

## Case report

### Pulmonary Alveolar Microlithiasis

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#### Abstract

Pulmonary alveolar microlithiasis (PAM) is an uncommon chronic disease characterised by calcifications within the alveoli and a paucity of symptoms in contrast to the imaging findings. Here we present two cases of PAM without significant respiratory complaints.

**Keywords:** Pulmonary, Alveolar, Microlithiasis, Calcification.

#### Introduction:

Pulmonary alveolar microlithiasis (PAM) is a rare idiopathic disease characterized by a diffuse bilateral filling of the majority of alveoli by calcific concretions called "Calcospherites". Patient remains symptom free until middle age when chronic respiratory failure and cardio-respiratory decompensation develop. The diagnosis of PAM is incidental in early age as in the present cases.

#### Case report 1:

A 19 years old male, student presented with history of mild chest pain for the last 3 months. He was a non smoker. Family history was also not significant. General examination revealed that patient was of thin built and well nourished. His resting oxygen saturation was 100% with a fall of 16% on six minute walk test. Examination of other systems was unremarkable.

His Hb was 14 gm%; Total Leucocyte Count was 8000/cmm: Neutrophils 47%, Lymphocytes 43%, Monocytes 7% and Eosinophils 3%. Sputum smear was negative for acid fast bacilli. Serum calcium was 8.8 mg %. Spirometry was normal

(FEV1 87%, FEV1/FVC ratio 82) with no significant bronchodilator reversibility (post bronchodilator FEV1 88%).

The chest radiograph revealed the presence of innumerable, wide spread fine nodular pattern ('Sand-storm') involving both lungs diffusely. The nodular opacity was sharply defined showing greater involvement of lower lung field than upper. There is a thin, lucent line on lateral chest walls between the calcific pulmonary parenchyma and chest walls 'Black pleura sign'

(Fig-1).



Figure 1

A high resolution CTscan of thorax was obtained at full inspiration at 10mm intervals in supine positions. It revealed diffuse, symmetric lung involvement characterized by ground glass attenuation and septal thickening with calcified nodules (representing microliths) leading to crazy-paving pattern (Fig-2).

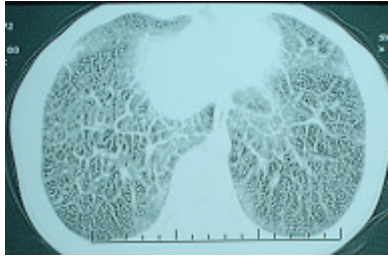


Figure 2

### Case report 2:

A 21 years old male presented with no respiratory complaints. On routine medical examination, he was of average built. Respiratory examination revealed bilateral normal vesicular breath sounds with no accompaniment. Family history was also unremarkable. His Hb was 13.2 gm%; Total Leucocyte Count was 6200/cmm: Neutrophils 57%, Lymphocytes 41%, Monocytes 2%. Sputum smear was negative for acid fast bacilli. Serum calcium was 9.6 mg %. Spirometry was normal (FEV1 83%, FEV1/FVC ratio 85) with no significant bronchodilator reversibility (post bronchodilator FEV1 84%).

Chest x-ray revealed bilateral diffuse symmetrical, dense, micro nodular pattern, more at lower and middle zones with sharply defined, black pleural line along lateral chest walls. High resolution CT thorax revealed widespread intra-alveolar calcifications (representing microliths) with ground glass attenuations and septal thickening resulting into a crazy-paving pattern.

### Discussion:

Pulmonary alveolar microlithiasis is a rare idiopathic disease<sup>1</sup>. Homozygous inactivating mutations in SLC34A2 are present in PAM, both familial and sporadic cases. This condition was first described in 1856 by Friederich as "Corpora-Amylacea in den lungen"<sup>2</sup>. In 1933, Pühr used the term as Micralithiasis alveolaris pulmonum<sup>3</sup>. In India, the first case was reported by Vishwanathan in 1962<sup>4-6</sup>. More than 500 cases have been reported in the world literature till now. The highest number of cases has been reported in Europe,

followed by Asia, especially Asia Minor, while the single nation with the greatest number of reported cases are Turkey, then Italy and the USA<sup>7</sup>.

Recent genetic study showed that defect in the SLC34A2 is the possible reason for PAM<sup>8</sup>. SLC34A2 is the only phosphate transporter that is highly expressed in the type II alveolar cells of the lung. The type II cells produce pulmonary surfactant, of which phospholipids are essential constituents. Outdated surfactant is taken up by type II cells for recycling and degradation and by alveolar macrophages for degradation. Degraded phospholipids release phosphate that should be cleared from the alveolar space. Dysfunction of SLC34A2 may reduce the clearance of phosphate and may lead to the formation of microliths. The aetiology and pathogenesis are obscure. But it may occur at any age between infancy and 80 years, while our cases were young with no significant respiratory complaints and without familial incidence. A report from Turkey indicates that the condition seems to be more frequent than would be expected on the basis of reports from elsewhere in the world, 52 cases having been described over 30 years, several of these were familial<sup>9</sup>.

Pulmonary Alveolar Microlithiasis is characterized pathologically by the accumulation of numerous, largely intraalveolar calcified bodies. Microliths range from 0.01 to 3 mm in diameter. The lungs are solid and may sink in water; throughout there are sand like grains diffusely distributed but maximum at bases<sup>1</sup>. Microscopically, there are onion-skin bodies, resembling corpora amylacea, in 30-80 % of the alveoli. Micro-chemical analysis has shown that these are composed of calcium phosphate. Emphysematous blebs may be seen at apex or anterior margin of the lungs. Some times these calcium bodies are also deposited in the lumbar sympathetic chain and probably in the testis<sup>10</sup>.

Majority of the patients with this disease are asymptomatic. Dyspnoea on exertion is the initial

symptoms which develop in advanced cases. Occasionally patients expectorate microliths. Haemoptysis occurs rarely<sup>11</sup>. Digital clubbing may be an occasional finding<sup>12</sup>. Recurrent pneumothorax may also occur<sup>13</sup>. There are no physical sign in chest when radiograph is grossly abnormal. Later there may be inspiratory crepitations and ultimately, the signs of cor pulmonale may develop. Death may occur resulting from respiratory or cardiac failure

The diagnosis of pulmonary alveolar microlithiasis is mainly radiological and based on characteristic radiological appearance and clinico-radiological dissociation. But the diagnosis is often confirmed by open lung biopsy or transbronchial lung biopsy. The chest radiographs in case of pulmonary alveolar microlithiasis are very characteristic and show very fine sand like micro nodulation diffusely involving both lungs<sup>14</sup>. The overall density is greater over the lower than the upper zones, probably because of increased thickness of lung. The distribution of the calcific nodules can also be explained by the relative higher blood supply to this area. The heart borders and the diaphragm are usually obliterated. Other typical findings include small apical bullae and black pleural line, which is demonstrated as an area of increased translucency between the lung parenchyma and ribs<sup>15-16</sup>. The chest radiograph of our patients showed diffuse symmetric lung involvement with dense micronodular pattern, explaining the pattern previously described and as shown in Figure 1. Pleural thickening has been described, although it is probable that this roentgenographic appearance is caused not by actual thickening of the pleura itself but by a visual effect produced by an exceptionally heavy concentration of microliths in the subpleural parenchyma<sup>17</sup>. Calcification of pericardium has also been described in a 13 year old child with this disease<sup>18</sup>.

The High Resolution CT Thorax shows that alveolar calcification is either micronodular or ground glass calcification may be uniform or may show some micronodular structure with

accentuation along the pleural margins and fissures adjacent to interlobular septa (giving polygonous structures) and bronchovascular bundles explaining the coarsely linear nodulations, reticulations and septal lines occasionally seen on chest radiograph<sup>19,20</sup>. There is a predominance of calcifications in the medial areas than lateral portions of lung<sup>21, 15</sup>. It may also reveal small cysts in the subpleural lung parenchyma, pleural calcifications and small calcispherite with in thickened pleura<sup>15-16</sup>. Many of these findings were also seen in our cases such as diffuse ground glass attenuation and septal thickening with calcified nodules. Murch and Carr described the crazy-paving pattern as characteristics of pulmonary alveolar proteinosis<sup>22</sup>. E.L.Gaspreto described that ground glass attenuation with superimposed septal thickening ('crazy-paving pattern) with calcifications along the interlobular septa on HRCT may also be considered diagnostic of pulmonary alveolar microlithiasis<sup>23</sup>, as also seen in our cases (Fig-2).

Pulmonary function tests are often normal or near normal even with extensive radiograph changes. However, with progression of disease restrictive pattern of lung volumes develops with impairment of gas exchanges<sup>12,24</sup>. Progression of the disease is generally very slow; some patients are followed up for more than 30 years without evidence of change. End-stage lung disease was reported to occur more frequently among the cigarette-smoking PAM patients. Sputum specimen showed microliths as rounded concentrically laminated masses. Broncho-alveolar lavage has also been used to recover microliths.

Regarding treatment usually no treatment is required. It is the radiological finding which prompts the first hand treating physician to seek an expert's opinion because of unawareness about the disease in general. Otherwise most patients remain asymptomatic and their diagnosis is made either accidentally during their medical examination or when chest x-ray is performed for some other reasons like surgery etc. In early

stages of the disease, therapeutic broncho-alveolar lavage has been shown to be effective<sup>11</sup>. While in advanced stage of the disease for severe dyspnea, the only management effective is lung

transplantation<sup>25</sup>. Recent genetic study showed that remedies that target phosphate metabolism rather than calcium metabolism may be beneficial for the treatment of PAM<sup>9</sup>.

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