Acute Silicosis Responding to Corticosteroid Therapy*

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The course of acute silicosis usually is relentlessly progressive. Death results from cor pulmonale and respiratory failure, with mycobacterial infection a frequent serious complication. Attempts to treat the illness generally have been unavailing. We report an unusual case of acute silicosis in which improvement in clinical status, chest x-ray film findings and pulmonary function occurred following therapy with corticosteroids. To our knowledge, this is the first such case reported in the medical literature.

(Chest 1992; 101:366-70)

Dco = diffusing capacity for CO; FEV_1 = forced expiratory volume in 1 s; FRC = functional residual capacity; FVC = forced vital capacity; PAS = periodic acid-Schiff; PMA = phorbol-12-myristate-13-acetate; PMNs = polymorphonuclear leukocytes; RV = residual volume; TLC = total lung capacity; VC = vital capacity

The risk of developing silicosis in underground coal miners, tunnel workers and some foundry workers is well-known. These persons generally develop the classic form of the disease over a prolonged period of time. Workers involved in abrasive blasting of bridges and those polishing tombstones have been reported to develop an acute form of silicosis within a few years of commencing exposure. Not well-appreciated is the potential for development of acute silicosis among drillers at surface coal mines. We report the case of a 33-year-old man who worked primarily at surface drilling, developed acute silicosis within three years of beginning exposure, and who initially responded dramatically to corticosteroid therapy.

Case Report

The patient is a 33-year-old white man who worked as a rock driller at a quarry and also at surface coal mines in western Pennsylvania since 1975. Prior to 1983, much of his work was done with a wet process in which water was applied to reduce dust generation. After 1983 he worked primarily as a driller at a surface coal mine using a dry process. He never wore a respirator. He described the dust as being so dense that he "couldn't see anything." In August 1986, he presented to his local physician with a complaint of pleuritic chest pain and shortness of breath. A chest x-ray film was obtained showing only a few p and q opacities. He continued working and these symptoms subsided, but the patient noted the onset of progressive weight loss. By May 1987, he had lost approximately 50 lb. In addition, he suffered profound malaise, dyspnea, migratory chest pain and arthralgia, fevers and drenching night sweats.

A course of erythromycin therapy given in the hospital resulted in only fleeting improvement. Studies for Legionella and Mycoplasma infections were negative, as was a tuberculin skin test. The patient was transferred to Allegheny General Hospital in Pittsburgh on June 4, 1987.

There was no history of serious medical illness, including tuberculosis. The patient admitted to smoking between 1 and 1½ packages of cigarettes daily for 2½ years prior to May 1987 when he stopped smoking. He denied intravenous drug abuse, homosexual activity or receiving transfusions of blood or blood products.

On physical examination the patient was a thin, febrile white man who appeared chronically ill. Bilateral axillary and cervical lymphadenopathy was present. Chest examination showed restricted expansion and bilateral crackles. Examination of the heart and abdomen disclosed no abnormalities.

Laboratory studies, including blood counts, serum chemistry studies, complement levels, protein electrophoresis and cryoglobulin determinations were all nondiagnostic. Initial pulmonary function studies shown in Table 1 were consistent with severe restriction. The diffusion capacity also was severely reduced, but in proportion to the reduced alveolar volume.

Figure 1 shows a chest x-ray film obtained upon the patient's admission to Allegheny General Hospital. Diffuse nodular infiltrates of q and r size were present in both lung fields. In addition, the base of the left lung contained a small alveolar infiltrate.

Bronchoscopy with transbronchial lung biopsy and later open-lung biopsy were performed. Microscopic examination of the biopsy specimens revealed interstitial inflammation and fibrosis without granulomas. Early silicotic nodules were evident. Birefringent needle-like particles were seen within macrophages, consistent with the appearance of silica particles (Fig 2). A cervical lymph node biopsy was performed and revealed only reactive hyperplasia. No birefringent particles or granulomas were seen in the cervical node tissue. Routine microbiologic studies, acid-fast and fungal studies failed to disclose any infecting microorganisms.

An open-lung biopsy was performed, with multiple specimens obtained from the lingula and left lower lobe. Microscopic examination again revealed interstitial inflammation and fibrosis. Early silicotic nodules and birefringent intracellular and extracellular needle-like particles consistent with silica were seen. No granulomas were seen. Periodic acid-Schiff stains were focally positive in some of the alveolar spaces where hemotoxylin-eosin staining showed granular eosinophilic material (Fig 3). Electron microscopic examination of this tissue revealed needle-shaped and polyhedral intracytoplasmic fragments within macrophages consistent with the appearance of silica particles.

Postoperatively the patient began receiving high-dose corticosteroids intravenously for several days and then prednisone orally. He

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Manuscript received August 17; revision accepted May 14.
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Table 1—*Pulmonary Function Tests*

	Allegheny General Hospital		West Virginia University Hospital		
Tests	6/9/87	8/5/87	9/14/87	12/1/87	2/2/90
FVC (% predicted) L	1.35 (25)	2.48 (47)	3.36 (62)	3.66 (67)	2.84 (53)
FEV_1 (% predicted) L	1.28 (30)	2.29 (56)	2.89 (68)	3.09 (73)	2.45 (59)
FEV_1/FVC	95%	92%	86%	84%	86%
TLC (% predicted) L	2.88 (40)	. . .	. . .	. . .	3.10 (43)
VC (% predicted) L	1.64 (31)	2.51 (47)	. . .	. . .	2.79 (52)
FRC (% predicted) L	1.95 (46)	. . .	. . .	. . .	2.19 (53)
RV (% predicted) L	1.24 (64)	. . .	. . .	. . .	0.31 (16)
Dco ml/min/mm Hg	10.2 (30)	18.0 (53)	21.0 (61)	19.5 (56)	17.8 (53)
Kco units	4.53 (81)	5.38 (97)	5.12 (92)	4.39 (79)	4.93 (90)
Therapy					
Prednisone	60 mg/day	40 mg/day	⟶	20-10 mg/day	None
Isoniazid	300 mg/day	None			
Rifampin	600 mg/day	None			

Numbers in parentheses are % predicted values.

also received isoniazid and rifampin until reports from acid-fast cultures were confirmed negative. On this regimen the patient defervesced, experienced subjective improvement and was discharged.

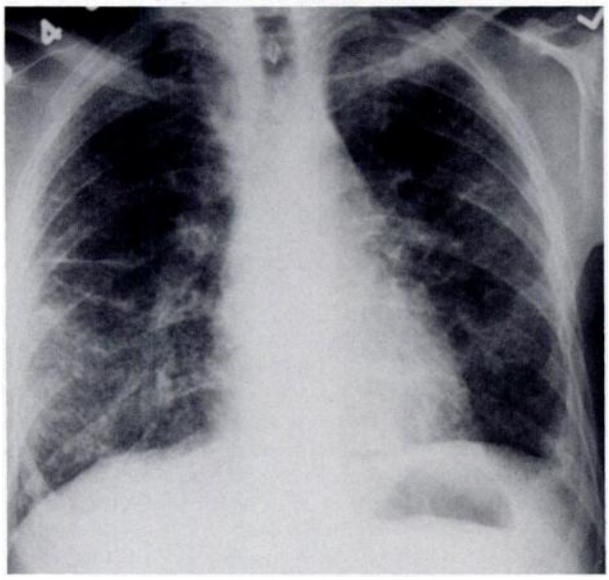

FIGURE 1. Chest radiograph of June 4, 1987, shows diffuse, nodular infiltrates of q and r size and an alveolar density at left base.

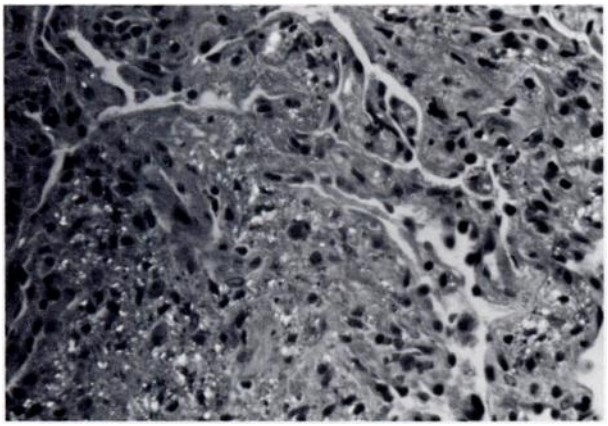

FIGURE 2. Transbronchial biopsy demonstrates birefringent particles observed with polarized light within nodules and interalveolar septae (hematoxylin and eosin, original magnification ×3,000).

He was seen again at Allegheny General Hospital on August 5, 1987, and reported enhanced exercise tolerance. Repeat pulmonary function studies (Table 1) showed considerable improvement in lung volumes and diffusion capacity. Therapy was continued with orally administered corticosteroids at a reduced dosage.

He was seen by the Pulmonary Service at West Virginia University Hospital on September 14, 1987. He reported continued subjective well-being and a weight gain of approximately 25 lb. Physical examination revealed clear lung fields. Repeat pulmonary function testing showed a further improvement in lung volumes and diffusion capacity (Table 1).

Of particular interest is the sequence of changes noted in the

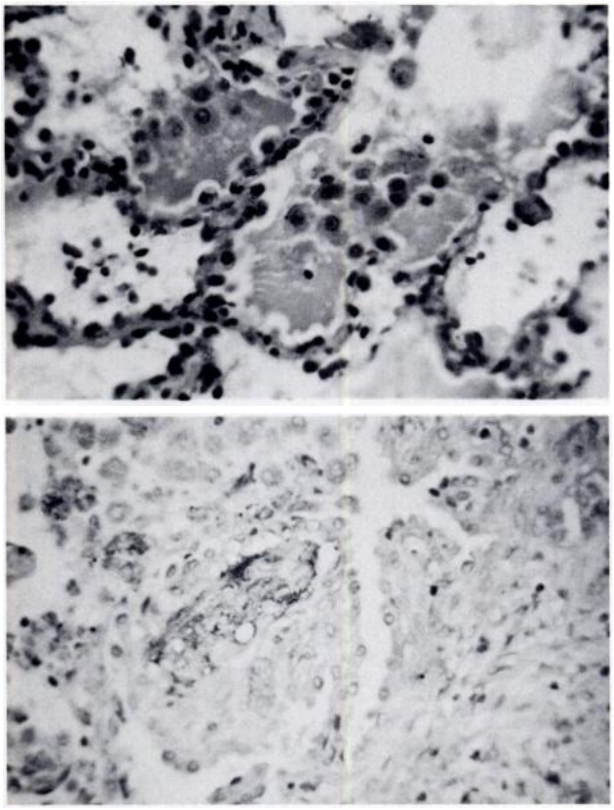

FIGURE 3. *Top,* Open-lung biopsy specimen shows granular eosinophilic material in alveolar spaces. Chematoxylin and eosin, original magnification ×3,000). *Bottom,* Open-lung biopsy specimen shows PAS-positive staining of the granular eosinophilic intra-alveolar material (original magnification ×3,000).

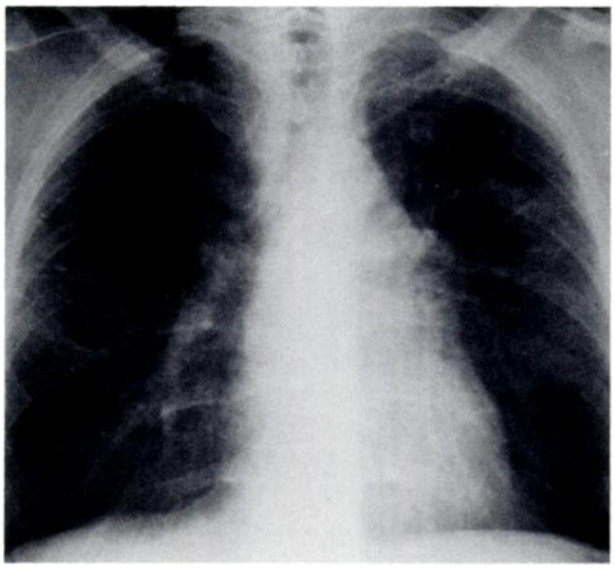

FIGURE 4. Chest radiograph of September 14, 1987, after three months of corticosteroid therapy, demonstrates marked reduction in nodule size and profusion as well as clearing of the basal alveolar infiltrate.

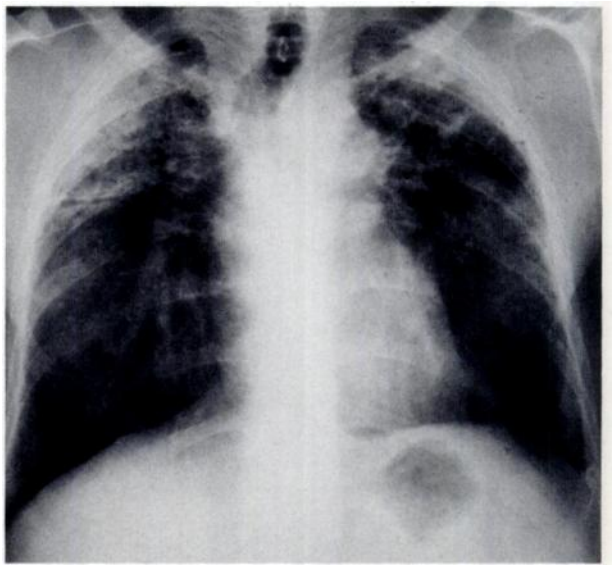

FIGURE 5. Chest radiograph of February 1990, shows the appearance of large masses in the upper zones consistent with complicated silicosis.

patient's chest x-ray films. On August 19, 1986, a year before the onset of acute illness, only a few p- and q-sized nodules were present, with profusion of 1/0 observed in the mid-zones. On the film of June 4, 1987, obtained at the height of his illness, the nodulation was primarily q but r opacities also were seen. The profusion increased dramatically to 3/3 observed in all zones. By September 14, 1987, after three months of steroid therapy, the nodulation was markedly reduced. Primarily q and secondarily p opacities were present with r nodules not seen. The profusion was reduced to 2/2. In addition, the left basal infiltrate cleared (Fig 4). Therapy was continued with orally administered prednisone.

To further characterize the inflammatory process involving his lungs, the patient underwent gallium 67 citrate scanning on December 4, 1987. The images obtained at 72 h after injection of radioisotope showed intense uptake diffusely in both lungs with measured target to background radioactivity ratios of 8.7 to 1 for the left lung and 9.7 to 1 for the right lung. These values are far in excess of the ratios normally observed using this method.[1,2]

We performed fiberoptic bronchoscopy with bronchoalveolar lavage. The counting and identification of cells obtained by lavage were performed using an electronic cell counter and sizer as previously described.[3,4] The results are displayed in Table 2. The numbers of lavageable macrophages, lymphocytes and neutrophils were increased by 32, 1,358 and 945 percent, respectively, compared with values observed in nonsmoking non-silica-exposed men of comparable age.[5] Sizing data indicated that the lavage specimen exhibited a high degree of contaminant with a small amount of particulate matter. The identity of these contaminating particles was determined by energy-dispersive x-ray analysis of the lavage supernatant after removal of cells by centrifugation. Analysis of the spectrum of energy emission from the samples indicated that the elemental composition of most of the particles was silicon having an emission of 1.84 kev. Occasionally, particles were observed where silicon was contaminated with aluminum or magnesium.

Table 2 also shows the results of chemiluminescence assays performed to determine the activity of cells obtained from the patient by bronchoalveolar lavage. We measured activity at rest and following stimulation of lavaged cells with either PMA (3×10^{-6}M) or zymosan (2 mg/ml).[6-8] The levels of resting and stimulant-induced chemiluminescence observed were much higher than observed in nonsmoking individuals without histories of occupational dust exposure.[5] Resting, PMA-stimulated and zymosan-stimulated chemiluminescence were increased by 436, 267 and 1,127 percent, respectively, in the patient with silicosis.

The patient was seen again on February 2, 1990. At this time his pulmonary function exhibited a decline from the levels measured two years prior (Table 1). Similarly, the chest radiograph showed large masses in the upper zones consistent with progression to complicated silicosis (Fig 5).

DISCUSSION

The risk of developing silicosis is well-recognized in

Table 2—*Characterization of Bronchoalveolar Lavage**

Group	Macrophages‡	Lymphocytes‡	Neutrophils‡	Resting Chemiluminescence§	PMA-Stimulated Chemiluminescence§	Zymosan-Stimulated Chemiluminescence§
Control†	7.4 ± 1.2	4.5 ± 0.8	2.9 ± 0.7	27.0 ± 6.0	68.2 ± 22.6	41.4 ± 12.4
Silicosis	9.8	65.6	30.3	144.6	250.2	509.0

*Mean volume of lavage return was 140 ml (70 percent of total lavage volume).

†Values are means ± standard errors of data for eight volunteers.

‡Cell counts and differential cell counts were determined using an electronic cell counter with sizing attachment. Cell counts are given as cells $\times 10^6$/subject.

§Total chemiluminescence generated by lavage cells (1.63×10^6 alveolar macrophages/0.6 ml of Hepes-buffered medium in the presence of 1.7 ml percent luminol was measured with a Berthold 9505 luminometer. Chemiluminescence measured in unstimulated cells (resting chemiluminescence) or in the presence of stimulants, *ie*, PMA 3×10^{-6} M), (PMA-stimulated chemiluminescence) or zymosan (2 mg/ml) (zymosan-stimulated chemiluminescence).

association with underground coal mining. A significant but less-appreciated risk exists among surface coal mine drillers as well.[9] We believe the diagnosis of acute silicosis in this case is firmly established. Our patient was exposed to silica dust over a period of 12 years. The temporal relationship of his work to the chest x-ray film changes observed suggests an acute insult superimposed upon a background of milder silica exposure. His course was marked by progressive dyspnea and weight loss and restrictive impairment. He also suffered a hectic phase with fevers and sweats, which are common symptoms in acute silicosis.[10] Lung tissue obtained by transbronchial biopsy and open-lung biopsy showed needle-like birefringent particles. Analysis of lavage supernatant confirmed the presence of silica particles in fluid obtained by bronchoalveolar lavage. Although evidence of infection was carefully sought, no acid-fast, fungal or bacterial organisms were isolated which might explain the clinical findings. The observation of intraalveolar accumulations of macrophages with intracytoplasmic birefringent particles is consistent with silicosis, as is the presence of nodules. The medical literature mentions that typical whorled silicotic nodules may not be observed in acute silicosis,[11,12] and they were not in our patient. The nodules observed here may reflect his prior mild chronic exposure. Noncaseating granulomas suggestive of sarcoidosis or hypersensitivity pneumonitis were not seen in the lung or cervical lymph node specimens.

We are unaware of a previously reported case documenting the efficacy of steroids in the improvement of this disease as evidenced on the chest radiograph and pulmonary function.[13] Xipell et al[14] reported a patient with acute silicoproteinosis in whom "minor behavioral disturbance and intellectual deterioration" improved with corticosteroid therapy. They did not mention observing either radiologic or pulmonary functional improvement. Sharma et al[15] reported significant improvement over three to six months in airway function and possibly alveolitis in patients suffering from simple and complicated chronic silicosis. In our patient we had the opportunity to monitor a therapeutic trial closely over a period of time. We initially observed a dramatic response to this therapy which the patient tolerated with minimal side-effects. However, the most recent pulmonary function tests showed deterioration (Table 1). A recent chest radiograph demonstrated changes consistent with progression to the complicated form of category A silicosis (Fig 5).

The alveolitis in our patient is unusual. The relative proportions of cells recovered are not those typically observed in bronchoalveolar lavage of individuals chronically exposed to silica. Several groups of investigators have reported lavage results from silica-exposed individuals.[16-18] None of these individuals was stated to suffer from acute silicosis. In all of these cases, the preponderant cell was the alveolar macrophage, averaging over half of the total cells recovered. In our patient alveolar macrophages were approximately 9 percent of the total with lymphocytes being the most plentiful cell type. Evidence that silica exposure is associated with a dramatic increase in the number of lymphocytes obtained by bronchoalveolar lavage has been reported in the rat and man.[19,20] Despite the small proportion of alveolar macrophages observed, their state of functional activation was high. Chemiluminescence studies demonstrated excessive oxidant activity at rest with a significant increase after stimulation. In this regard, it is interesting that although steroids are anti-inflammatory, they fail to inhibit chemiluminescence from human phagocytes.[21]

The preponderant cell in this lavage specimen was the lymphocyte (62 percent of total cells) but PMNs were also increased in absolute and relative terms compared with what was found in control subjects.[5] The predominantly lymphocytic alveolitis we observed may be related to the acuteness of our patient's silica exposure. It is possible that the steroid therapy he received prior to lavage modified the alveolitis. It is of interest that at a time when the patient continued to show evidence of alveolitis by gallium scan and bronchoalveolar lavage he had already demonstrated functional improvement with an increase in FEV_1 and FVC of approximately 2 L over values obtained originally. There was also radiologic improvement with decreased nodule size and profusion and clearance of a basal infiltrate. It is possible that the focal material that was PAS-positive on the patient's open-lung biopsy accounted for the appearance of larger nodules and the soft basal infiltrate seen on the x-ray film of the chest on June 4, 1987. If so, the clearing of this material could explain the radiographic improvement seen.

Finally, we note that the improvement with steroid therapy was only transient. By February 1990, both pulmonary function tests and the chest radiograph indicated deterioration in the patient's condition (Table 1, Fig 5) consistent with progression to category A complicated silicosis.

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