A 71-year-old white female with a history of chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, and right total knee and hip replacement was admitted with right lower extremity cellulitis. A right lower extremity Doppler examination was negative. Administration of cefazolin produced improvement of the cellulitis. The patient complained of shortness of breath and a nonproductive cough. She was evaluated by a pulmonologist for intermittent hypoxia despite a clear chest radiograph. A ventilation-perfusion scan was negative, and the shortness of breath, hypoxia, and cough were attributed to COPD. Chest computed tomography (CT) demonstrated emphysematous changes, atelectasis at the lung bases, and mediastinal and hilar lymphadenopathy. The patient also admitted to having fevers up to 38.9°C intermittently for 3 months. She had been maintained on approximately 10 mg of prednisone for at least 6 months and had travelled to Arizona, California, Chicago, and Spain. She had no pets nor any known tuberculosis contacts.

The patient’s physical examination was notable for a temperature of 38.3°C and a respiratory rate of 24 breaths per minute. Her lungs showed rhonchi bilaterally, her right lower extremity was mildly erythematous and warm, with no cords.

Laboratory studies were remarkable for a white blood cell count (WBC) of 3.7 × 10^3/mm^3, lactate dehydrogenase (LDH) 1062 units/ml, aspartate transaminase (AST) 47 units/ml, arterial blood gases (ABG) on room air: pH 7.51, HCO_3^- 19 meq/L, CO_2 14.7 mm Hg, PO_2 84 mm Hg, O_2 saturation 97%.

A gallium scan was obtained, which showed increased uptake of the right paratracheal, bilateral hilar and carinal lymph nodes. A thoracotomy was performed for a biopsy of a mediastinal lymph node. The biopsy demonstrated necrotizing lymphadenitis with hematoxylin bodies but no granulomas (Figure 1). Special stains showed no acid-fast organisms, yeasts, or fungi. The patient was started on solumedrol 30 mg intravenously every 6 hours for a COPD exacerbation. The dosage was subsequently tapered to 10 mg orally once a day. Defervescence followed, and her shortness of breath resolved.

**DIFFERENTIAL DIAGNOSIS**

The differential diagnosis of this patient, an older woman with mediastinal and hilar adenopathy and fever, initially included Wegener’s granulomatosis, silicosis, sarcoidosis, lymphoma, cryptococcosis, nocardiosis, tuberculosis, histoplasmosis, coccidioidomycosis, and blastomycosis. In addition, since she had been taking steroids for years (recently tapered), *Pneumocystis carinii* pneumonia (PCP) also was considered.

Lack of lung uptake on the gallium scan virtually excluded PCP. Wegener’s granulomatosis was unlikely, since renal function was normal. There was no history of silica exposure and, therefore, no reason to suspect...
Sarcoidosis is a systemic disease with protean manifestations, including lymphadenopathy and constitutional symptoms; therefore, sarcoidosis was a possibility in this patient, though her age and lack of pulmonary infiltrate were contraindications. The patient's symptoms and radiographic findings were consistent with tuberculosis as well as lymphoma, since both can cause fever and adenopathy. Her travel history to the southwest and midwest United States led to a concern for coccidiomycosis and blastomycosis, respectively.

The lymph node biopsy demonstrated necrotizing lymphadenitis. The following disease entities can cause necrotizing lymphadenitis: toxoplasmosis, Epstein-Barr virus (EBV), lymphogranuloma venereum (LGV), Yersinia enterocolitica infection, cat scratch disease, carcinoma (including lymphoma), human immunodeficiency virus (HIV), Kikuchi's disease, systemic lupus erythematosus (SLE).²

Lymphadenopathy is the most commonly recognized clinical manifestation of acute toxoplasmosis. Fever, mental status changes, myalgias, rash, headache, and hepatosplenomegaly may occur. Epstein-Barr virus infection classically presents with fever, lymphadenopathy, pharyngitis, heterophile antibodies, and atypical lymphocytes. Hilar and mediastinal adenopathy without additional systemic symptoms made toxoplasmosis and EBV infection unlikely diagnoses.

Lymphogranuloma venereum is a sexually transmitted infection caused by Chlamydia trachomatis. The most common presenting picture is painful inguinal lymphadenopathy. This patient did not have inguinal adenopathy or recent sexual activity.

Yersiniosis is a bacterial infection in which organisms penetrate the ileal mucosa, localize in the ileocecal lymph nodes, and produce an acute mesenteric adenitis, generally accompanied by vomiting, abdominal pain, diarrhea, fever, and leukocytosis. This patient had adenopathy without accompanying gastrointestinal manifestations, making yersiniosis an unlikely diagnosis.

Cat scratch disease is an infection characterized by indolent, occasionally suppurative regional lymphadenitis, usually occurring following a scratch or close contact with a cat. This patient denied recent exposure to a cat.

Carcinoma and lymphoma were possible diagnoses, ruled out by pathology. Human immunodeficiency virus infection was also possible, but the patient tested negative.

Kikuchi's disease predominately produces disease in cervical lymph nodes, affects young women, usually Asian or Caucasian, and causes systemic symptoms. It can be confused with SLE. However, these two entities can usually be differentiated pathologically, since hematoxylin bodies are absent in Kikuchi's lymphadenopathy. The presence of necrotizing lymphadenitis accompanied by hematoxylin bodies was highly suggestive of lupus lymphadenopathy. Hematoxylin bodies are almost exclusively seen in SLE. They are believed to represent degenerated nuclei that have reacted with antinuclear antibodies.

The following serologies were performed: antinuclear antibodies 1:40, anti-double stranded DNA (anti-DNA), negative; anti-Smith antibody (anti-Sm), negative; anti-RNP, negative; complement C₃ 44.6 mg/dL (92-202), complement C₄ 10.7 mg/dL (26-79), urine Histoplasmosis antibody, negative. A serum cryptococcal antigen was not obtained.

**DIAGNOSIS**

Systemic lupus erythematosus (SLE).

**DISCUSSION**

This patient had fever of unknown origin with pulmonary lymphadenopathy. The major considerations were infection and tumor until the results of the biopsy suggested lupus erythematosus. Systemic lupus erythematosus is a connective-tissue disease that usually occurs in women of child bearing age, but children, men, and the elderly can be affected.¹ Tissues are damaged by deposition of autoantibodies and immune complexes. Systemic lupus erythematosus can cause a myriad of disease manifestations, since it can involve multiple organ systems. Systemic symptoms are usually prominent and include fatigue, fever, weight loss, and anorexia. Cutaneous, rheumatologic, gastrointestinal, renal, cardiac, neurologic, ocular, vascular, and hematologic manifestations can occur. A positive antinuclear antibody (ANA) is sensitive, but not specific. Antibodies to double stranded DNA and anti-Smith are specific. Low complement levels correlate with disease activity. The hematoxylin body, an amorphous aggregate of basophilic material, is pathognomonic of lupus lymphadenitis.² Most individuals experience exacerbations interspersed with periods of quiescence. The overall survival rate is 71% over 10 years.

This patient was 71 years old. She most likely had SLE as a young woman, was treated with prednisone for a diagnosis of rheumatoid arthritis, and therefore, her SLE was inadvertently treated. Interestingly, her double stranded DNA and anti-Smith antibodies were negative. Anti-DNA is positive in approximately 70% and anti-Sm in 30% of patients with SLE.¹ Therefore, although both tests were negative, this does not exclude the diagnosis. Low complement levels and a positive ANA are consistent with the diagnosis. Although SLE can cause lymphadenopathy, it usually causes axillary, cervical, and inguinal adenopathy. Hilar or mediastinal lymphadenopathy is a rare presentation for SLE. In fact, few cases have been reported.²⁻⁶ The patient discussed here
presented with fever and cervical and hilar adenopathy; she had a lymph node biopsy consistent with SLE and improved with corticosteroid therapy.

CONCLUSION

Systemic lupus erythematosus should be considered in the differential diagnosis of any individual presenting with enigmatic hilar or mediastinal adenopathy.

REFERENCES


