Cavitary Lung Disease with Skin Lesions*

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A 51-year-old nonsmoking white woman presented with abnormal chest x-ray film findings and skin lesions. Five years earlier, she developed recurrent bouts of productive cough diagnosed as bronchitis and treated with antibiotics. Five months earlier, she developed skin lesions (Fig I) and mild breathlessness. Chest x-ray examination revealed bilateral cavitary lesions and left lung nodules (Fig 2). In addition to her skin lesions, she was noted to have diffuse coarse rhonchi, expiratory wheezing, and a soft systolic murmur. Her hematocrit was 34.5 and urinalysis revealed 1+ proteinuria, trace hematuria, and 10 to 15 WBC and RBC per high power field. A wedge skin biopsy was performed (Fig 3).

The most likely diagnosis is:

a) Wegener’s granulomatosis
b) Sarcoïdosis
c) Tuberculosis
d) Lymphomatoid granulomatosis
e) Lymphoma
f) Goodpasture’s syndrome

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Figure 1. Multiple skin lesions (initially subcutaneous nodules) were present on both lower extremities. Shown are lesions present in the patient’s lower right leg.

Figure 2. Chest radiograph taken at time of presentation. Several nodules are demonstrated in the left lung (arrows) as well as a thin-walled cavitary lesion in the left costophrenic angle. On the right, a large soft tissue density is present in the right middle lobe. A large thick-walled cavitary mass is present in the right lower lobe, and an additional soft tissue mass is within the center of this lesion. A second, smaller mass lesion is present just above the right hemidiaphragm (arrows).

Figure 3. Wedge skin biopsy from a lower extremity lesion.
The answer is d) Lymphomatoid granulomatosis (LYG).

Lymphomatoid granulomatosis is a multisystem disorder of unknown etiology described by Liebow et al. in 1972. The term lymphomatoid granulomatosis (LYG) was coined due to histologic similarities with lymphomas and clinical and roentgenographic relationships to Wegener's granulomatosis. It is characterized by angiitis and granulomatosis, and although it may affect any organ, its hallmark is pulmonary, skin and CNS involvement. Histopathologically, it is a granulomatous process with a polymorphic lymphohistiocytic infiltration which is both angiocentric and angiodestructive in nature. Atypical and occasionally bizarre lymphohistiocytic cells are often seen, often with mitoses. 1,4

Most patients present in the third to sixth decade, although patients from 7 to 85 years old have been reported. There is a male predominance of approximately 1.7:1. Skin involvement in LYG is common with up to 43 percent of patients presenting with skin lesions. 1,2,3 Most common are erythematous, macular, or plaque-like lesions, usually on the extremities; however, subcutaneous nodules can occur as well. Skin biopsy can establish the diagnosis of LYG, although lung biopsy is often required to rule out associated pulmonary lymphoma. Skin lesions usually occur with pulmonary disease but can precede or follow the lung manifestations by months or years. Prognosis is not affected by the presence of skin lesions (ie, similar mortality is noted in patients with and without skin disease).

Pulmonary involvement is almost invariably present, although it can occasionally be asymptomatic. 1,4 Fever and cough (sometimes productive) are the most common presenting features. Other pulmonary symptoms include dyspnea, chest pain (sometimes pleuritic), transient or rarely fatal hemoptysis. Pulmonary function testing usually reveals a restrictive defect with decreased diffusing capacity for carbon monoxide. Chest roentgenogram typically reveals peripheral and lower lung field nodular lesions which cavitate in roughly one third of cases. Massive infiltration with respiratory failure also occurs. Most patients have bilateral nodules, but one fifth have unilateral disease. Up to one third have small pleural effusions and although rare, hilar adenopathy has been reported.

Central nervous system complications occur in up to 30 percent and are characterized by extensive infiltration of the meninges, blood vessels, and parenchyma with mass lesions sometimes described. Peripheral and cranial neuropathies occur as well. CNS LYG disease is a very poor prognostic sign with most patients dying even with immunosuppressive therapy. 1

In contrast to Wegener's granulomatosis, clinical renal disease is uncommon, although histologic evidence of disease is present in 40 percent. Atypical lymphohistiocytic infiltrates with necrosis and angiitis are recognized; however, strikingly absent is glomerulonephritis, with only rare cases reported. Other features include hepatomegaly (seen in 12 percent and carrying a worse prognosis) and lymphatic, splenic and marrow involvement which are less common. Histologic evidence of disease in the heart, adrenal glands, pancreas, and gastrointestinal tract is documented in 7-9 percent of subjects with LYG at necropsy, but clinical manifestations appear to be absent or rare. Other rare manifestations include subcutaneous masses, retroperitoneal fibrosis and bone lesions.

The diagnosis of LYG can be strongly inferred from clinical and radiographic data. Nonetheless, tissue confirmation is necessary to confirm the diagnosis and exclude lymphoma, Wegener's granulomatosis, or an infectious granulomatous disease. Skin biopsy can be diagnostic, but lung biopsy is usually required. Scattered reports suggesting that transbronchial biopsies are useful can be found, but they are rarely definitive. Even with a generous biopsy specimen, LYG can be difficult to diagnose and appropriate cultures of tissue should be taken. Consequently, open lung biopsy is the recommended procedure for establishing the diagnosis and ruling out other processes, especially lymphoma. 8

Overall mortality is roughly 60 percent; however, the clinical course can be extremely variable. Most patients have a relentless downhill course with more than 50 percent dying of respiratory failure, while others have mild disease, do not require therapy, and survive for many years. Bad prognostic features include neurologic involvement and large numbers of atypical lymphohistiocytic cells on biopsy.

No clearly effective treatment has evolved. There are some reports of steroid responsiveness, but long-term remission is unusual. Cytotoxic agents have been used with limited success. The combination of prednisone and Cytoxan has resulted in long-lasting remission in some patients. 7 Malignant lymphoma develops in 10-15 percent of patients and is frequently the cause of death. There are reports of success with radiation therapy for localized lesions; however, the role of radiation therapy has yet to be defined. 3,4

References
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