

Case report

Pulmonary alveolar microlithiasis: an overlooked disease in Iraq

W. Al-Kubaisi,¹ N. Al-Alwan² and K. Al-Nu'aimi³

Introduction

Pulmonary alveolar microlithiasis (PAM) is a rare disease of unknown etiology and pathogenesis, where the pathological substrate is composed of calcium microconcrements inside the alveoli [1]. Examination of bronchial lavage fluids from affected patients usually reveals spherical or ovoid-shaped microliths composed of calcium and phosphate deposits in a ratio of 2:1 [2]. The essential features of the disease include a characteristic radiographic appearance of a sand-like opacity in both lungs with linear densities similar to beads on a string along the heart pleura and interlobar fissures. There are few clinical signs and almost no laboratory abnormalities [3].

The term pulmonary alveolar microlithiasis was first introduced by Pühr in 1933 and since then sporadic cases have been reported in different countries [4-10]. In the Eastern Mediterranean Region, reports of the disease in Egypt were published by Abdel-Hakim et al. and Madkour et al. [5,6]. In 1993, Ucan et al. estimated that of only 173 cases recorded worldwide, approximately 30% came from Turkey [11]. To our knowledge this is the first report on PAM from Iraq, and this study describes the clinical presentation, typical roentgeno-

graphic appearance of the chest and the pathological diagnosis of five patients.

Patient case reports

Case 1

In 1978, a 22-year-old single woman was referred from Al-Anbar province to the Tuberculosis Institute as a case of miliary tuberculosis. Her chief complaint was dyspnoea on exertion. On clinical examination she was well built with no cyanosis, clubbing or oedema. Her chest was clear and her heart was normal with no abnormal findings in any other body systems. A chest X-ray showed disseminated minute miliary densities in both lung fields, mostly at the hilum and in the middle and lower zones (Figure 1). A tuberculin test was negative. Sputum examination for acid-fast bacilli was also negative on two separate occasions. Her complete blood picture was normal and serum calcium, serum sodium and serum potassium levels were 10 mg/100 mL, 138 mEq/L and 3.8 mEq/L respectively.

As PAM was our provisional diagnosis, the case was referred to the Department of Thoracic Surgery in the Medical City Teaching Hospital for a lung biopsy which

¹Department of Community Medicine, Saddam University Medical College, Baghdad, Iraq.

²Department of Pathology, Baghdad University Medical College, Baghdad, Iraq.

³Tuberculosis Institute, Ministry of Health, Baghdad, Iraq.

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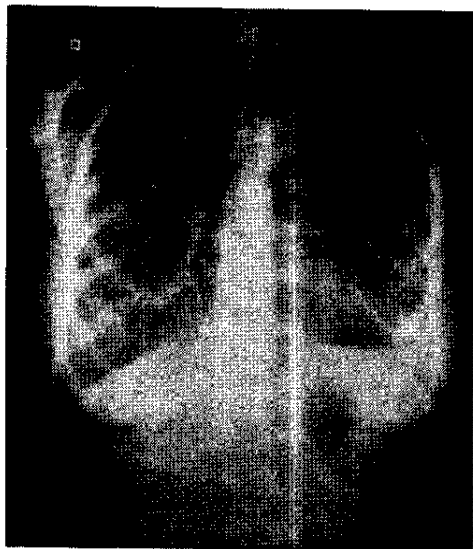


Figure 1 Chest X-ray showing disseminated minute miliary deposits in both lung fields, mostly at the hilum and the middle and lower zones

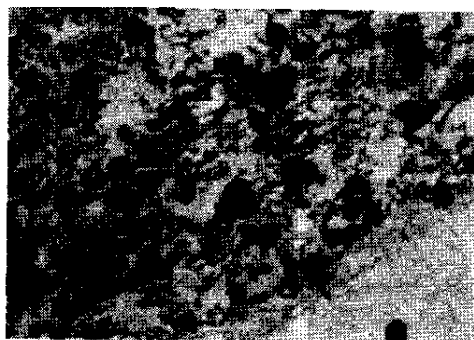


Figure 2 Lung biopsy—histopathological section showing multiple calcified intra-alveolar deposits (H&E x 180)

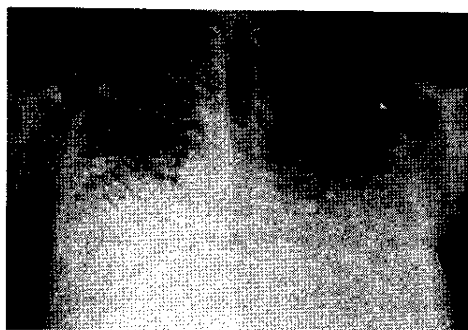


Figure 3 Chest X-ray showing confluent calcified opacities uniformly involving both lung fields

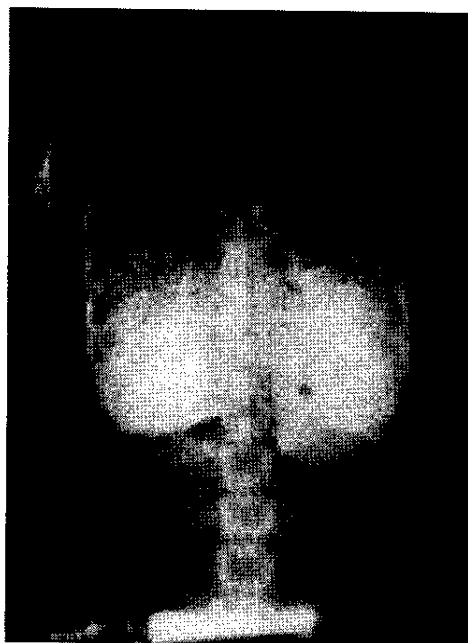


Figure 4 Total obliteration of the mediastinal and diaphragmatic contours

confirmed our diagnosis (Figure 2). Regrettably, no further follow-up was possible as the patient came from Al-Anbar province.

Case 2

In November 1995, a 48-year-old man was officially referred for opinion from the Medical Committee Department to the Tuberculosis and Chest Disease Centre in Baghdad. His history and clinical examination revealed no abnormal signs or symptoms apart from dyspnoea. On consultation it transpired that he was a known case of PAM, originally diagnosed in 1976 in the United Kingdom by lung biopsy. His chest X-ray findings are shown in Figure 3.

Cases 3 and 4

In 1986, a 20-year-old woman presented complaining of having renal pain for 1 week. Her history and clinical examination were normal and a general urine examination revealed 10–15 pus cells/high-power field and 5 red blood cells/high-power field. Her kidney, ureter and bladder did not show any stones, although there were confluent densities of calcification at the bases of both lungs. The patient had no respiratory symptoms. Her chest X-ray showed confluent calcified opacities spread uniformly across both lung fields. Further investigations, including a complete blood picture, serum calcium, serum phosphate and pulmonary function tests were all normal. The patient, who had no family history of the disease, was diagnosed as a case of PAM. One month later a histopathological examination of her lung biopsy confirmed our diagnosis.

The patient subsequently married in 1992 and after delivery of her first child in 1993 started to complain from dyspnoea on exertion. A chest X-ray showed total obliteration of the mediastinal and diaphragmat-

ic contours (Figure 4). During one visit in August 1995, she was accompanied by her 19-year-old brother. His routine chest X-ray showed minute miliary dissemination with hairline densities transversing from the hilum to the peripheral parts of both lungs (Figure 5). Because he had no respiratory complaints, he refused further investigations and never returned. We later understood from his sister that he had been mistreated as a case of miliary tuberculosis.

Case 5

In this case a diffuse but sharply defined micronodular pattern was accidentally discovered on the routine chest X-ray of an asymptomatic 33-year-old man. The patient had a long history of heavy exposure to sand particles. Cytological examination of a bronchioalveolar lavage specimen showed concentrically laminated oval calcified microliths, making the diagnosis of PAM more likely (Figure 6). However, the diagnosis was histologically confirmed by findings of multiple, differently sized, rounded, haematoxylin-stained deposits or calcospherites, which were located within the alveolar spaces.

Discussion

As a disorder, PAM is characterized by the progressive formation of intra-alveolar calcified microgranules in response to an unknown stimulus. Several hypotheses on the etiopathogenesis have been put forward, such as increased calcium resorption and retention [12]. However, there was no evidence in the cases reported of either calcaemia or calcium deposits in any other organ of the body.

Environmental factors have also been postulated as a possible cause and previous theories have linked microlithiasis to exter-

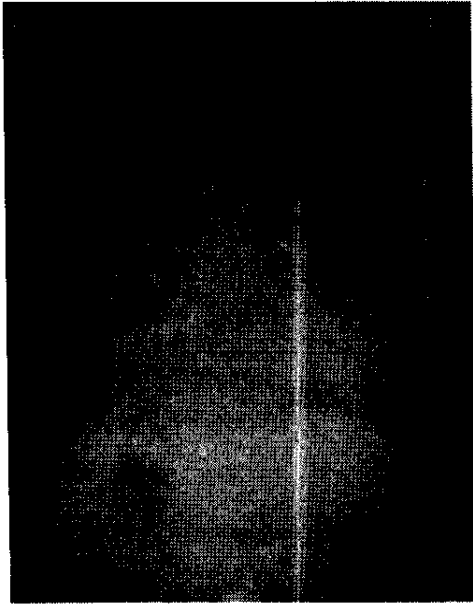


Figure 5 Chest X-ray showing hairline miliary nodular densities in both lungs transversing from the hilum to the peripheral parts



Figure 6 Calcospherites—concentric laminated oval bodies in smears obtained from bronchioalveolar lavage (Papanicolaou stain $\times 400$)

nal irritants. For example, cases have been reported in snuff dippers in Thailand, and in Saudi Arabia diagnosis of the disease in desert inhabitants suggests the possibility that sand particles might be responsible for triggering a hyperimmune response resulting in the formation of microliths [7,13]. If this is so, the condition may have similarities with desert lung syndrome, a disease definitely caused by the deposition of sand silica within the lungs [14]. This etiology may be responsible for the development of the disease in Case 5, and the role of the pebble factory in Al-Anbar, the residence of Case 1, should also be considered.

PAM has been diagnosed in patients of all ages, even in infants, and there is no obvious sex predominance [15]. A familial tendency has, however, been noted in many published reports and was evident in Cases 3 and 4 [7,16,17]. This familial incidence, which has been mostly restricted to siblings, suggests a possible genetic etiology with autosomal recessive inheritance [1,16–18].

The disease usually follows a slow course, which may extend over 20 years [1]. In the majority of cases, patients are asymptomatic when the disease is first discovered and respiratory findings are normal (e.g. Cases 4 and 5) [16,18]. Others may present with a chronic and persistent cough, which could be a direct consequence of the disease [19].

Interestingly, the disease may become arrested (as in Case 2), where changes apparent on X-ray remain stable for up to 20 years. But in other patients the microliths may continue to form and increase in size as the disease progresses. The lungs may then suffer deterioration of the respiratory mechanism, which results in the development of ventilation and perfusion disorders. This was illustrated in Case 3 as the patient's follow-up showed a deterioration in

chest X-ray findings with the opacities becoming more confluent and distributed over a larger area within the lung tissue. A high resolution computed tomography scan revealed that the pleural line on the chest X-ray was caused by a fat-dense layer between the ribs and the calcified parenchyma [20]. Following such deterioration, patients may develop dyspnoea, hypoxia and even cyanosis [21]. Eventually, some might end up with pulmonary hypertension and chronic cor pulmonale. Also, the development of emphysematous bullae and pneumothorax has been recorded [22]. In such conditions pulmonary function tests may show signs of hyperventilation and airway dysfunction in the presence of restrictive ventilatory defects [23].

No effective specific treatment is so far known, and it has been proposed that a combined heart/lung transplant might be the only therapy that could prolong a patient's life. However, the possible use of di-

phosphonate to inhibit microcrystal growth formation has also been given consideration [24,25].

In conclusion, we can confirm that this pulmonary disorder is present in Iraq. For its diagnosis, the radiological picture is quite characteristic and should consequently obviate the need for a lung biopsy. Essential knowledge of the disease process is therefore recommended and PAM should be taken into consideration in the differential radiological diagnosis of any diffuse mottling opacities radiating from the hilum of the lungs or symptoms simulating pulmonary oedema.

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