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Case report

Pulmonary microlithiasis – A case report

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ABSTRACT

Pulmonary alveolar microlithiasis is a rare diffuse lung disease characterized by widespread sand-like intra-alveolar calcifications (calcospherites composed of calcium and phosphorus). Around 800 cases have been reported in the literature to date. We report here a case of a 35 years old female with prolonged h/o of exertional dyspnoea and mild cough. Clinical examination was mostly normal. Her Chest X-Ray revealed bilateral multiple nodular opacities (sand storm appearance). CT Scan chest showed diffuse micronodular calcifications with septal thickening, compatible with alveolar microlithiasis. Pulmonary function tests showed moderately restrictive lung disease. Bronchoscopic alveolar lavage revealed calcospherites in the alveloli and bronchi confirming the diagnosis of pulmonary alveolar microlithiasis.

1. Case report

A 25 years old married female, mother of two children came in the outpatient clinic with complaints of persistent cough for the last 10 years and breathlessness for six years with off and on fever during this period. According to the patient she was well 10 years ago when she started getting bouts of dry cough especially at night so much so that she used to wake up from sleep. Also she started having episodes of fever along with cough which sometimes resolved spontaneously (after variable periods of time) and at other times she took treatment from a doctor for which she had to travel far as she resided in a far flung area of Baluchistan desert in Pakistan with almost no medical facilities. After few years of intractable cough, she as well started noticing breathlessness which was initially on exertion and later on at rest also with exacerbations at the time of fever. She never had hemoptysis but had history of passing gritty particles in sputum. There was no history of orthopnea, paroxysmal nocturnal dyspnoea, body swelling, urinary or gastrointestinal complaint and she was never hospitalized. For ten years, she consulted many general practitioners and consultants and considering her chest Xrays has tuberculosis like radiological appearance, she was prescribed anituberculous therapy thrice, each upto 8–9 months duration. In addition, she has had multiple courses of antibiotics and both oral and inhaled corticosteroids. There was no improvement from any of these drugs.

She presented to us with severe exertional dyspnoea for the last 2 weeks. On examination, she was afebrile, tachypnoeac with respiratory rate of 32 breaths per minute with normal blood pressure and pulse. Her Chest examination revealed scattered crepitations all over the chest but otherwise no other abnormality. Rest of her systemic examination was normal. Her blood oxygen saturation while breathing room air was 82% while arterial blood gas analysis showed low pressures of Oxygen.

Her laboratory tests showed hemoglobin level of 11.5 gm/dl, TLC of 9500/cmm with 60% neutrophils and 25% lymphocytes and elevated ESR of 30 mm in 1st hour. Liver function tests, serum electrolytes, renal function tests, serum parathyroid hormone and vitamin D were all within normal range. Pulmonary function tests showed moderately restrictive lung disease which was not reversed with bronchodilators Sputum smear for AFB was negative three times and culture showed no growth. Her Chest Xray (Fig. 1A, B and C) showed bilateral diffuse fine nodules predominantly in the middle and lower Zones (Sand Storm Appearance). Her CT Scan Chest images (Fig. 2A, B and C) demonstrated widespread tiny micro calcifications throughout the lungs with septal thickening and ground-glass opacification. Later on, Bronchoscopic alveolar lavage was performed which revealed rehtypical microliths and cytologic smears showed extracellular and intracellular concentrically round microliths confirming the diagnosis of pulmonary alveolar microlithiasis. She was symptomatically treated by Intravenous Moxifloxacin to cover possible infections and oxygen

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therapy via nasal cannula at 3 lit/min and later on discharged with advice of long term oxygen therapy at home. Because of her travel logistic difficulties, she is on 4 monthly (May 2015, September 2015, January 2016 and May 2016) follow up and regular till now.

2. Discussion

Pulmonary alveolar microlithiasis (PAM) is a rare diffuse lung disease characterized by widespread sand-like intra-alveolar calcifications (calcospherites composed of microliths composed of calcium and phosphorus). First described in 1856 by Friederich [1], and then by Harbitz [2] (hence some times also known as Harbitz Syndrome); It was named Pulmonary alveolar microlithiasis by PUHR in 1933 [3]. Around 800 cases have been reported till date in medical literature with two third in Europe and Asia, particularly Italy, Turkey and Japan [4,5].

PAM is an autosomal recessive disease with Sporadic and familial cases accounting for 30–50% [6,7] of the cases with no specific sex predilection but male predominance has been described in sporadic cases [8]. PAM is thought to be caused by mutations of the SLC34A2 gene. It encodes a type IIb sodium-dependent phosphate co-transporter (NaPi-IIb). SLC34A2 is primarily expressed in the lung and only in type II pneumocytes [9,10]. These cells are responsible for production of surfactant. Loss of function of the

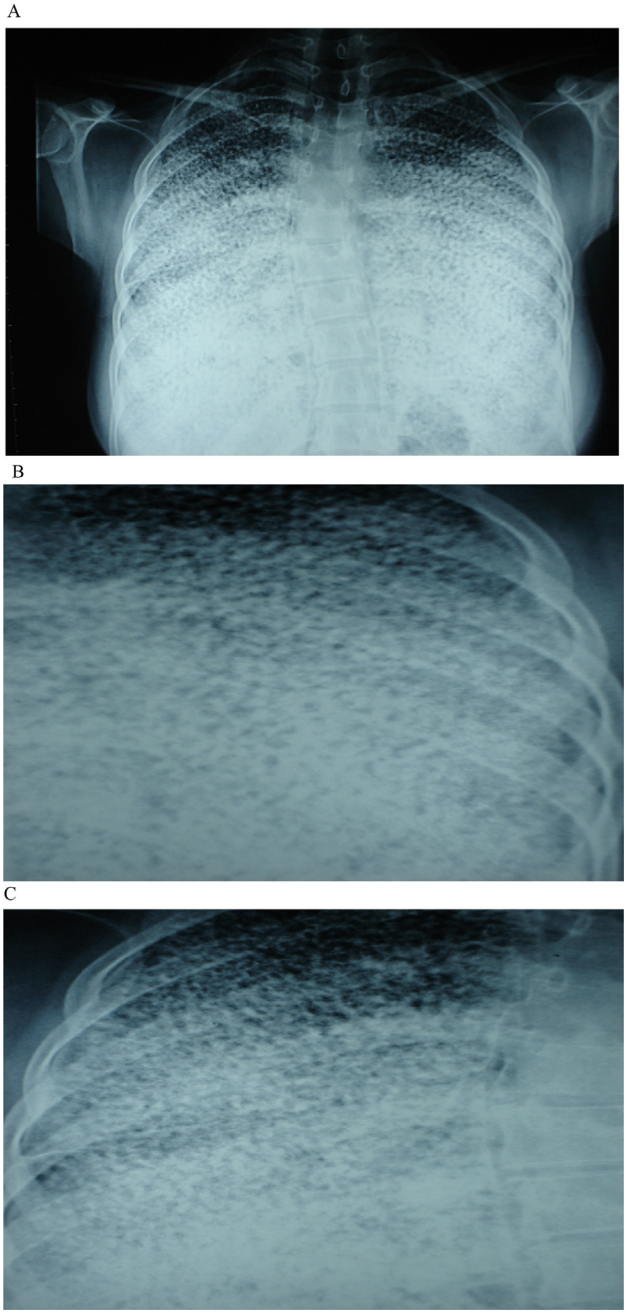

Fig. 1. A. Chest x ray showing bilateral diffuse fine nodules predominantly in the middle and lower Zones (Sand Storm Appearance). **B**. Close view of left upper zone. **C** Close view of right upper zone.

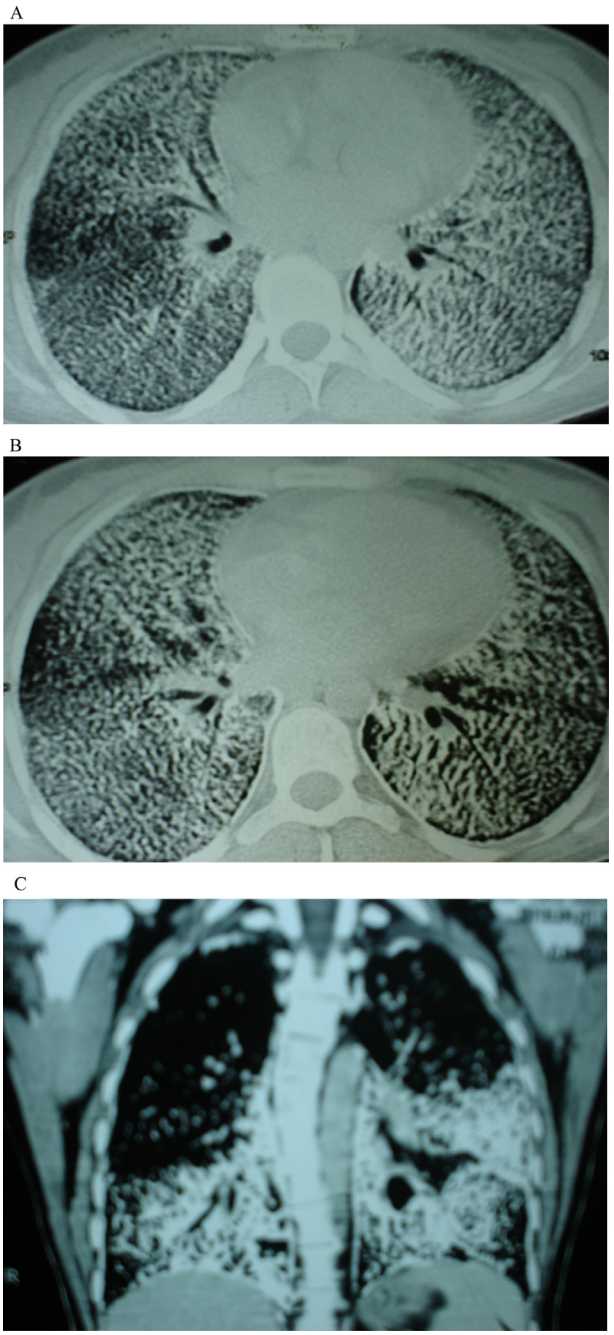

Fig. 2. A & B. Axial view of CT Scan Chest showing widespread tiny micro calcifications throughout the lungs with septal thickening and ground-glass opacification. **C**. Coronal View of CT Scan Chest showing micro calcifications.

gene due to mutations lead to a decreased cell uptake of phosphate, which in turn may lead to formation of intra alveolar microliths (calcospherites) as a result of phosphate-chelating calcium in the extracellular fluid [11].

PAM is a disease with clinical and radiological dissociation and is mostly diagnosed incidentally during pulmonary radiography of the chest for other reasons while many patients have no clinical symptoms [12,13]. The disease is usually discovered from birth up to 40 yrs of age. In symptomatic patients, typical complaints are dyspnoea, cough, chest pain and asthenia [16]. Cough may occur at any stage of disease even with expectoration of microliths. The disease is usually indolent with slow progression and leads to pulmonary fibrosis, respiratory failure and cor pulmonale [14].

The characteristic picture of PAM on the chest radiograph shows infiltrates as fine sand-like calcific micronodules also called 'sand-storm lung', diffusely involving both lungs and usually more marked in middle and lower zones [15].

Differential diagnosis include miliary tuberculosis, sarcoidosis, pneumoconiosis, pulmonary hemosiderosis, amyloidosis, and metastatic pulmonary calcifications associated with chronic renal failure.

The characteristic CT chest findings are calcified thickening of interlobular septa, bronchovascular bundles, and pleura [16]. CT shows symmetrical abnormalities in the lungs, usually as marked calcifications. The calcifications are most prominent in peripheral, mediastinal and fissural subpleural regions and each lobe is surrounded by a fine dense outline, giving the overall appearance of a stony lung with areas of ground-glass opacity commonly visible. Subpleural multiple small cysts are also present.

Extrapulmonary calcifications can occur with PAM, like medullary nephrocalcinosis nephrolithiasis, calcification of the lumbar sympathetic chain, possible testicular involvement, punctate calcifications in the seminal vesicles, epididymal and periurethral calcifications causing obstructive azospermia [17,18].

Routine blood biochemistry including serum calcium concentration, hepatic, renal and parathyroid functions are usually normal. The deterioration of the pulmonary function may be useful to monitor disease activity and disease progression. Most of the cases either have normal pulmonary function or a mild restrictive pattern The identification of the SLC34A2 gene mutation (where available) also suggests the diagnosis. Serum concentrations of the surfactant proteins A and D(SP-A and SP-D) are elevated in the patients with PAM, and can be the markers to monitor the activity and progression of the disease [19].

The Radiology is usually pathognomonic for diagnosis but sometimes fibreoptic broncoscopy with BAL or lung biopsy showing microliths is required to confirm the diagnosis. The microliths are rounded, oval and lobular concentric laminated in appearance. The composition of the calcifications is calcium and phosphate, in a ratio of 2:1.

There is no known effective treatment for PAM, with the exception of lung transplantation [20]. Home-based oxygen therapy is often necessary as the disease progresses. Symptomatic and some radiological improvement with use of steroids, disodium etidronate and therapeutic BAL has been observed in very few cases till date [21]. Long-term survival time is still uncertain but is usually more than 20 years.

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