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A case of pulmonary alveolar microlithiasis and rheumatoid arthritis

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Introduction

Pulmonary alveolar microlithiasis (PAM) is a rare disease characterized by widespread localisation of calcispheritis in the alveolar spaces. Chest X - ray is the most important tool to diagnose PAM revealing a sandstorm picture while the clinical state undergoes to a slow and progressive impairment resulting in respiratory failure at the end stage.

Case report

A 17-year-old young girl was admitted to the chest department with a 8 months history of pain and swelling in her knees, ankles, and hands. She had had a severe pneumonia 7 years ago. There was no family history of PAM . She was asymptomatic for pulmonary system. Her pulse was 100 beats per minute, the blood pressure was 110/70 mm Hg, the respiratory rate 24 breaths per minute, and the temperature was 37.5 ^{o}C. There was swelling and tenderness on palpation of her knees and slightly diminished breats sounds at the both lung bases. There was no crackles. The WBC was $8.1x10^{9}$/L, the hemoglobin value 10.8g/dl, PPD 10mm. Rheumatoid factor was 664 IU/ml (normal: 0-10 IU/ml), CRP 53.6 mg/L (normal: 0-5.00), Ig G 2507 mg/dl (normal: 800-1700), Ig M 463.8 mg/dl (normal: 60-370), C_3 109 mg/dl (normal: 50-90), C_4 69.4 mg/dl (normal: 10-40). Serum calcium level was 7.7 mg/dl, and phosphorus 5.2 mg/dl in admission, and calcium 8.0 mg/dl, phosphorus 4.7 mg/dl in discharging. Synovial fluid analyses yielded 75700 cells/mm^3 with a predominance of neutrophils (87%), protein 5.7mg/dl, glucose 59 mg/dl, and cholesterole 75mg/dl. The Pa O_2 was 82 mm Hg, the Pa CO_2 was 35 mm Hg, Sa O_2 was 96%, and the pH value was 7.38. Pulmonary function test revealed a mild restrictive pattern. A chest roentgenogram (picture 1) was interpreted as showing diffuse bilateral micronodular opacities of calcific dansity. CT scan (picture 2) demonstrated a fine diffuse reticulonoduler pattern most prominent in the middle and lower lung zones with greatest concentrations in the subpleural paranchyma and along the bronchovascular bundles. Fiberoptic bronchoscopy (FOB) revealed that the orifices of segmental bronchi gained a whitish appearance. After taking a transbronchial biopsy microlits were seen macroscopically, and histopathologic examination showed microcalcifications in lung paranchyma (Picture 3). An antirheumatic therapy was instituted with indomethacin, prednisolon, salasopyrine. There were clinically significant improvements in rheumatic symptoms.

Discussion

Pulmonary alveolar microlithiasis is a rare disease characterized by widespread localisation of calcipheritis in the alveolar spaces. PAM can be seen in any age group, and disease typically follows a protracted course. The mean age at diagnosis is 35 years. Males and females are affected with equal frequency. The cause of this process remains unclear. One hypothesis is that an abnormal inflammatory response to irritants or infection leads to formation of an exudate that is not easily absorbed and ultimately undergoes calcification (1,2). In our country infectious diseases such as measles in childhood and tuberculosis in both childhood and adulthood are very common. As we know, these infections may easily infect the other children of the family and then a post infectious autoimmune inflammatory process develops. So this explains the reason for familial association in approximately half of the reported cases and that the affected relative is sibling (3,4,5).

It is also possible that inborn errors in metabolism at the alveolar interface leading to increased alkalinity or that mucopolysaccaride deposition may promote the local accumulation of salts. As extrapulmonary calcifications are unusual, and calcium an phosphorus levels in our case have been sometimes abnormal, it is likely that the disease is due to a local derangement of calcium metabolism.

Although not usually required bronchoalveolar lavage or transbronchial biopsy can confirm the diagnosis. Biopsy shows the calcified spherules filling alveolar spaces (Picture 3). There may or may not be interstitial fibrosis and inflammatory cell infiltration. There are usually no changes in other organs although calcium deposits have been reported in one patient (6).

A striking feature of this disease is the frequent discordance between the clinical and radiographic manifestations. Many patients display only minor symptoms despite impressive radiographic features.

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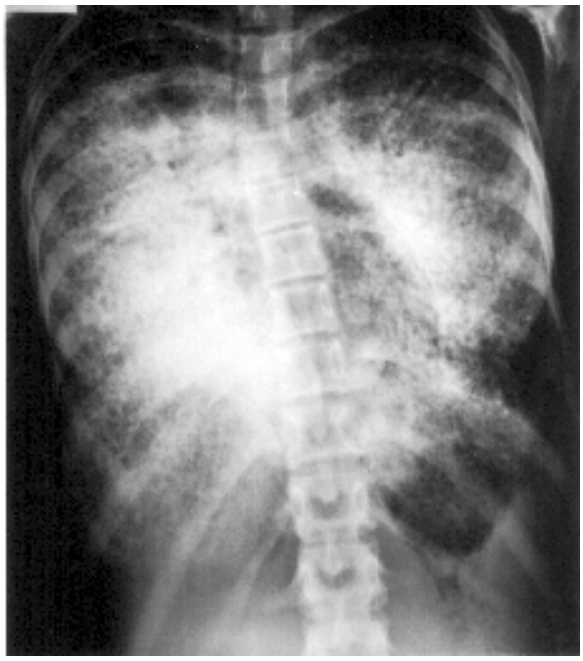
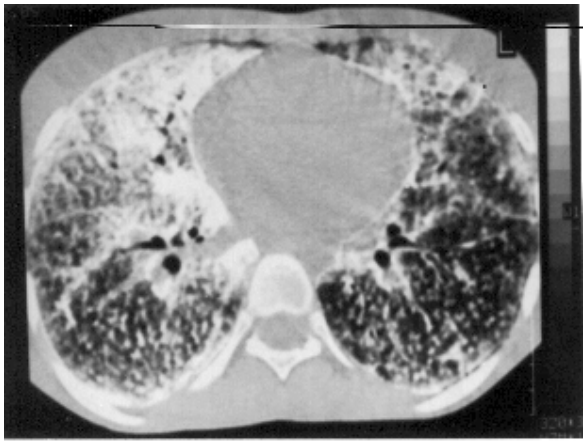
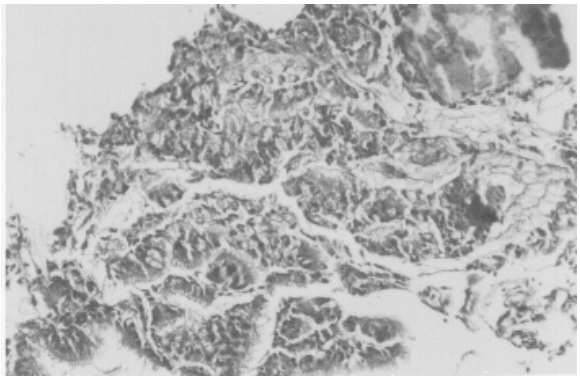
Those patients who are symptomatic typically complain of dyspnea and nonproductive cough, and the disease may develop slowly and progressively culminating in cor pulmonale (5).



Picture 1. Chest radiography shows diffuse bilateral micronodular opacities.



Picture 2. CT scan shows diffuse distribution of micronodular calcific densities in the subpleural parenchyma and along the broncho-vascular bundles.

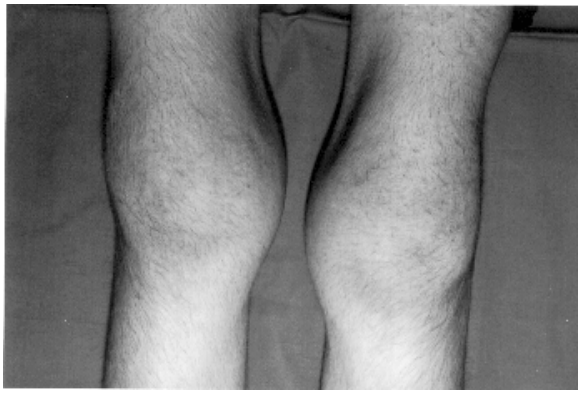


Picture 3 Biopsy specimen taken from bronchial tissue shows microcalcification at the righ upper corner (H.Ex100).

The typical finding on chest roentgenogram of bilateral infiltrates with a fine sandlike micronodular appearance and greater density in the lower and middle lung fields is considered to be diagnostic (Picture 1).

CT scan demonstrate diffuse distribution of micronodular calcific densities which are usually most prominent in the middle and lower lung zones with greatest concentration in the subpleural parenchyma and along the broncho-vascular bundles (Picture 2). Although usually asymptomatic at the time of presentation, alveolar microlithiasis rarely produces functional abnormalities. When it does, these findings are restrictive pulmonary function tests or exercise-induced pulmonary hipertension.. Respiratory function tests are often normal even with extensive radiographic changes. With progression of disease, a restrictive pattern of lung volumes develops, and gas transfer is disturbed and respiratory failure ensues. No therapy, including therapeutic bronchoalveolar lavage, has proven effective (7).

In the differential diagnosis, pulmonary dystrophic and metastatic calcification should be taken into consideration. Dystrophic calcification refers to the deposition of calcium salts in dead tissue, such as within the healing granulomas of tuberculosis. Metastatic calcification refers to the deposition of calcium salts and occurs in association with some derangement of calcium salts metabolism, such as hyperparathyroidism, hypervitaminosis D, the milk alkali syndrome, sarcoidosis, increased bone turnover due to multiple myeloma or metastatic carcinoma, or chronic renal failure (1).

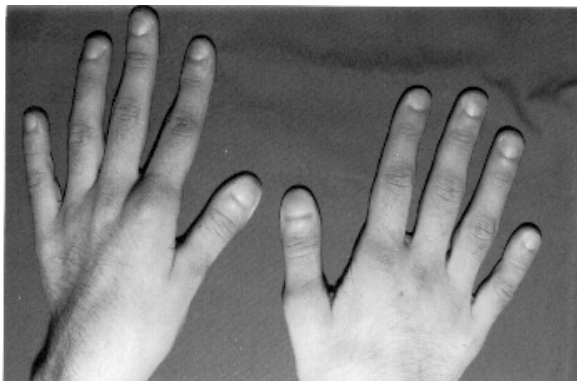


Picture 4. Bilateral swelling in the knees.

In this patient we think that PAM itself caused an otoimmune rheumatic process to start. The patient complained mostly of symptoms of poliarthritis (Picture 4,5). Clinical and laboratory findings strongly suggested a rheumatic process. Results

revealed Rheumatoid Arthritis. In our knowledge, this is the first report on PAM associated with RA.

This patient gave rise to an opinion that local inflammatory response caused to the development of PAM, and PAM itself started an otoimmune rheumatic process . In our knowledge, this is the first report on PAM associated with RA. We think that further cases are needed to explain this association.



Picture 5. Phalangeal and metacarpo-phalangeal deformities.

At present, no medical therapy has been shown to definetely alter the progression of this disease. Therapeutic modalities including corticosteroids, calcium chelating agents, and bronchopulmonary lavage have been shown to be ineffective (1,8). Two reports discussed the use of etidronate disodium to treat PAM patients (5,9). Bilateral lung transplantation would appear to be the procedure of choice as a treatment of advanced lung disease (4). In order to maximize the chances for a successful outcome, the patients should be referred to the operation before the development of severe right ventricular disfunction.

In the case reported we based our diagnosis on the chest roentgenogram and computed tomography scan and pathological findings obtained at FOB avoiding open lung biopsy. The dens alveolar filling pattern, with the presence of numerous parenchymal calcifications was sufficient to the diagnosis.

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