CASE REPORT

SUCCESSFUL DIAGNOSIS OF PULMONARY ALVEOLAR MICROLITHIASIS BY A NEW MODALITY

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ABSTRACT

Pulmonary alveolar microlithiasis is a rare disease with an almost unheard of pathogenesis. With very few cases to document worldwide, predominantly being discovered in Turkey, Italy, and America, it has been nearly impossible to determine a concrete etiology. However, one standout biochemical finding most cases of PAM have in common is a mutation in the SLC34A2 gene coding for the sodium-phosphate cotransporter found in Type II alveolar cells. This cotransporter is responsible for maintaining equilibrium of phosphorus which is a vital component of surfactant. Diagnostic exploration is achieved via radiological imaging, bronchoalveolar lavage and above all, transbronchial lung biopsy. However, in this particular case, due to the patient's hypoxic condition, Technetium 99m diphosphonate scanning was employed in place of the biopsy. A non-invasive procedure, technetium 99m can detect extensive pulmonary uptake, hereby diagnosing the patient and protect against the physical damage and accompanying side effects inflicted upon the patient by various invasive procedures. In future, to avoid wastage of resources, the use of technetium 99m diphosphonate scanning should be more prevalent in the diagnosis process of PAM.

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INTRODUCTION

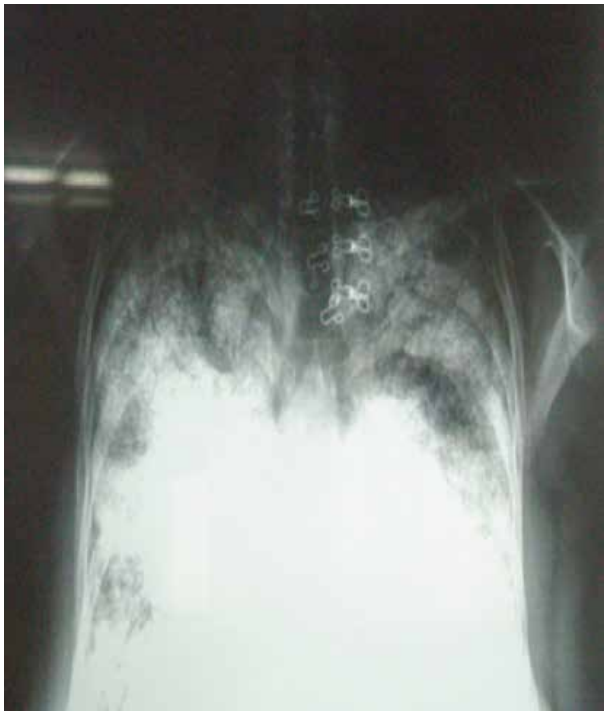
Pulmonary alveolar microlithiasis is a rare autosomal recessive disease characterized by the precipitation of calcium phosphate microliths throughout the respiratory tree. Despite having a relatively unknown etiology, research leans towards mutations in the SLC34A2 gene, which codes for a sodium-phosphate cotransporter found in Type II pneumocytes[1,8] Less than 600 cases have been reported worldwide[7,8,11] mainly from Japan, Turkey, Italy, and USA[2-7]. In this particular case the patient was incidentally diagnosed with pulmonary alveolar microlithiasis on the basis of a recently approved modality; Technetium 99m diphosphonate scintigraphy.

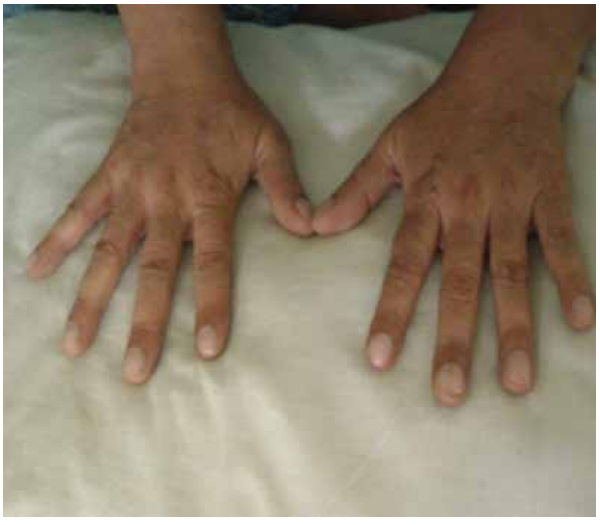
CASE REPORT

A 38-year-old female, with an unremarkable family history, presented with a four-year history of progressive dyspnea (mMRC class III) in the Pulmonology Department of JPMC. She also complained of orthopnea. She was a non-smoker. There was no evidence of any other known pulmonary disease. She had been diagnosed with hypothyroidism four years back. General physical examination noted a young, overweight female with a blood pressure of 140/90 mmHg; pulse 110/ min, respiratory rate 30/min. Grade IV clubbing and cyanosis were present. Auscultation of the chest revealed coarse crackles. The rest of the systemic examination was unremarkable.

Lab reports were as follows:

CBC: Hb 20.6gram/dl Hct 62 WBC 4.1/Cmm TSH Platelets 109/Cmm
Thyroid Function test: FT3:5.5pmol/L Renal, liver functions and electrolytes were normal.
Arterial Blood Gases pH 7.36 PCO2 47.9mmHg PO2 52.8mmHg HCO3 28mmol/L SO2 86.4





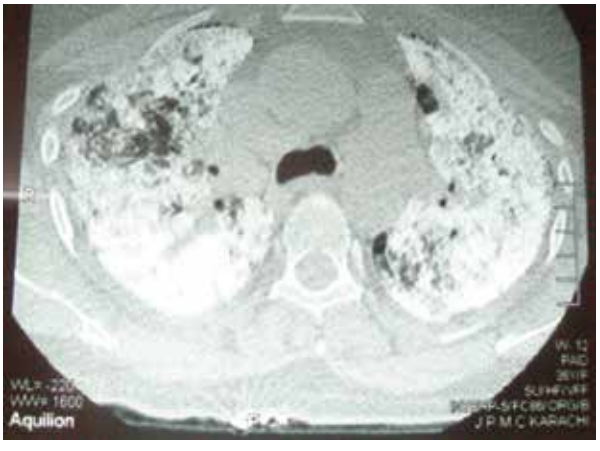
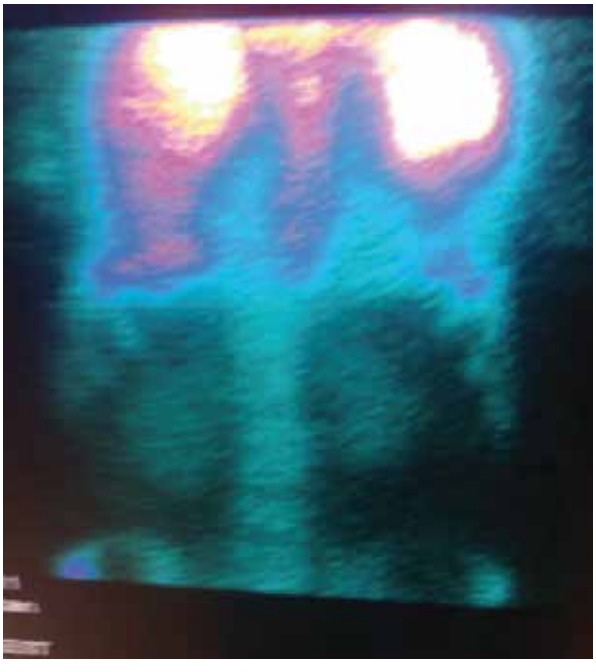


Figure 1: Chest radiograph revealed diffuse bilateral areas of micronodular calcification with black pleura and HRCT showed a mosaic-like pattern present in the interlobular area



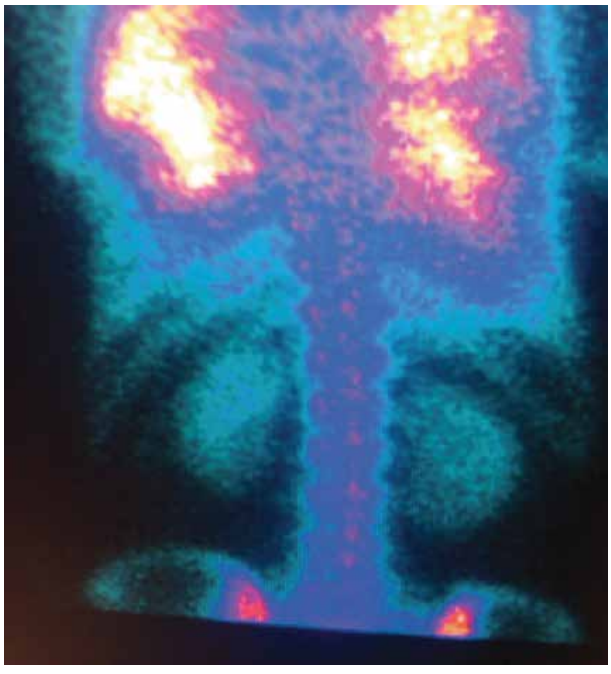


Figure 2: 99m technetium diphosphonate scanning detected extensive pulmonary uptake

Chest radiograph revealed diffuse bilateral areas of micronodular calcification with black pleura and HRCT showed a mosaic-like pattern present in the interlobular area (Figure 1). Bronchoalveolar lavage did not show acid-fast bacilli, fungi or any atypical cell. Transbronchial lung biopsy could not be performed due to hypoxia. However, 99m technetium diphosphonate scanning detected extensive pulmonary uptake as shown in the image above (Figure 2). These findings confirmed the diagnosis of pulmonary alveolar microlithiasis.

DISCUSSION

Pulmonary alveolar microlithiasis is a rare chronic disease of unknown etiology, consisting of numerous small alveolar calculi (composed of calcium and phosphorous) in the absence of a known calcium metabolism disorder. There have been fewer than 160 reported cases in previous literature[19]. It can be familial or sporadic[9].

The previous literature identifies a mutation of the SLC34A2 gene, encoding a type IIb sodium-dependent phosphate cotransporter (NaPi-IIb) in Type II alveolar cells. This transporter is involved in phosphorus metabolism in vivo.[18] Type II pneumocytes not only produce surfactant (composed of phospholipids and Ca-dependent binding proteins SP-A and SP-D) but are also responsible for its recycling and degradation[20]. A mutation of SLC34A2 decreases the cellular uptake of phosphorus leading to its accumulation in the alveoli and subsequent chelation with calcium in the extracellular fluid. As a result, microliths are formed. It is now believed that this mutation of SCL34A2 gene is responsible for the parenchymal changes seen in the lungs of patients with PAM[18].

The patient is initially asymptomatic, with restrictive type lung impairment appearing in the third or the fourth decade. The usual course of PAM is progressive deterioration of lung function with the development of corpulmonale, and respiratory failure which leads to death in midlife[10-12]. Following this trend, our patient was 38 years old with complaints of dyspnea developing over the past four years. A familial occurrence in one-third of known cases has been reported, with an autosomal recessive inheritance pattern and no apparent gender predisposition[8]. However, the family history of our patient for the disease was negative.

The chest radiograph of our patient mimicked a typical PAM chest radiograph, which shows: bilateral infiltrates of fine, sand-like calcified micronodules (< 1 mm) mostly in the middle and lower zones of the lung. Obliteration of heart border and diaphragm is also seen[11, 13].

The most common HRCT findings in patients of PAM are ground-glass opacities, calcified micronodules, interlobular septal thickening, pleural and subpleural calcification and pulmonary cysts. Calcifications along bronchovascular bundles and tree have also been noted. Our patient's radiograph displayed a mosaic pattern, which is pathognomonic for PAM on HRCT[10]. Possible differential diagnoses with similar nodular calcifications are tuberculosis, metastatic osteosarcoma, and amyloidosis. Dense consolidations are also noted in metastatic pulmonary calcification, talcosis and amiodarone lung toxicity. Therefore, to rule-out probable conditions, clinical features and CT findings should be carefully correlated with those typical of PAM.

The bronchoalveolar lavage did not show acid-fast bacilli, fungi or any atypical cells. Due to hypoxia, transbronchial lung biopsy a routine procedure for PAM was unadvised. Technetium 99m diphosphonate scan was used for final confirmation and depicted bilateral pulmonary uptake of the radioisotope 99mTc. Technetium 99m diphosphonate compounds bind to calcified soft tissue, this is vital in detecting early-stage PAM21. In cases where CT scan findings are nonspecific, the bone scintigraphy is very useful in the detection of early pulmonary calcifications, which are missed in the CT scan because of their small size[14]. When the bone scan was done in our patient, it showed extensive uptake as described in the literature, thus confirming our diagnosis.

PAM does not have an effective medical therapy. Alendronate sodium has been tried in some patients which provided symptomatic relief but no

reversal. Corticosteroid therapy has not shown much benefit either. Lung transplantation is the only choice12.

CONCLUSION

Specific diagnosis of PAM is usually confirmed by histopathological evaluation of the lung tissue via transbronchial/tracheal or open lung biopsy. This case shows that this diagnosis can also be made through correlation of clinical and radiological findings and confirmed by performing tech 99 bone scan in suspected cases thus eliminating the need of subjecting patients to invasive procedures. Tech99 is especially useful for diagnosing this rare disease in those patients who are not fit for invasive procedures, as seen in our case.

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