Pulmonary Alveolar Microlithiais

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ABSTRACT

Pulmonary Alveolar Microlithiasis (PAM) is a rare, slowly progressive lung disease, characterised by widespread intra-alveolar accumulation of minute calculi called microliths. It is caused by mutation in SCL34A2 gene encoding sodium phosphate cotransporter in alveolar type II cells. Herein, we report a case of PAM, diagnosed incidentally showing "Sandstorm" appearance on chest X ray. Diagnosis was confirmed based on characteristic features of PAM on HRCT Chest scan and striking clinico-radiological dissociation.

Keywords: Microlithiasis, Pulmonary, alveolar, Sandstorm, SCL34A2 gene, microliths

INTRODUCTION

Pulmonary Alveolar Microlithiasis (PAM) is a rare, autosomal recessive, genetic and/or sporadic disorder with high penetrance characterized by diffuse, bilateral intra-alveolar accumulation of innumerable minute calcium phosphate calculi called microliths or calcispherites[1,2]. It is caused by inactivating mutations in the gene "solute carrier family 34 member 2" encoding a sodium-dependent phosphate co-transporter (SLC34A2, Npt2b, NaPi-2b) expressed predominantly in type II alveolar cells and is responsible for uptake of phosphate released from phospholipids in outdated surfactant[3]. As a result of failure to uptake phosphate, calcium is chelated and leads to formation of microliths[1].

PAM has been reported from all the continents, with majority of cases reported from Turkey, followed by China, Japan and India[1]. It may affect people of any age, ranging from premature infants to the elderly; the youngest reported case was of premature twins, and the eldest was an 84 year female[1]. The hallmark of PAM is the striking Clinico-radiological dissociation, meaning that a patient may present with a paucity of symptoms in contrast to image findings[4]. Frequently, patients may have no chest symptoms, such that diagnosis is often fortuitous, as in our case. In symptomatic cases, dyspnoea is the most frequently encountered symptom, followed by cough, chest pain and asthenia[4].

CASE REPORT

A 23 years male, car driver by occupation was referred to our department for evaluation of an abnormal chest X-ray done for routine check up following a road traffic accident. He was admitted in the Neurosurgical intensive care unit for conservative management of Sub-arachnoid and sub-dural hemorrhage. Patient was asymptomatic and the general physical examination was unremarkable. He maintained a normal oxygen saturation of 98% at room air. Respiratory examination showed bilateral air entry and normal vesicular breath sounds. Chest X ray revealed bilateral diffuse hyper-dense sand like micro nodular opacities, more so in the middle and lower zone with partial sparing of upper zone with obliteration of heart borders and hilar vessels & diaphragm ("drowned heart syndrome")[5], giving a typical appearance of "sandstorm"[2,5] with thickened septae [Figure 1]. Blood investigation were all within normal limits, HIV test was non reactive. Possibility of PAM was considered and patient was subjected to High resolution Computed tomography (HRCT) chest scan. HRCT chest showed bilateral diffuse hyperdense micro nodular opacities predominantly in middle and lower lobes with interlobar septal thickening, calcification along interlobular septa, ground glass opacities (crazy pavement pattern, considered pathgnomonic)[5,7,8], sub pleural small cyst with sub pleural sparing, appearing like black pleura line[2,5] or negative pleura sign[5]. Diagnosis was confirmed based on the above mentioned characteristic HRCT findings[Figure 2&3]

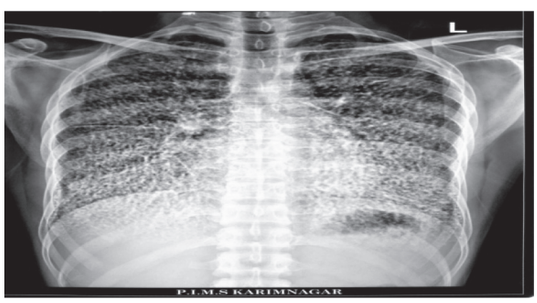

Figure 1: Chest X ray showing sandstorm appearance

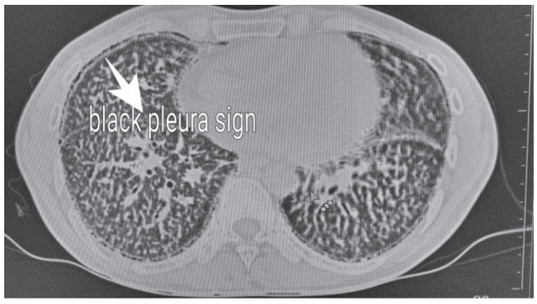

Figure 2: HRCT image showing black pleural sign

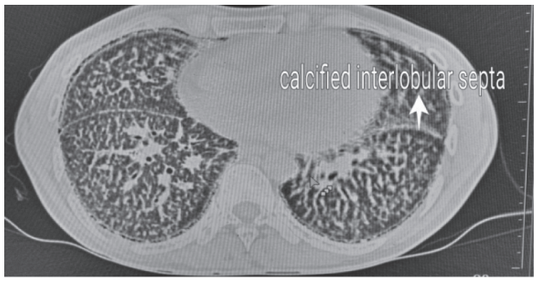

Figure 3: HRCT image showing calcified areas

DISCUSSION

PAM is rare disease with over all incidence of 1022 cases reported worldwide (upto Dec-2014)[1]. It is characterised by the formation of widespread laminated microliths or calcispherites in alveolar spaces with no underlying disorder of calcium metabolism[2]. It presents as both sporadic & familial autosomal recessive inheritance pattern. PAM occurs in both sexes equally, though predominance in males is reported[1,2,6]. It is most frequently diagnosed from birth to 40 yr of age.

The defective mutation of the solute carrier family 34(sodium phosphate), member 2 gene (SLC34A2 gene) is the possible cause of the disease[3]. This cotransporter usually clears phosphate generated from recycling of outdated surfactant. Defect in this cotransporter leads to loss of function, result in inability of type II alveolar cells to clear phosphate ion, resulting in accumulation, and chelation of calcium leading to formation of microliths or calcispherites[2].

The hallmark of this disorder is clinico-radiological dissociation i.e lack of significant symptoms (asymptomatic) despite extensive radiological changes[2,4,7,8]. Symptoms of dry cough and progressive dyspnoea manifest in the third and fourth decade. A few cases of expectoration of microliths have been reported[2,7]. The progressive disease leads to fibrosis and cor pulmonale[1]. In most cases, its an incidental finding of a Sandstorm-appearance on chest X ray. Pulmonary function test remains normal or slightly impaired initially but later restrictive ventilatory defect with reduced diffusion capacity develops[2]. Apical blebs and bullae may cause recurent pneumothorax in these cases[7,9]. Extrapulmonary calcifications have been reported in mammary glands, small intestine, pancreas, liver, ovaries, placenta, prostate including nephrolithiasis, testicular calcification, and sympathetic chain calcification[2,5]. Comorbidities, such as Mitral stenosis, autosomal recessive Waardenburg anophthalmia syndrome, Lymphocytic interstitial pneumonitis (LIP), Milk-alkali syndrome and Diaphyseal aclasia are reported[1,5].

The diagnosis of PAM can be made based on 2 findings

1. Characteristic radiological appearance in Chest X ray and HRCT scan Chest[7].

2. Striking clinico-radiological dissociation [7].

The diagnosis of PAM can be established on the basis of typical radiological characteristics, which includes interlobular septal thickening and calcification along the septa, ground glass opacities, calcified micronodules, pleural and subpleural linear calcification and cysts[2,5,7,8] ,giving overall the appearance of “stony lung”[9]. Other findings include diffuse ground glass opacities attenuation with septal thickening and calcified nodules referred to as crazy paving pattern[1,5,6,8]. Even if the histopathological examination remain as gold standard for the diagnosis of PAM, the typical HRCT finding are so characteristic that, when present, can rule out the need for lung biopsy. Some authors believe that the HRCT findings are pathgnomonic for PAM and the lung biopsy may be avoided[1,6,10].

The mircoscopic 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[5]. It is always advisable to confirm the diagnosis of nodular lesion on CXR by HRCT scan of chest as the later is more sensitive[2]. In Saudi Arabia, differential diagnosis has also been made with “desert lung syndrome” (due to inhalation of the desert sand)[9].

There is no specific treatment available for PAM. Lung transplantation is the treatment of choice for end stage disease[1,4,6]. To date, no recurrence after transplantation has been reported[1,5]. Disodium etidronate, which inhibits the microcrystal growth of hydroxyapatite has been tried in some patients with doubtful outcome[1,2,4,6]. Supportive management with home oxygen therapy may be necessary for patients with respiratory failure[1,2,4,11]. According to a study, low phosphate diet may be helpful[4]. Corticosteroids and hydroxycholoquine are generally ineffective[4,6].

Recent advances

Surfactant protein-A and surfactant protein-D are potential serum markers to monitor the disease activity and progression[5,9]. Drugs targeting phosphate metabolism rather

than calcium metabolism could prove beneficial[5].

CONCLUSION

Though PAM is a rare disease, should be considered as one of the possible diagnosis for nodular opacities on CXR. In a tuberculosis endemic country like India, where other possiblities like miliary tuberculosis have been excluded based on clinical presentation, PAM should be considered.Whenever possible a HRCT chest should be performed. High degree of suspicion in a clinco-radiological dissociation with characteristic HRCT chest finding would obviate the need for invasive procedure like Lung biopsy. Genetic counseling of families affected with PAM should be done.

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