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Absence of pulmonary uptake of Tc-99m methylenediphosphonate in alveolar microlithiasis

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Pulmonary alveolar microlithiasis (PAM) is a rare disease of unknown etiology characterized by accumulation of calcific concretions in the alveolar spaces. The paper reports a case of PAM in a 56-year-old male. The patient had persistent dry cough, and gradually progressive dyspnea on exertion. The diagnosis was established on the basis of roentgenography and confirmed by the sputum and transbronchial biopsy findings. Scintigraphy revealed the absence of Tc-99m methylenediphosphonate uptake of lungs. Familial occurrence was not observed. Chest roentgenogram, pulmonary function, and clinical status of the patient have remained stable for 41 months. Radiological and clinical follow-up of the disease continues.

Key words: pulmonary alveolar microlithiasis, Tc-99m MDP bone scintigraphy, lung

INTRODUCTION

Pulmonary alveolar microlithiasis is a rare disease of undetermined cause characterized by the presence of microliths within the alveoli of the lungs. Although the disease shows no clear geographic distribution,[2] most of the reported literatures were from Turkey.[1] The disease affects both sexes equally, afflicts patients primarily between in 4th and 6th decades.[2] The diagnosis is usually made on the basis of the typical radiological pattern, namely a very fine, sand-like micronodulation of calcific density diffusely involving both lungs with basal predominance.[3] After the disease is diagnosed in a given patient, other family members should be screened by chest roentgenography, and parents should be counseled that future children are also at risk of developing the disease.[4] Although some patients present with progressive respiratory symptoms, the discovery is in most cases an incidental finding on a chest radiograph. Tc-99m diphosphonate scanning usually reveals diffuse intense uptake throughout both lungs.[5]

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The patients are symptomless for a long time. Nevertheless, this disease slowly develops into pulmonary fibrosis and cardiac failure.

CASE REPORT

A farmer, a 56-year-old man, presented to our outpatient clinic on 2 October 2000 complaining of persistent dry cough and gradually progressive dyspnea on exertion. His symptoms had been presented for 6 months, but had recently worsened. He did not have a smoking history. Vital signs were normal. His temperature was 36.7°C, pulse rate was 88 beats per minute, respiratory rate was 18 per minute, and blood pressure was 110/70 mmHg. There was no peripheral adenopathy. Results of complete physical examinations were normal except for a palpable thyroid (cystic goiter). Thyroid function tests (T_3, T_4, TSH) were normal. No specific metabolic abnormalities were identified. Serum calcium, phosphorus, alkaline phosphatase, parathyroid hormone levels, and urinalysis were normal. There was no hepatosplenomegaly, and no clubbing, cyanosis, or edema of the extremities. Hemoglobin and white blood cell count were normal at 13.9 g/d*l* and 6.9×10^3/m*l*, respectively. Resting arterial blood gas values in room air were as follows: pO_2: 83.2 mmHg, pCO_2: 35.1 mmHg, O_2 hemoglobin saturation: 96.5%, and pH: 7.41. Pulmonary function test results were within

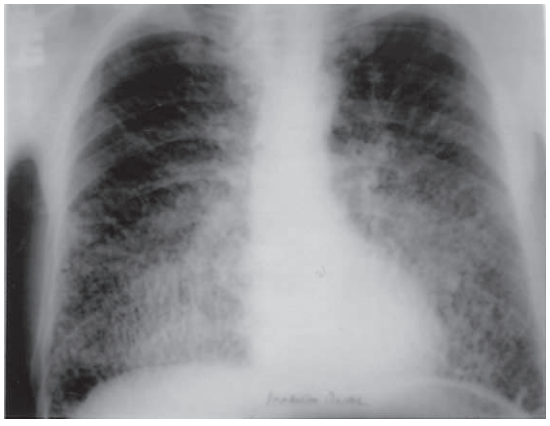

Fig. 1 Chest roentgenogram showing diffuse interstitial pattern.

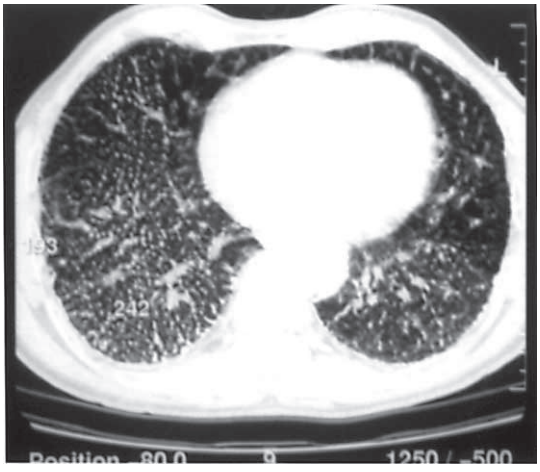

Fig. 2 Computed tomography of the chest showing diffuse interstitial pattern and fine punctate nodular densities.

normal limits. The chest radiogram revealed diffuse high-density sand-like micronodules and reticular lines throughout the lung fields (Fig. 1).

High-resolution CT of the chest (Fig. 2) showed a unique and characteristic calcified reticular pattern and thickening of the interlobular septa of the lung parenchyma, with predominant basal and peripheral lung distribution. There was no hilar or mediastinal lymphadenopathy.

Whole body bone scintigraphy was performed 3 hours following I.V. injection of 740 MBq (20 mCi) of technetium-99m methylene diphosphonate using a gamma camera with a low energy, high resolution collimator (Toshiba GCA-901/SA). The photopeak was centered at a 20% window in the camera. In obtained images, the radiotracer was distributed normally in systemic bones, and symmetric uptakes with increased activities were seen in joints and junctions. Also bone scintigraphy showed the absence of Tc-99m methylenediphosphonate uptake of lungs (Fig. 3).

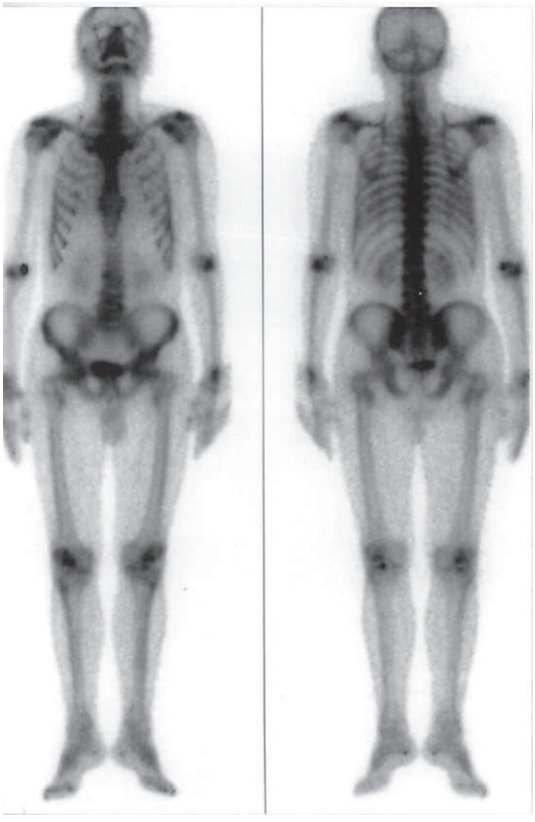

Fig. 3 Tc-99m diphosphonate bone scan revealing absence of lung uptake.

Histopathological examination of the transbronchial lung biopsy specimen showed the characteristic calcispherites in the alveolar space but not in the interstitium. In microscopic examination some of the alveoli contained laminated eosinophilic calcispherites with Von-Kossa (Fig. 4).

His three brothers, two sisters, two sons, two daughters, and four grandchildren underwent chest radiography. There were no abnormalities suggesting alveolar microlithiasis. The last follow-up radiographs and pulmonary function studies were available on 15 March 2004 to document the clinical progression of the disease. His clinical status has remained stable for 41 months. No differences were seen on chest radiographs, lung function tests or arterial blood gas measurements. There was no progression in symptom severity. Vital signs and physical examination were also normal. Follow-up regarding the radiological and clinical course of the disease continues.

DISCUSSION

Pulmonary alveolar microlithiasis is a rare disease entity of unknown etiology that affects individuals of all ages, from the very young to elderly. A review in 2002 described 300 cases of PAM reported in the literature.[6] To our knowledge, only two PAM cases with absence of

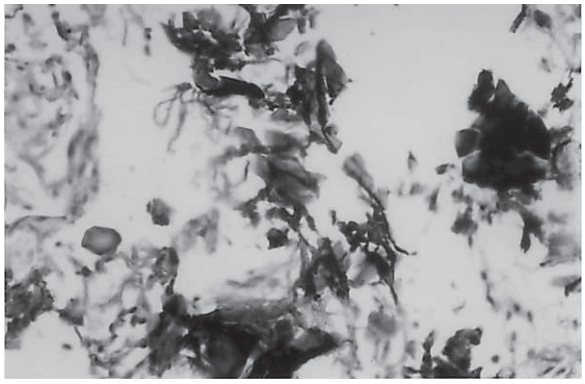

Fig. 4 One of the airspaces contained laminated eosinophilic bodies representing the microliths, with surrounding lung parenchyma showing inflammatory and fibrotic changes. Von-Kossa × 200

pulmonary uptake of Tc-99m diphosphonate have been reported previously in the literature.[7,8]

Most patients with this disorder have no symptoms when their disease is discovered. Our patient had persistent dry cough and gradually progressive dyspnea on exertion. A familial occurrence is a notable feature and has been observed in more than half of the reported cases.[7,9,10] The family history of our patient was negative for the disease.

Although the radiographic appearance is typical, CT, pulmonary uptake of Tc-99m diphosphonate, bronchoalveolar lavage, and transbronchial biopsy help confirm the diagnosis.[11–13] Although lung biopsy might be avoided in the presence of the typical radiological pattern, we also performed transbronchial lung biopsy to confirm the diagnosis.

Examination of the transbronchial lung biopsy specimen showed PAM. Although microliths can be found in the sputum, they are not diagnostic, and Tao found that the sputum of 26% of patients with chronic obstructive pulmonary disease contained microliths.[13] In our case, sputum examination also confirmed the diagnosis of PAM besides the transbronchial lung biopsy.

Results of pulmonary function studies in patients with pulmonary alveolar microlithiasis vary, depending on the presence or absence of interstitial fibrosis, but they are normal in the early stages. No abnormal pulmonary function was noted in our patient.

In PAM patients, bone scanning agents should be taken up in lung due to chemisorption on the surface of calcium salts because microliths consist principally of calcium salts.[14] In our case, no lung uptake with technetium-99m diphosphonate was detected on the bone scintigraphy. In the study of Caffrey and Altman,[15] histological examination suggested that the microliths originated in the alveolar septal cells and were extruded into the lumen. Although no microliths were detected in the alveolar septum by transbronchial biopsy in our patient, Sears et al. revealed calcispherites not only within alveoli but also in bronchial walls and in fibrosed interstitium.[16] The decreased intensity of the microliths in the alveolar septal cells and the absence of any communication with the systemic circulation may explain the absent lung Tc-99m diphosphonate uptake.

There is currently no effective medical therapy for PAM, but whole lung lavage and bilateral sequential lung transplantation have been considered as options.[17,18]

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