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PULMONARY ALVEOLAR MICROLITHIASIS (A CASE REPORT)*

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Pulmonary alveolar microlithiasis (PAM) is a very rare autosomal recessive disorder characterized by intra-alveolar calcified microgranules called calcospherites. The causative mechanism of this disorder is still unknown and diagnosis is generally based on typical radiological and lung biopsy findings which are usually confused with pulmonary tuberculosis[1]. In this article, we presented a case of PAM in a four-year-old boy in which two other family members had the same disorder; however they received unnecessary antituberculosis therapy for various durations.

Case Report

A four-year-old male child was admitted to the hospital with complaints of headache, fever and vomiting. It was discovered that the left part of his face had been swollen three days before and had been diagnosed as mumps. However, for the past two days, the symptoms had become more severe. His developmental history was normal and he did not have any significant illnesses except for pneumonia when he was seven-months-old.

Physical examination revealed a child with a temperature of 38 °C (axillary), pulse of 112/min, respiration rate of 24/min, and blood pressure of 100/50 mm Hg. His general condition was good except for some weakness. Both parotid areas were swollen, without pain. There was nuchal rigidity but all other systemic findings were normal.

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Laboratory findings included; hemoglobin 13.50 g/dl, White Blood Cell count 6400 per mm^3 and a normal peripheral blood smear. Routine urinalysis, serum sodium, potassium, chloride, calcium, phosphorus, alkaline phosphatase, total protein, albumin, and glucose levels were all within normal limits. The serum amylase level was 380 Somogy units. The cerebrospinal fluid was clear with polymorphonuclear leukocytes 275 per mm^3, protein 48 mg/dl, and glucose 60 mg/dl. Bacteriological examinations of the throat and CSF were normal. The PPD test was negative. Chest x-ray revealed bilateral, diffuse calcified micronodules which resembled a miliary reticulonodular pattern and overlayed heart contours (Fig. 1).

The patient's parents were healthy. The father was the son of the grandchild of the patient's grandmother's uncle. The maternal grandmother and the patient's father were cousins (Fig. 2). We learned that the child's aunt had been in the hospital two years ago and on the basis of biopsy findings was diagnosed as having PAM (Fig. 3). She had pulmonary symptoms between the ages of 9-10 years and died of cor pulmonale at the age of 34. The mother's nephew, whose chest x-ray also revealed PAM, received unnecessary antituberculosis treatment during his military service (Fig. 4).

On the basis of the family history and typical chest x-ray findings, the patient was diagnosed as having PAM. He was treated for fever and vomiting in the course of mumps meningo-encephalitis. When his general condition improved, the patient was discharged from the hospital. He is being followed up as an outpatient.

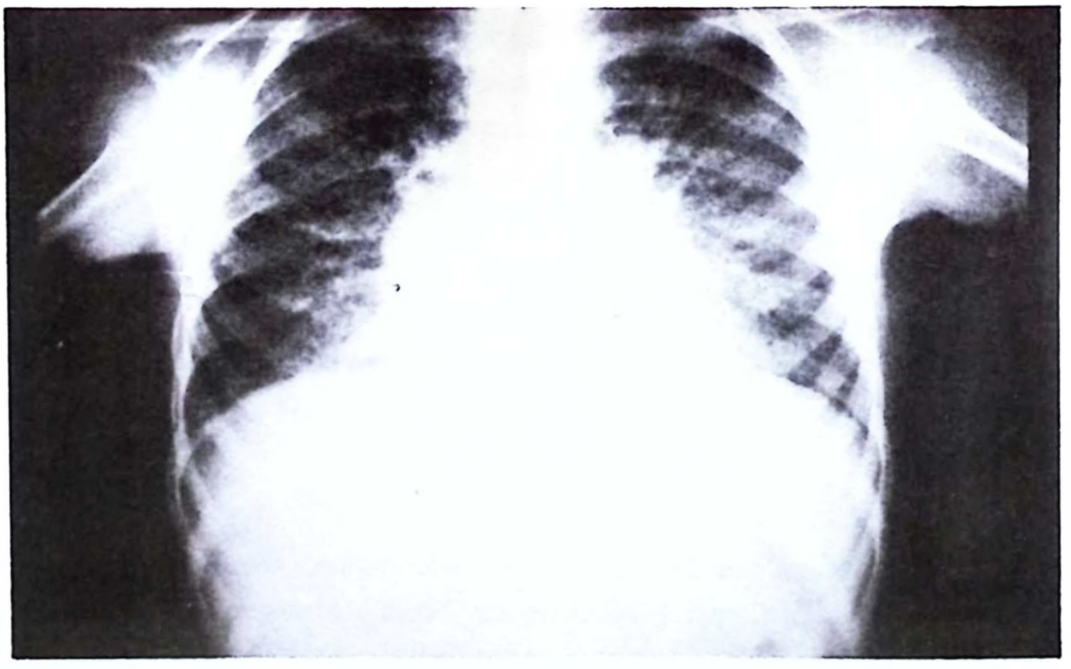

Fig. 1: Chest x-ray of the patient. Bilateral, diffuse calcified micronodules.

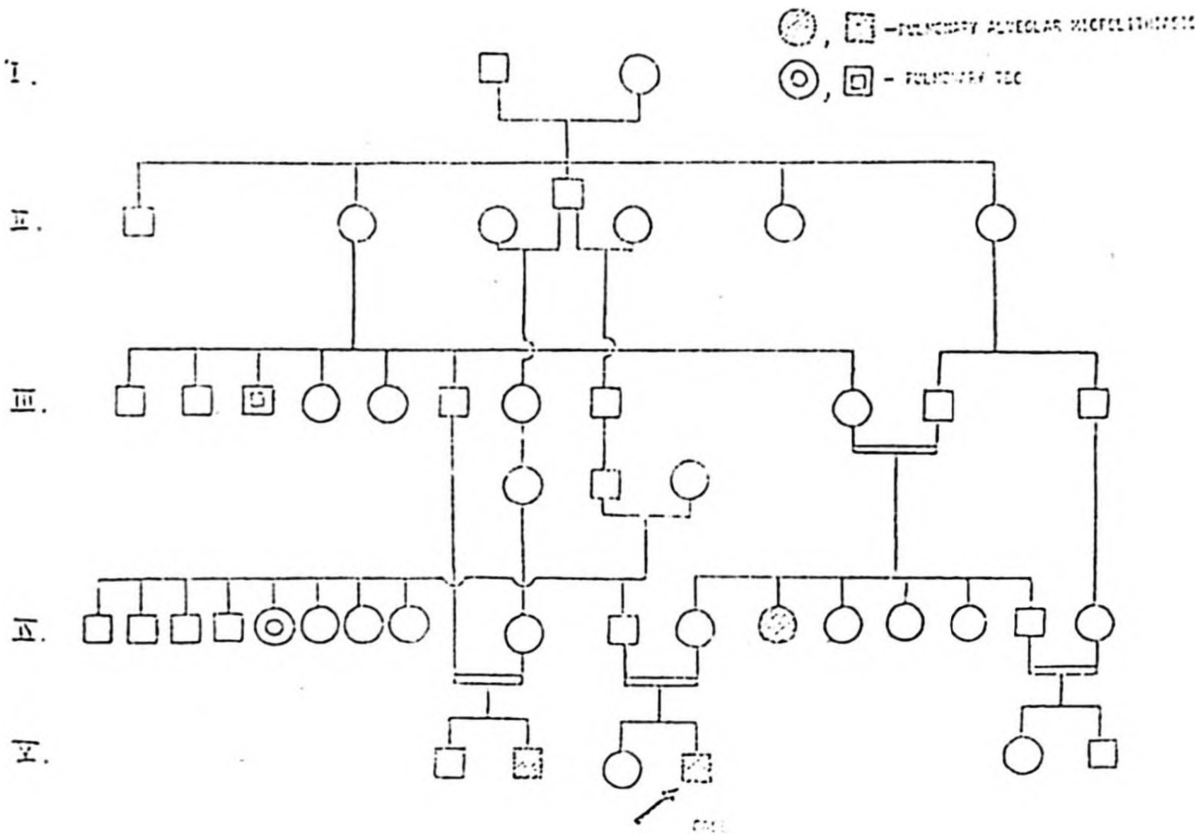

Fig. 2: Pedigree of the patient.

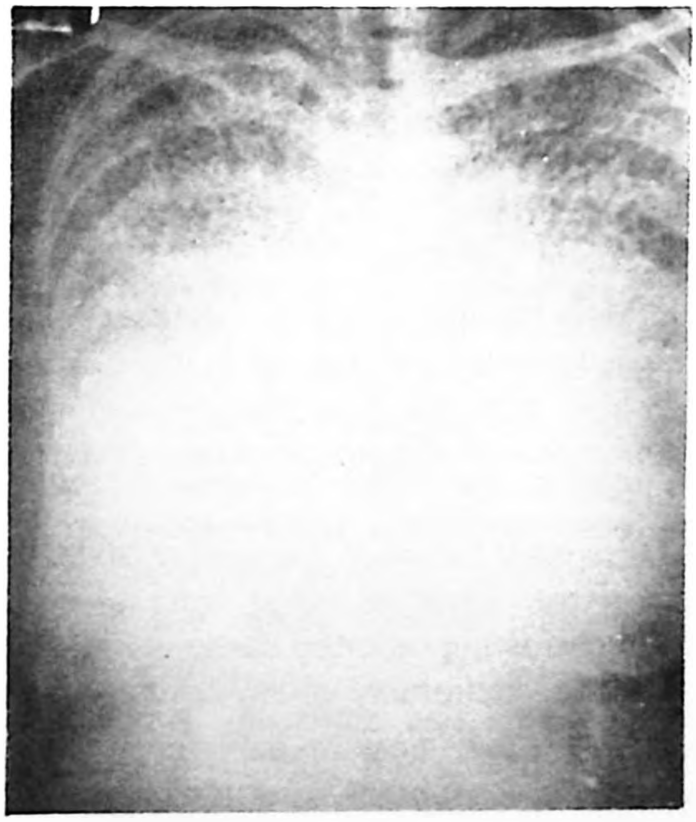

Fig. 3: Chest x-ray of the patient's aunt.

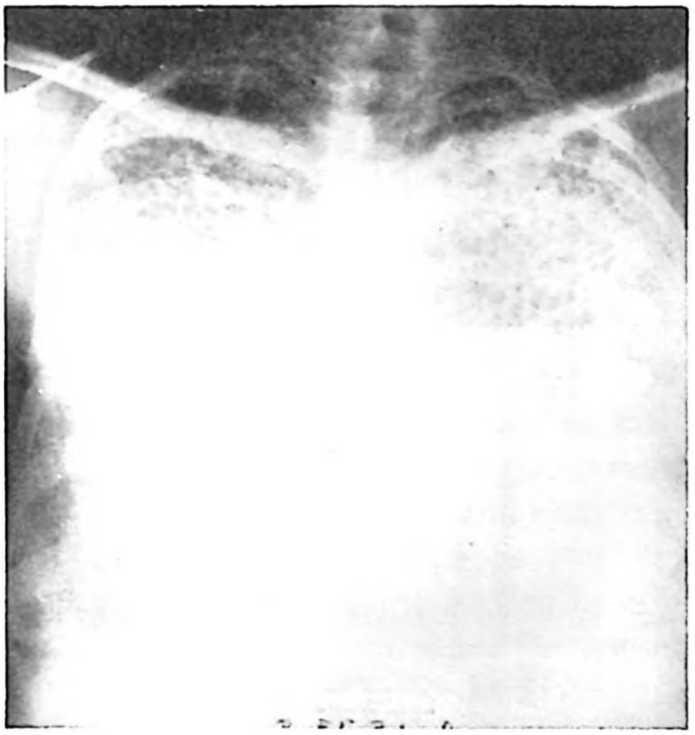

Fig. 4: Chest x-ray of the patient's maternal nephew.

Discussion

PAM was first described in 1918 by Harbitz[2]. Puhr[3] was the first one to use this terminology in 1933. In 1957 Sosman et al[4] reported 23 new cases along with the 21 already reported. One hundred and twenty cases of PAM were reported in 1981. It is believed that the total number of cases has reached 200 in the world, predominanting in Asians and Caucasians[1,5]. Environmental causative agents, such as toxic materials or airborne agents have not been specified and neither have infectious agents been identified[1].

Familial predisposition to the disease suggests a genetic inheritance of autosomal recessive order[6-8]. Family histories are positive in more than half of the patients, with siblings usually being affected. The disease is not sex dependent. Our findings support the hypothesis of an autosomal recessive mode of inheritance of this disorder.

The incidence of PAM is highest between the ages of 30-50 years but the ages of the patients reported in the literature range from birth to 80 years[1,9]. The youngest, and the most interesting reported cases were premature twins[10]. The presented case is one of the extremely young cases reported in the literature.

Histopathologic findings of the lung reveal alveoli covered with calcified microgranules known as calcospherites assuming concentrically laminated patterns. These deposits are generally spheroidal and ovoid in shape with

diameters between 0.01-3.0 mm. They are irregular and surround an amorphous nucleus-like electron dense fragment. Calcospherites are mainly deposits of calcium and phosphorus ions, which occur as Ca_2PO_3 complexes[11,12].

The initial symptom of this disease is usually characterized by a cough and in the later course, pulmonary insufficiency develops into cor pulmonale. Besides the cases which remain asymptomatic and stabile for long periods, there are also those which develop pulmonary insufficiency quite rapidly. But generally the disease progresses slowly and clinical findings can develop several years after the radiologic findings[1,12].

The pathogenesis of the disease is still unknown. Some investigators have observed calcospherites in the testis[13], lumbal sympathetic chain[13], kidney[14] and prostate[15]. Although all these findings suggest a possible defect in the calcium metabolism in this disorder, the data is insufficient to verify this. In our patient the serum calcium, phosphorus and alkaline phosphatase levels were within normal limits, as reported in the literature.

Some environmental factors may affect the onset of the disease. Chinacinoti and Tangchai[16] found radiologic abnormalities in nine males who had inhaled snuff in the Far East. PAM was diagnosed in one of them from the biopsy material. Another case had been exposed to printer's ink for a duration of nine months[5]. However, no correlation could be made between these materials and PAM. In some published reports, it is suggested that the microgranules are a result of a hyperimmune reaction to various irritants and they form as a result of an inflammatory process or an exudative response to pneumonia or rheumatic fever[11,12,17].

The typical radiologic findings of PAM are calcified opacities resembling a sandstorm, calcified micronodules at the basal section of the lung, hilar trabecular pattern pleural lining in each lobe surrounded by an opaque line formed by microgranules in the subpleural area. Moreover, some cases have been reported which present Kerley B lines that are findings of lung edema. These criteria can change with the addition of inflammatory and necrotic findings in later stages[18,19].

These typical radiologic findings of PAM are mostly mistaken for miliary tuberculosis. For example in Mayo Clinic, it has been reported that more than half of the cases were initially diagnosed as miliary tuberculosis[5]. In the present case, two other members of the family received unnecessary antituberculosis treatment for various durations.

Although it is not diagnostic, microliths can be seen in the sputum[20] and bronchoalveolar lavages[21]. But it should be recalled that salivary microliths have been observed in 26% of cases with obstructive lung disease and chronic tuberculosis.

There is no specific therapy for PAM. Corticosteroids and chelating agents have not proved to be valuable in the treatment of some patients. Bronchopulmonary lavage has been applied, however, the course of the disease could not be reversed. Symptomatic treatment is directed towards pulmonary failure and cor pulmonale[1]. No course of treatment was planned for our patient. Since there was consanguinity in the patient's family, they received genetic counselling. We believe that more research is needed to find a parallel between a calcium-phosphorus metabolism disorder in the lung and the etiology of the disease. The development of proper treatment will follow the determination of the etiology.

Summary

A case of pulmonary alveolar microlithiasis in a four-year-old male child diagnosed by chest x-ray is presented. This rare autosomal recessive disorder was also detected in two other members of the family. It is emphasized that in differential diagnosis this disorder must be distinguished from tuberculosis.

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