Case Report

Mica-associated Pulmonary Interstitial Fibrosis[1,2]

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SUMMARY We present the clinical and biopsy findings of a 63-yr-old white male with interstitial pulmonary fibrosis and a long history of extensive exposure to mica while working in the rubber industry. The patient presented 30 yr after the initial exposure with complaints of progressive shortness of breath and a chronic nonproductive cough. Pulmonary function testing revealed restrictive lung function with a mild reduction in the total lung capacity (80% of predicted) and a moderate-to-severe reduction in the diffusing capacity of carbon monoxide (50% of predicted). The chest radiogram and high-resolution chest CT scan showed diffuse fibrosis and focal honeycombing involving the upper and lower lung zones bilaterally. Bronchoalveolar lavage revealed 20% neutrophils in the lavage fluid with abundant rectangular flaking crystals. Open-lung biopsy exhibited extensive fibrosis and architectural remodeling with abundant sheets and fragments of engulfed polarizable crystalline material. Energy-dispersive spectroscopy and electron diffraction studies confirmed the material to have the features of mica. Asbestos and other silicates were not identified. The documentation of prolonged exposure to mica, the clinical and radiographic features of severe interstitial fibrosis, and the histopathologic delineation of the interstitial lesion, including spectroscopic and crystallographic verification of crystalline mica, support the causal relationship between mica and interstitial fibrosis.

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Introduction

There are few well-documented reports describing the clinical and pathologic features of interstitial fibrosis associated with mica inhalation (1-4). Only six previous cases of mica-associated interstitial fibrosis are documented histologically. The relation of mica to pulmonary interstitial fibrosis has been the subject of a number of experimental and epidemiologic studies (5-11). However, the fibrogenic properties of pure mica exposure remain unresolved (3, 4).

Mica is a group of silicates with unique physical properties yielding sheetlike crystals. Exposure to mica dust occurs in various industries and was cited as a potential occupational health hazard as early as 1932. Some of the earlier studies of groups of workers exposed to inhaled mica dust offer incomplete or imprecise characterization of occupational exposure, however, often with confounding accompanying exposure to other fibrogenic agents (12-15).

We report an individual with severe interstitial fibrosis who had extensive exposure to mica while working in the rubber industry. Elemental and crystallographic analysis indicate that mica is present in the alveoli and lung parenchyma, suggesting that mica is the likely fibrogenic agent in this particular patient.

Case Report

The patient is a 65-yr-old, never smoking, white male who developed mild dyspnea in 1968 but continued to work relatively free of symptoms until 1986, when he was 62 yr of age. Following retirement, the patient noted that he was more breathless than expected with exertion. This dyspnea slowly progressed, and he developed a dry bothersome cough. In mid-1988, he realized that he became dyspneic while walking up a flight of steps. A chest radiograph in January 1989 revealed marked interstitial fibrosis involving the upper and lower lobes with more extensive disease in the right lung. Be-

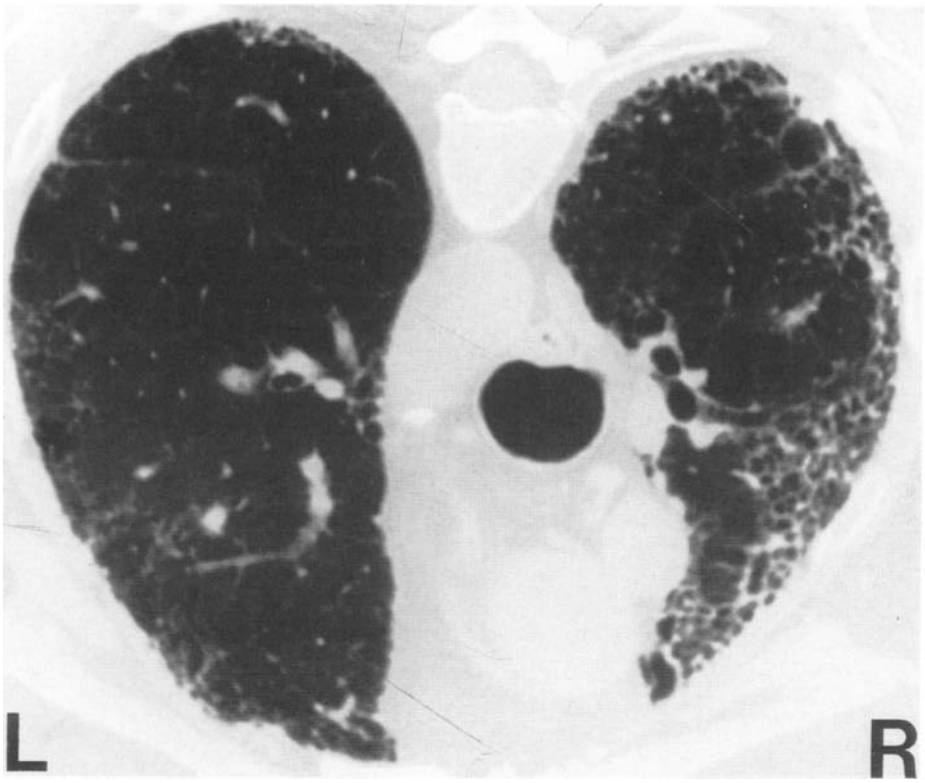

Fig. 1. High-resolution chest CT exhibits architectural remodeling and "honeycomb" change, especially in the right lung.

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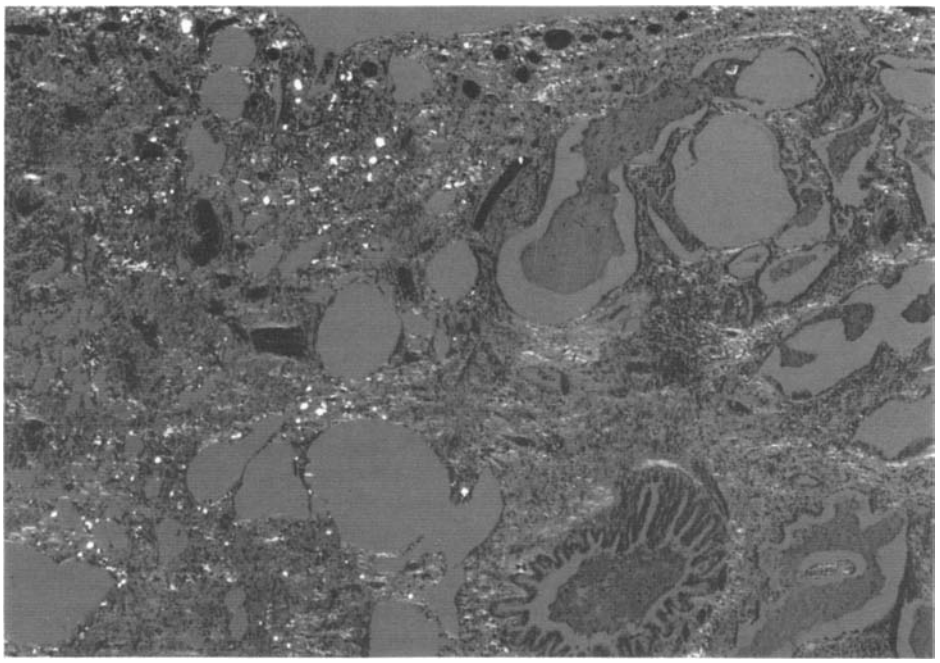


Fig. 2. The open-lung wedge biopsy exhibits architectural remodeling with very large, often debris-filled airspaces yielding a honeycombed appearance. The large airspaces are intermixed with dense and fibrotic scarred parenchyma. Polarizable crystalline mica fragments (bright, white granules and fragments) are densely deposited and spatially associated with the regions of fibrous scarring. The morphologic features reflect the radiographic findings. (Hematoxylin and eosin; ×10; polarized light microscopy.)

cause of his occupational exposures, he was referred to the Occupational Medicine Clinic at the University of Iowa for further evaluation.

The patient worked in a rubber manufacturing plant for approximately 40 yr (1946–1986). Between 1946 and 1951, he worked in the core department, where he was exposed to mica dust, process oils, carbon black, and "blowing agents." During this period, he reports shoveling mica into the Banbury mixing chambers and being exposed to visible clouds of mica dust. From 1951 to 1968 he worked in the maintenance department, where he was exposed to the preceding agents and to urethane foam manufacturing, including toluene diisocyanate (TDI). He developed some mild dyspnea and wheezing in 1968 and was transferred to the engineering department, where he worked until his retirement in 1986.

The physical examination revealed a well-developed, well-nourished male in no acute distress who had a respiratory rate of 20 and was not using his accessory respiratory muscles. He had bibasilar late inspiratory rales but showed no signs of right heart failure and did not have clubbing. A chest X-ray confirmed the presence of diffuse interstitial lung disease, and pulmonary function tests revealed mild restrictive lung function (TLC = 77% of predicted, residual volume [VR] = 69% of predicted, and FVC = 73% of predicted) and a prominent reduction in carbon monoxide diffusing capacity (65% of predicted). A high-resolution chest computed tomographic (CT) scan (figure 1) demonstrated an interstitial fibrotic process and peripheral honeycombing that was more prominent on the right side. A bronchoscopy was notable for normal airway anatomy, an increase in lavage neutrophils (20%), and nondiagnostic transbronchial biopsies.

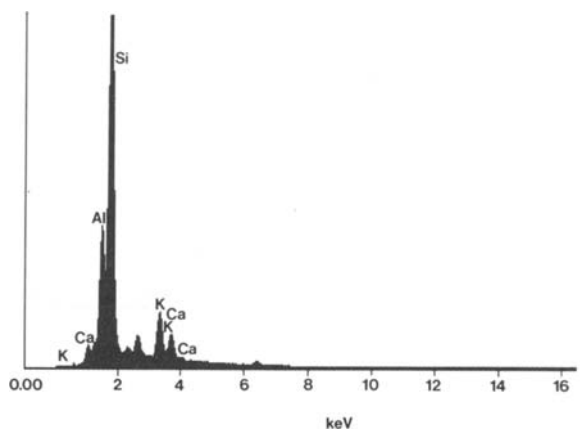


Fig. 3. The spectrum represents the relative numbers of X-rays emitted from the crystal as it was probed by the electron beam (the various peaks) plotted against the energies of the same, emitted X-rays. Spectral analysis confirms characteristic "peaks" representing silicon (Si), aluminum (Al), potassium (K), and calcium (Ca).

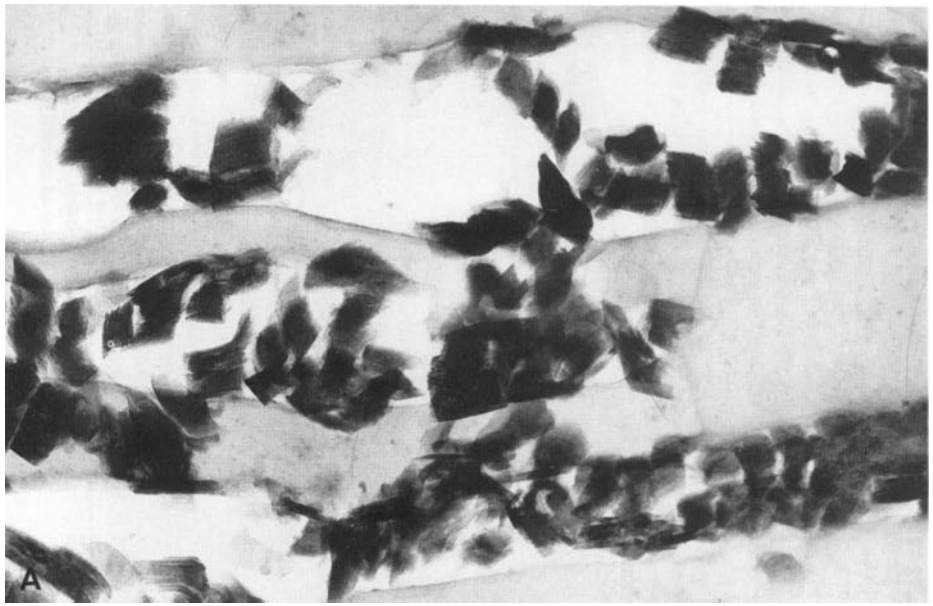
An open-lung biopsy was performed and exhibited extensive interstitial fibrosis and architectural remodeling (figure 2). There was abundant polarizable crystalline material, much of it engulfed within individual histiocytes (rarely within giant cells), often appearing as multiple crystalline sheets or partially disrupted, "flaking" laminar plates. The crystalline material was often present in two or more parallel sheets. No ferruginous bodies were identified, and no polarizable silica component distinct from the laminar material was evident. A small amount of anthracotic pigment was present. Individual crystals were examined by scanning electron microscopy, and energy-dispersive spectroscopy exhibited the spatial features and elemental composition of mica (figure 3). Electron diffraction analysis (figure 4) was performed, and the data indicated the interplanar distances and angles expected of mica (muscovite). Review of the cytospin preparation from the bronchoalveolar lavage demonstrated similar polarizable crystals (figure 5) within alveolar macrophages.

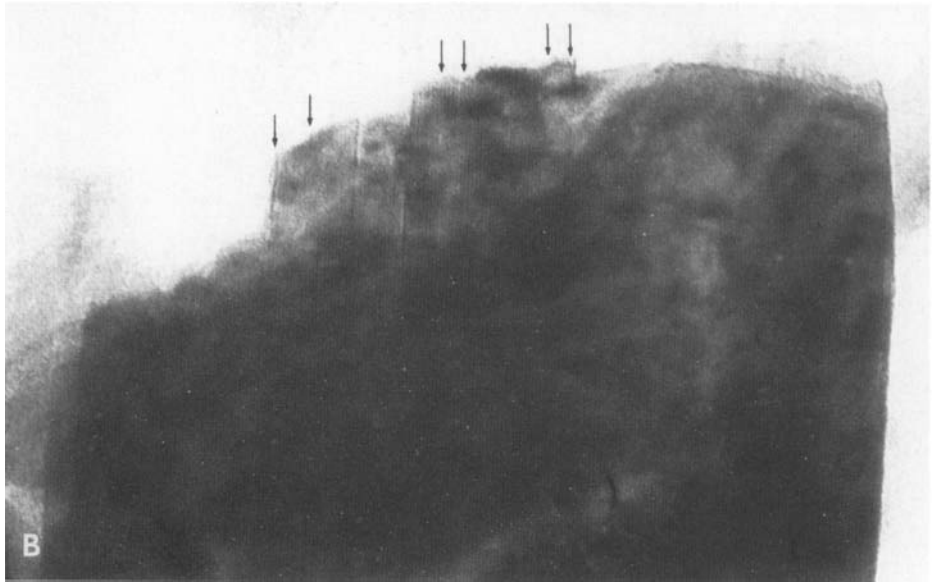
Although his lung volumes have remained stable during the follow-up 2-yr interval, he has experienced a progressive decline in his diffusing capacity and has become increasingly dyspneic. In fact, because of these changes, he was placed on corticosteroids (60 mg prednisone every day) for 3 months in the first 6 months of follow-up. This treatment had no effect on his symptoms or lung function, however. At a clinic visit in March 1990 his oxygen saturation was found to decrease from 92 to 80% with walking on level ground, and he was placed on supplemental oxygen.

Discussion

It is necessary to carefully document cases of mica-associated pulmonary interstitial fibrosis, excluding those cases in which coincidental exposures confound the putative association of mica inhalation and disease. The chronic exposures and long latency associated with development of disease in these patients suggest that mica is not as fibrogenic as other pneumoconiotic agents. On the other hand, the few well-documented cases of "pure" mica exposure indicate that mica is not harmless. An exposure sufficient to produce serious pulmonary fibrosis can predate the appearance of even early clinical signs and symptoms.

Our report represents an additional case with carefully investigated occupational and environmental exposure history, documentation of radiographic and physiologic data, description of bronchoalveolar lavage findings, and presentation of anatomic features. This patient had a protracted course of mica inhalation and was not exposed to other established fibrogenic agents. The increased numbers of neutrophils, macrophages, and polarizable, platelike, intracellular mica crystals in the bronchoalveolar lavage specimen suggest this technique may be a useful screening tool in similar cases. The biopsy exhibited extensive interstitial fibrosis and architectural remodeling with spatial association of heavy mica deposition in regions of dense fibrosis. The markedly asymmetric distribution of the interstitial fibrosis lends further support that it was caused by an environmen-





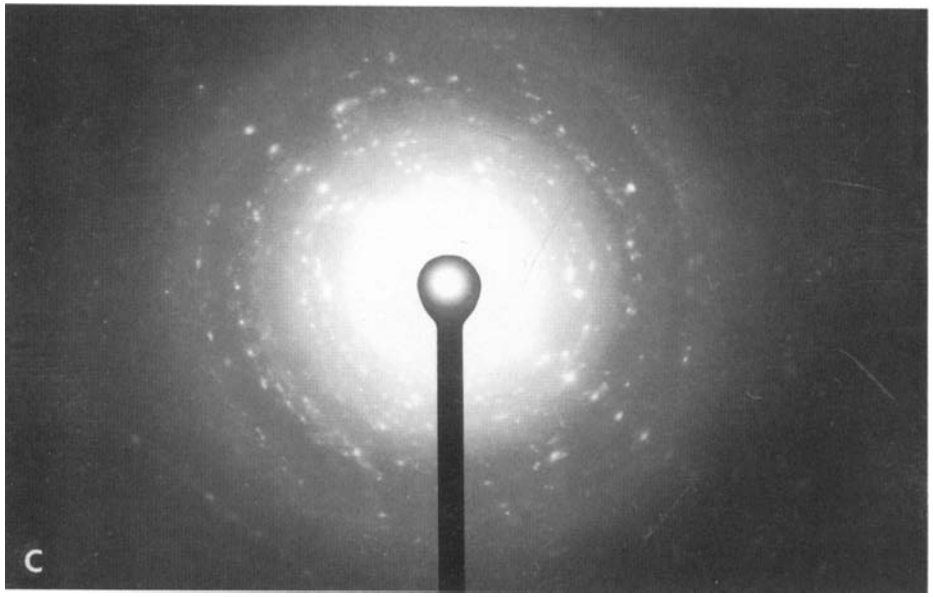


Fig. 4. Transmission electron microscopy allows observation of "individual" fragments of mica that at high magnification (*A*, ×45,000) appear as flaking sheets or shelves of crystalline material. Individual layers of atoms are represented (*B*) by the image of the parallel lines (×230,000; *arrows*) with interplanar spacing of approximately 10 Å. The electron beam diffraction patterns (*C*) generated by the various mica crystals yield data consistent with and confirmatory of muscovite.

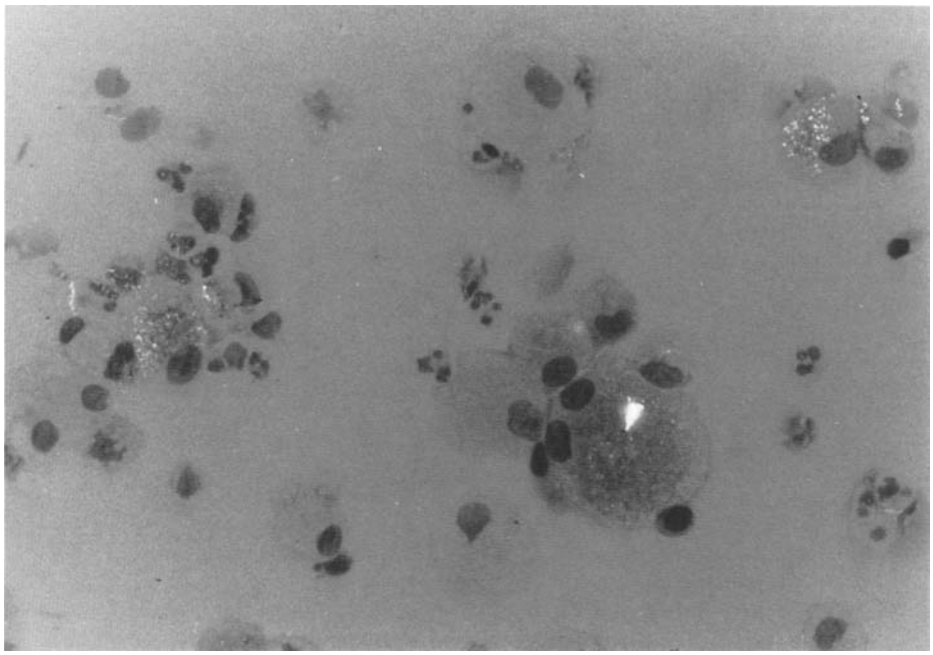


Fig. 5. The bronchoalveolar lavage contained numerous neutrophils as well as polarizable mica crystals within macrophages (bright, white material, ×75).

tal agent. The predominance of right lung involvement may be due to tracheobronchial geometry or asymmetric diaphragmatic excursion.

There remains a theoretical possibility that small quantities of other fibrogenic silicates, masked by the abundance of mica, are responsible for the genesis of interstitial lung disease in such patients. This would be testable by experimental studies employing stringently tested, pure mica chronic exposure or dosing and long-term observation. Resolution of this issue would clarify whether mica-associated lung disease is, as it appears, a specific pathologic entity or merely a reaction to other fibrogenic silicates in "dirty" mica.

The pathogenicity of mica and the demonstration of a cause-and-effect relationship between mica inhalation and interstitial lung disease remains controversial. Clearly, one could argue that this case is consistent with idiopathic pulmonary fibrosis. However, documentation of prolonged exposure to mica, characterization of the clinical and radiographic features of severe interstitial fibrosis, and the histopathologic delineation of the interstitial lesion (including spectroscopic and crystallographic verification of mica) provide evidence in this case for a causal relationship between mica and interstitial pulmonary fibrosis.

References

1. Davies D, Cotton R. Mica pneumoconiosis. Br J Ind Med 1983; 40:22-7.
2. Lapenas DJ, Davis GS, Gale PN, Brody AR. Mineral dusts as etiologic agents in pulmonary fibrosis: the diagnostic role of analytical scanning electron microscopy. Am J Clin Pathol 1982; 78:701-6.
3. Pimentel JC, Menezes AP. Pulmonary and hepatic granulomatous disorders due to the inhalation of cement and mica dusts. Thorax 1978; 33:219-27.
4. Skulberg KR, Glyseth B, Skaug V, Hanoa R. Mica pneumoconiosis—a literature review. Scand J Work Environ Health 1985; 11:65-74.
5. LeBouffant L, Daniel H, Martin JC. The value and limits of the relationship between cytotoxicity and fibrogenicity of various mineral dusts. In: Brown RC, Chamberlain M, Davies R, Gormley IP, eds. The in vitro effect of mineral dust. London: Academic Press, 1980; 333-8.
6. Brambilla C, Abraham J, Brambilla E, Benirschke K, Bloor C. Comparative pathology of silicate pneumoconiosis. Am J Pathol 1979; 96:149-70.
7. Goldstein B, Rendall REG. The relative toxicities of the main classes of minerals. In: Shapiro HA, ed. Pneumonoconiosis: proceedings of the international conference, Johannesburg. London: Oxford University Press, 1970; 429-34.
8. King EJ, Gilchrist M, Rae MV. Tissue reaction to sericite and shale dusts treated with hydrochloric acid: an experimental investigation on the lungs of rats. J Pathol Bacteriol 1947; 59:324-7.
9. Lemon WS, Higgins GM. The tissue reactions of the lung to the intratracheal injection of particulate sericite. Am Rev Tuberc 1935; 32:243-56.
10. Policard A. The action of mica dust on pulmonary tissue. J Ind Hyg 1934; 16:160-4.
11. Shanker R, Sahu AP, Dogra RKS, Zaidi SH. Effect of intratracheal injection of mica dust on the lymph nodes of guinea pigs. Toxicology 1975; 5:193-9.
12. Middleton EL. Industrial pulmonary disease due to the inhalation of dust with special reference to silicosis. Lancet 1936; 2:59-64.
13. Smith AR. Pleural calcification resulting from exposure to certain dusts. Am J Roentgenol 1952; 67:375-82.
14. Heimann H, Moskowitz S, Iyer CRH, Gupta MN, Mankiker NS. Silicosis in mica mining in Bihar, India. Arch Ind Hyg Occup Med 1953; 8: 420-35.
15. Heimann H, Moskowitz S, Iyer CRH, Gupta MN, Mankiker NS. Note on mica dust inhalation. Arch Ind Hyg Occup Med 1953; 8:521-32.