transbronchial biopsy. Lung biopsy remains the most definitive procedure for confirmation of PAM. In centers where open lung biopsy is not feasible, a transbronchial biopsy may be performed. The pathological features are mostly limited to the lungs, and the microliths are almost invariably intralveolar. The microscopic picture shows alveolar spaces containing typical laminated calcific microliths with fibrosis and thickening of the alveolar walls.

A number of conditions can resemble PAM radiologically. These include miliary tuberculosis, metastatic calcification, amiodarone lung toxicity, and amyloidosis. It is always advisable to confirm the diagnosis of nodular lesions on CXR by a CT scan of the chest.

There is no specific treatment available for PAM. Unlike pulmonary alveolar proteinosis broncho alveolar lavage of the whole lung is not effective for PAM. The calcium embedded microliths are not easily dislodged by BAL. Home oxygen therapy may be necessary for patients with respiratory failure. Disodium etidronate, which inhibits the micro-crystal growth of hydroxyapatite has been tried in some patients.¹⁵ Lung transplant may be needed for end-stage disease.

CONCLUSION

PAM though is a rare disorder, should be considered as one of the possible differential diagnosis of nodular opacities on CXR. In a tuberculosis endemic country like India, there are chances for wrong treatment with ATT. Whenever possible a HRCT thorax should be performed.

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