what's your diagnosis?

A 32-year-old male with progressive pulmonary symptoms and disseminated small radio-opacities throughout both lung fields

Mohammad A. Rajabi

From the Department of Surgery, Isfahan University of Medical Science, Isfahan, Iran

Correspondence and reprints: Mohammad Ali Rajabi, MD · Associate Professor of Surgery, Isfahan University of Medical Science Sofe St. Al Zahra Hospital · PO Box 901 Isfahan, Iran · T: +983-11-668-7611 F: +983-11-668 7611 · rajabi@med.mui.ac.ir · Accepted for publication January 2008

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A 32-year-old man who suffered from repeated periods of fever, dizziness and increasing respiratory symptoms was admitted to Shariati General Hospital of Isfahan in December 1993. He had a history of recurrent febrile lower respiratory infection. He also had a history of exposure to mustard gas in 1988, during the Iraq-Iran war. There were no hereditary respiratory diseases in his family. His entire medical record, including chest x-rays and laboratory tests before 1988 were normal.

After exposure to mustard gas, the patient had dermatitis and conjunctivitis, cheilitis and pneumonitis, which healed after about 2 months but the patient had progressive respiratory complications including productive cough, dyspnea and repeated periods of pneumonia. Asthmatic-like symptoms and signs continued but were relatively controlled through corticosteroid therapy. The patient needed to be hospitalized 2 to

3 times a year. In the first 3 to 4 years of the disease course the patient had no cyanosis or clubbing of the fingers, but later he manifested cyanosis and clubbing and in the last 4 months of his life he experienced orthopnea. In the fifth year following mustard gas exposure the patient's chest x-ray revealed remarkably uniform opacification of both lungs produced by disseminated, very fine sand-like, discrete radio-opaque micro-nodules of almost equal sizes throughout both lungs; thus the lungs appeared to be sprinkled with sand, predominantly in the lower zones. Apical bullae were present on both sides (Figure 1). Routine lab tests including complete blood count, erythrocyte sedimentation rate, blood urea nitrogen, blood sugar and urinalysis exhibited normal values; however, a certain tendency to polycythemia in the hemogram was detected. Spirometry showed a severe restrictive pattern consistent with an end-stage pulmonary condition: forced

Figure 1. Chest x-ray showing dense micronodular pattern.

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vital capacity (FVC) was 49% (2.23 L), forced expiratory volume in one second (FEV_1) was 53% (2.08 L) and FEV_1/FVC was 93.1%. On rigid bronchoscopy, there was no tumor, mass or signs of tuberculosis, but there was mucosal atrophy and areas of edema without any specific findings in bronchial biopsy and in lavage fluid examination. The patient was treated with diphosphonates, bronchodilators, glucocorticoids and bronchoalveolar lavage, but his condition deteriorated over the next several months and he died in November

2001 due to cardiopulmonary failure.

- What is your diagnosis?
- What do you think of the efficacy of the suggested treatment?

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errata

Volume 28; Issue 3 (May/June 2008) - In the article entitled "Lichen scrofulosorum in a Saudi adolescent with multifocal tuberculosis", the following errors appeared:

On page 213, the author's name should have been Mushira A. Enani. The unit for leukocyte count "a leukocyte count of $8.7 \times 10^9/dL$ " should have read $8.7 \times 10^9/L$. The unit for erythrocyte sedimentation rate should have read mm/h. The reference ranges for each laboratory parameter are as follows: leukocytes (normal range, $4.0-11.0 \times 10^9/L$), hemoglobin (normal range, 11.5-16.5 g/dL), platelets (normal range, $150-450 \times 10^9/L$), erythrocyte sedimentation rate (normal range, 0-15 mm/h)

On page 215, the last sentence of the first full paragraph should have read: In a prospective study from India with 402 patients and conducted over 20 years, Kumar and Muralihar found that lupus vulgaris was the commonest (55%), followed by scrofuloderma (26.8%), tuberculids (6.8%), TB verrucosa cutis (6%) and TB gumma (5.4%).⁹ In the next paragraph, reference 11 should have been 10, and reference 12 should have been 11.

On page 216, reference 10 should have read: McKee PH. Infectious Diseases: Tuberculids. In: Pathology of the Skin with Clinical Correlations (2nd edition.), Mosby-Wolfe, London (1996), pp. 4.1-4.91.

what's your diagnosis?

Diagnosis: Pulmonary alveolar microlithiasis after exposure to mustard gas

Mohammad A. Rajabi

From the Department of Surgery, Isfahan University of Medical Science, Isfahan, Iran

Correspondence and reprints: Mohammad Ali Rajabi, MD · Associate Professor of Surgery, Isfahan University of Medical Science Sofe St. Al Zahra Hospital · PO Box 901 Isfahan, Iran · T: +983-11-668-7611 F: +983-11-668 7611 · rajabi@med.mui.ac.ir · Accepted for publication January 2008

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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.

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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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