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Worsening Shortness of Breath in a 62-Year-Old Man

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Patient
62-year-old man.

Chief Complaint
Worsening shortness of breath.

History of Present Illness
The patient had experienced worsening shortness of breath (dyspnea) over the past 2 years. Based on clinical and radiographic evidence, it was thought that his shortness of breath was secondary to progressive interstitial lung disease. Therefore, he was referred by his pulmonologist to a thoracic surgeon for video-assisted thoracoscopy with lung biopsy.

Past Medical/Surgical History
The patient had a history of coronary artery disease with myocardial infarction over 10 years ago with no recent history of angina. In addition, he had a history of hypertension, gastroesophageal reflux disease (GERD) with Barrett's esophagus, cholecystectomy, and a lumbar laminectomy. Because of pneumonia, he had been hospitalized 18 months prior to this most recent presentation.

Social History
The patient had been a cigarette smoker, but discontinued smoking after being diagnosed with heart disease. His occupation had subjected him to significant inhalational exposure to graphite dust. There was no history of occupational exposure to any other agents.

Physical Examination
Vital signs: temperature, 98.8ºF; heart rate, 76 beats per minute; respiratory rate, 16 breaths per minute; blood pressure, 142/81 mmHg. The patient was in no acute distress. He had mild rattles with coughing on pulmonary auscultation. The remainder of the physical examination was unremarkable.

Principal Laboratory Findings
Table 1

Results of Additional Diagnostic Procedures and Tests
Preoperative chest radiograph showed increased interstitial markings, consistent with interstitial lung disease (**Image 1**). Compared to previous radiographic findings, these radiographic changes had become more prominent over the past 2 years. Electrocardiogram (ECG) showed a normal sinus rhythm with a heart rate of 89 beats per minute, and was unchanged from past ECGs. Video-assisted thoracoscopic biopsy of the right lung showed interstitial fibrosis and emphysema as well as abundant black pigment within macrophages and multinucleated giant cells (**Images 2 and 3**). No polarizable material suggestive of silica was identified in these cells, nor was there evidence of neoplasm, granulomatous disease, vasculitis, viral cytopathic effect, or the presence of microorganisms. Microbiological culture studies performed on lung tissue were negative.

Questions:

1. What are this patient's most striking clinical, laboratory, and radiographic findings?
2. What purpose does video-assisted thorascopic lung biopsy serve in a patient with this constellation of findings?
3. What disease category does this patient's radiographic and biopsy findings suggest?
4. What is this patient's most likely diagnosis?
5. What are the most common signs, symptoms, laboratory, and radiographic features associated with this patient's condition?
6. What are the most appropriate treatment and follow-up for this patient?

Possible Answers:

1. Progressive shortness of breath, rattles with coughing, worsening features of interstitial lung disease on chest radiograph, and decreased oxygen saturation (SaO_2). This patient's laboratory findings are striking for what they do not show (ie, except for a modestly decreased SaO_2 value, all other laboratory test results shown in **Table 1** are within the "normal" reference interval for these tests).

2. The video-assisted thoracic surgery (VATS) technique has become the standard for obtaining lung biopsy material in patients with interstitial lung disease, since it allows the surgeon to visually inspect the lungs to choose a biopsy from the most likely abnormal area and because it has less morbidity (postoperative pain) and results in a shorter hospital stay than more invasive surgical procedures.[1] Interstitial lung disease refers to the presence of inflammation, fibrosis, or both between the tiny air spaces or alveoli of the lungs (the area known as the pulmonary interstitium), causing a distortion of the normal pulmonary microarchitecture.[2] The damage to the pulmonary microarchitecture can be secondary to a wide variety of chronic and acute conditions, including infection, neoplasm, drug reaction, occupational exposure, sarcoidosis, collagen vascular disease (such as rheumatoid arthritis), and numerous others.[2] Because conditions of such differing etiology and treatment implications can cause similar clinical and radiographic findings (**Image 1**), surgical lung biopsy is often necessary to establish or exclude the etiology of these findings.[1]

3. Pneumoconioses. The lung biopsy in this case did not show evidence of an infectious condition, neoplasm, vasculitis, or granulomas such as those seen in patients with sarcoidosis.

Table 1_Principal Laboratory Findings

Test	Patient's Result	"Normal" Reference Range
Hematology		
WBC count	5.0	4.8-10.8 x10^3/μL
RBC count	4.72	4.70-6.10 x10^6/μL
Hemoglobin	14.5	14.0-18.0 g/dL
Platelet count	168	130-400 x10^3/μL
Coagulation		
PT	12.0	10.9-12.9 sec
INR	1.0	
PTT	27	21-31 sec
Chemistry		
Sodium	139	133-145 mEq/L
Potassium	4.4	3.5-5.0 mEq/L
Chloride	104	96-108 mEq/L
CO_2	24	22-29 mEq/L
BUN	16	6-20 mg/dL
Creatinine	1.1	0.5-1.2 mg/dL
Glucose	118	70-105 mg/dL
Calcium	9.5	8.4-10.2 mg/dL
Total protein	7.7	6.4-8.3 g/dL
Albumin	4.3	3.5-5.0 g/dL
Total bilirubin	0.8	0.0-1.0 mg/dL
ALP	58	40-129 U/L
AST	19	0-37 U/L
ALT	30	0-41 U/L
SaO_2	97%	100%
Microbiology		
Tissue (right lung) culture	No growth	No growth

WBC, white blood cell; RBC, red blood cell; PT, prothrombin time; INR, International Normalized Ratio; PTT, partial thromboplastin time; CO_2, carbon dioxide; BUN, blood urea nitrogen; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; SaO_2, oxygen saturation

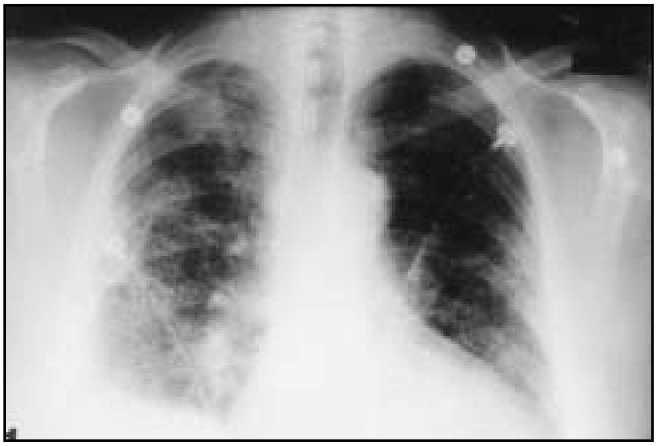

Image 1_Preoperative chest radiograph showing increased white markings in the lungs, especially the right lung, indicative of interstitial lung disease.

The lung biopsy did show interstitial fibrosis and most strikingly, the presence of an extensive amount of dark black pigment within macrophages and multinucleated giant cells (**Images 2 and 3**). These histopathologic features suggest a pneumoconiosis (ie, any nonmalignant chronic lung disease resulting from inhalation and deposition of mineral, metallic, or dust particles in the pulmonary interstitium).[3] The most common environmental agents causing pneumoconiosis are asbestos, silica, and coal,[3] although a variety of other inhaled, dust-borne agents, including forms of carbon other than coal, less commonly cause pneumoconiosis.[4,5] The pneumoconioses are most often seen in the context of occupational lung disorders (ie, any pulmonary disease felt to have been caused by an occupational exposure to any of the aforementioned agents).[4]

4. ***Most likely diagnosis:*** *complicated graphite pneumoconiosis due to occupational exposure to graphite dust.*

As with all of the pneumoconioses, a careful clinical history as to environmental and/or occupational exposure is of paramount importance.[6] In this case, the patient had documented occupational inhalation of graphite dust. Anthracosis, the inhalation and deposition in the lungs of dusts consisting predominantly of carbon, is common in cigarette smokers and those living in urban/industrialized areas. With the exception of the well-known deleterious effects of cigarette smoking, anthracosis due to such environmental exposure generally causes few health problems.[7] Inhaling greater quantities of carbonaceous substances, however, can lead to pulmonary disease, and is often the result of environmental exposure.[7] Although coal miners' pneumoconiosis is the most prevalent occupational exposure-related pulmonary disease due to carbon-based dusts, occupational exposure to other substances such as graphite can less commonly lead to significant health problems.[7] Natural graphite is a crystalline form of carbon which may contain significant quantities of silica.[5,8] Therefore, graphite mining can result in exposure to silica as well as carbonaceous dust.[8] Synthetic graphite is derived from heated coal or coke, and is virtually free of silica.[5,7] Occupational exposure to synthetic graphite (as in the patient presented in this case study) can be seen in the manufacture of steel, lubricants, pencils, electrodes, and other products.[7,8] Millions of workers in the United States may be subject to occupational exposure to natural and synthetic graphite, but the prevalence of pneumoconiosis is probably very low.[8] The pathologic findings are similar in exposure to large amounts of carbon in any form.[7] Simple pneumoconiosis involves deposition of carbon pigment without fibrosis, often as macules scattered throughout the pulmonary parenchyma.[7] Complicated pneumoconiosis (as in the patient presented in this case study) refers to the development of progressive massive fibrosis, defined as a focus of fibrosis and black pigment deposition larger than 1 cm in size.[7]

5. Most patients with graphite pneumoconiosis experience cough, sputum production, and dyspnea, which often worsen as the disease progresses and can lead to right-sided heart failure.[7] On physical examination, the patient may have decreased breath sounds and a few crackles.[7] There are no specific laboratory tests that aid in the diagnosis of graphite pneumoconiosis, although non-specific acute phase reactants such as C-reactive protein (CRP) and fibrinogen may be elevated, hypergammaglobulinemia may be present, and elevated serum rheumatoid factor and antinuclear antibody levels are common.[7] Other laboratory studies may help exclude the many other causes of interstitial lung disease. Radiographic findings vary depending upon the degree of pulmonary damage, and can include small rounded opacities, large nodules, and interstitial fibrosis.[4] Graphite pneumoconiosis is similar clinically and radiographically to coal workers' pneumoconiosis.[5,7,8]

6. There is no specific treatment for pneumoconiosis due to the deposition of carbon dusts.[4] Elimination of the causative agent to avoid further exposure is often helpful, although there can be disease progression even after exposure is eliminated.[3] With progressive massive fibrosis, there is increased risk for

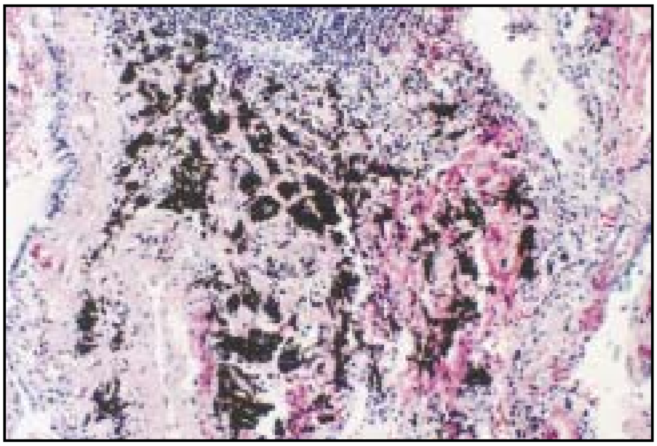

Image 2_Interstitial fibrosis and abundant black pigment [hematoxylin and eosin (H&E) stain, 100x magnification].

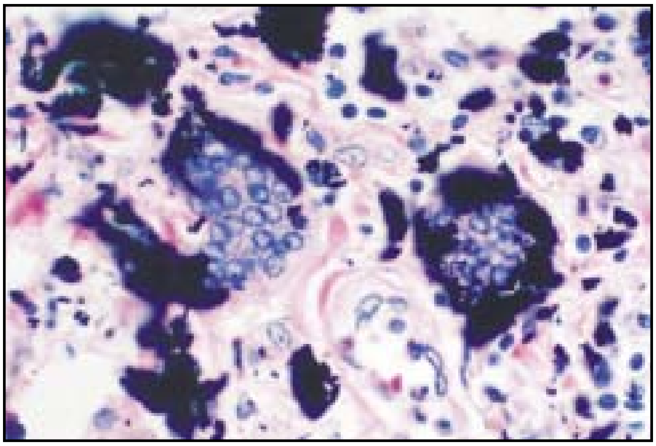

Image 3_Detail of the black pigment, including pigment within the cytoplasm of multinucleated giant cells (H&E stain, 400x magnification).

chronic respiratory failure, possibly requiring use of supplemental oxygen therapy. In addition, some patients with cough and dyspnea associated with airway limitation may benefit from bronchodilator medications, and patients with hyperresponsive airways may benefit from inhaled corticosteroids.[3] Despite such treatments, patients with progressive massive fibrosis have significantly increased mortality.

Patient's Treatment and Course

The patient had already retired from his job at the graphite factory, thereby eliminating the possibility of further graphite exposure. He was discharged home with oxygen therapy and no steroid therapy on the fourth postoperative day following his lung biopsy. He continues to be followed clinically and radiographically, and his disease has remained stable 6 months later.

Keywords

video-assisted thoracoscopy, graphite, pneumoconiosis, interstitial lung disease

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