A 36-year-old woman presents with dry cough and dyspnea on exertion, which have progressed over the past 2 years. She is dyspneic after climbing two flights of stairs. This surprises her because she was able to run an 8-min mile 2 years ago. She does not have wheezing, fever, chills, weight loss, skin rash, or joint pain, but she does have conjunctival injection. She is a life-long nonsmoker and has no pets. She does not have any history of asbestos exposure and works as a diamond polisher for a large-volume diamond buyer. Physical examination shows mild clubbing, conjunctival injection, and dry crackles bilaterally in the lower third of the lung fields. She does not have hepatosplenomegaly or a skin rash. Her chest radiograph is shown in Figure 1. Pulmonary function tests show FVC of 2.67 L (60% of predicted), FEV₁ of 2.35 L (63% of predicted), and oxygen saturation by pulse oximetry of 93% at rest and 87% after walking 300 feet in 3 min. Bronchoscopy with BAL and transbronchial lung biopsy are performed. A few hours later, the pathologist calls to report bizarre-appearing, multinucleated giant cells with a cell within a cell, or a “cannibalistic” appearance in the BAL specimen (Fig 2). Which of the following diseases is most likely?

A. Chronic beryllium disease
B. Bronchoalveolar carcinoma
C. Desquamative interstitial pneumonitis
D. Hard metal disease
E. Sjögren syndrome

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Answer: D. Hard metal disease

This patient has hard metal disease or cobalt-related interstitial lung disease. The essential elements in making the diagnosis are the appropriate cobalt exposure and the characteristic pathologic findings of giant cell interstitial pneumonia or the discovery of multinucleated “cannibalistic” appearing cells in BAL fluid. This patient is a diamond polisher and uses cobalt-containing tools for diamond polishing. Cobalt is widely used as a hardener and binder in metal alloys of tungsten, aluminum, chrome, and molybdenum. Tungsten carbide, the “hard-metal” that gives this disease its name, is made by mixing minute particles of tungsten, carbon, and up to 25% cobalt, and then sintering the mixture at high temperature to produce an extremely hard and heat-stable alloy. Occupations associated with cobalt-related interstitial lung disease include those associated with the maintenance and resharpeling of hard metal tools, the production of hard metals, diamond tooling (grinding wheels and stone saws), work utilizing cemented tungsten carbide (oil well drilling sites), armored plate production (tanks, naval ships), and the manufacture and maintenance (grinding/polishing) of cutting tools and loops for fishing poles. Figure 3 shows thickening of interalveolar septae with chronic inflammatory cells, consistent with an interstitial process, plus giant multinucleated cells with engulfed inflammatory cells lying within air spaces.

These multinucleated giant cells stain positive for cytokeratin and may represent epithelial cells. Giant cell interstitial pneumonia is almost pathognomonic for hard metal disease. The diagnosis of hard metal disease can be made on BAL findings alone in the presence of an appropriate clinical setting. Giant cells may comprise up to 15% of the BAL cell differential count. Epidemiologic data show that hard metal disease occurs in approximately 5% of exposed workers, with fibrosis seen in < 3%. The pathogenesis of the disease is not worked out but may include a delayed-type hypersensitivity/cell-mediated immune response. The natural history of this disease is variable, and if cobalt exposure continues, progressive fibrosis with respiratory failure may develop. Treatment of hard metal disease is total cessation of cobalt exposure. Although no controlled clinical trials have been reported, patients may respond to oral corticosteroids. Inhaled corticosteroids and cyclophosphamide have also been utilized. Avoidance of oxidant stress may also be important.

Cobalt may also cause occupational asthma, bronchitis, bronchiolitis obliterans-organizing pneumonia, and an acute chemical pneumonitis if there is an acute high-level cobalt exposure. Cobalt is a skin sensitizer, so skin hypersensitivity and conjunctivitis (as in our patient) may be seen. Occupational hygiene is vital in preventing this disease.

Giant cell interstitial pneumonia has not been reported in any of the other conditions listed. For instance, patients with chronic beryllium disease have pathologic findings similar to those of sarcoidosis and have an exposure history to beryllium (nuclear weapons, ceramics, computer parts, and electronic equipment manufacturing in the aerospace industry). Sjögren syndrome may be associated with interstitial pneumonia and interstitial fibrosis, especially if another rheumatic disease is present; however, the pathology findings seen in this case are not consistent with Sjögren syndrome.

**SELECTED READINGS**


