Diagnosis: Pulmonary alveolar microlithiasis after exposure to mustard gas

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Pulmonary alveolar microlithiasis (PAM) is a rare disease of unknown etiology and pathogenesis.^{2,3} This disorder is characterized by intra-alveolar development and deposition of microliths or calcispherytes containing calcium phosphate.^{2,3} The age range of patients is from newborn to 80 years. The mean age at presentation is in the third to fourth decade with no sexual predominance, but in approximately half the reported cases a familial pattern has been found. Most of the patients have few or no symptoms despite the gross radiographic changes. The dissociation between the definite x-ray pattern of the lungs and the relatively poor clinical symptoms is the most common characteristic of this disease. However, a certain degree of dyspnea with productive cough may occur together with a sporadic hemoptysis, thoracic pain and sometimes spontaneous pneumothorax.^{4,5} The lungs are hardened with associated deterioration of pulmonary hypertension and thus cor pulmonale occurs.⁶ Pulmonary fibrosis is also observed in association with PAM.^{7,8} In such cases, as in our patient, a posteroanterior chest x-ray shows a dissemination of radio-opaque nodules of almost equal sizes and the lungs appear to be sprinkled with sand. Very fine sand-like micronodulations with calcified densities were observed throughout both lungs fields (Figure 1). Histological examination demonstrated onion-skin-like microliths occupying the alveoli. Amorphous eosinophilic material filled the alveoli (Figure 2).

Some authors suggested that PAM may be a peculiar exudative response to a variety of insults, which include pneumonia and rheumatic fever.⁹⁻¹¹ Our report describes PAM after exposure to mustard gas. In other cases of microlithiasis sandstorm-associated, the exact cause has not been proved; only in 50% of cases has a genetic or familial factor been reported, but other causes have not been confirmed. In all cases, either acquired or genetic, it can be assumed that there is a disorder in the bronchial cilia or alveolar endothelium. Therefore, it can

be concluded that acquired causes can induce enzymatic disorders similar to those in genetic defects.⁴

Although the clinical features of this disease have been well described, the mechanism which may induce microliths to form is unknown. Inhalation of specific powders was thought to be involved in the origin of microliths as some patients lived in the same rural district and worked on the same farmlands. In addition, the pattern of serial scans clearly indicated that the lung mucociliary function was impaired in patients with microlithiasis. This may suggest that slowing of the clearance may represent a pathogenetic factor capable of favoring the formation of alveolar microliths. In patients who smoke "snuff" (a particular mixture of tobacco and oriental gum) this hypothesis is favored. Finally, cases of PAM secondary to lung cancer, tubercular remains and pleural mesothelioma have also been reported.⁴

Figure 1. Chest x-ray showing bilateral apical bullae, disseminated sand-like discrete radio-opaque micronodules predominantly in the lower zones. Lungs appear to be sprinkled with sand.

what's your diagnosis?

Figure 2. Photomicrograph showing laminated appearance of a microlith (hematoxylin-eosin, $\times 40$).

The etiology of pulmonary alveolar microlithiasis has remained obscure;¹⁻¹⁵ however, familial occurrence is a notable feature and has been observed in more than half of reported cases.¹⁵ However, our patient did not have a familial history of PAM or any other pulmonary disorders. His previous lab tests and chest roentgenograms showed a normal pulmonary condition before the exposure to mustard gas. His symptoms and roentgenographic changes appeared after the exposure to mustard

gas. The pattern observed in his chest x-ray consisted of disseminated uniform fine radio-opaque nodules. Our initial diagnosis was miliary tuberculosis as the radiologic pattern is somewhat similar.¹¹⁻¹⁴ However, as the patient did not have other features of tuberculosis, the diagnosis of microlithiasis was suggested and then confirmed by lung biopsy. The diagnosis of microlithiasis can be confirmed by bronchoalveolar lavage (BAL) or lung biopsy.^{13,14}

It is notable that a miliary pattern on chest roentgenograms may be seen in disseminated tuberculosis, fungal infection, neoplastic processes, sarcoidosis, pneumoconiosis, hemosiderosis, amyloidosis and metastatic pulmonary calcification associated with chronic renal failure and hemodialysis.^{3,14} These diseases, however, are usually associated with severe respiratory symptoms, whereas the peculiar feature of PAM is its asymptomatic nature and the paucity of physical signs, which are difficult to correlate with the gross roentgenographic abnormality.^{15,16}

For treatment of pulmonary microlithiasis, the use of diphosphonate to reduce calcium phosphate precipitation in pulmonary alveolus is suggested.¹⁻¹⁷ This treatment would have induced only a trivial improvement in the x-ray pattern without any improvement in the evaluative course of the disease.³⁻¹⁶ The use of steroids is ineffective and the use of therapeutic bronchoalveolar lavage fluid (BAL) is controversial.¹⁻¹⁹ There are reports of lung transplantation for end-stage lung diseases.^{13,19}

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