

CLINICAL VIGNETTE

Pulmonary Cryptococcus Mimicking Community Acquired Pneumonia in an Immunocompromised Patient

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Case Report

A 26-year-old female with systemic lupus erythematosus (SLE) and secondary Sjogren's syndrome presented to the emergency room with dyspnea on exertion, pleuritic chest pain, and fever for five days.

The patient was born in Korea and has lived in California for the last 6 years. She was diagnosed with lupus and secondary Sjogren's syndrome seven months prior. At that time, she was started on prednisone and hydroxychloroquine, and subsequently prescribed azathioprine for ongoing active disease.

The patient's current symptoms began approximately 6 months after she started treatment for SLE. She was awakened from sleep by severe left sided chest and back pain. One day prior to presentation, the pain reoccurred with a temperature of 38.5 degrees Celsius. Review of systems was positive for new headache, associated with onset of fever. She did not have cough, rash, neck stiffness, photophobia, diarrhea, dysphagia,

and joint pain.

At the emergency room, she was afebrile with normal O₂ saturation on ambient air. Her physical exam included normal respirations with crackles over the left posterior lung field. Labs included a white blood cell count of 11.78, but were otherwise normal. A CT angiogram of the chest (Figure 1) was negative for pulmonary embolism but showed dense consolidation within the apical segment of the left lower lobe and a trace left sided pleural effusion. She was admitted with presumed community acquired pneumonia and treated with ceftriaxone and azithromycin. Her chest pain and dyspnea persisted after 48 hours of antibiotics. Additional testing for opportunistic infections were obtained given her immunocompromised status. Urine Histoplasma antigen and blood Coccidioides antibody were negative. Blood cryptococcal antigen (CrAg) returned positive, with a titer of 1:1280.

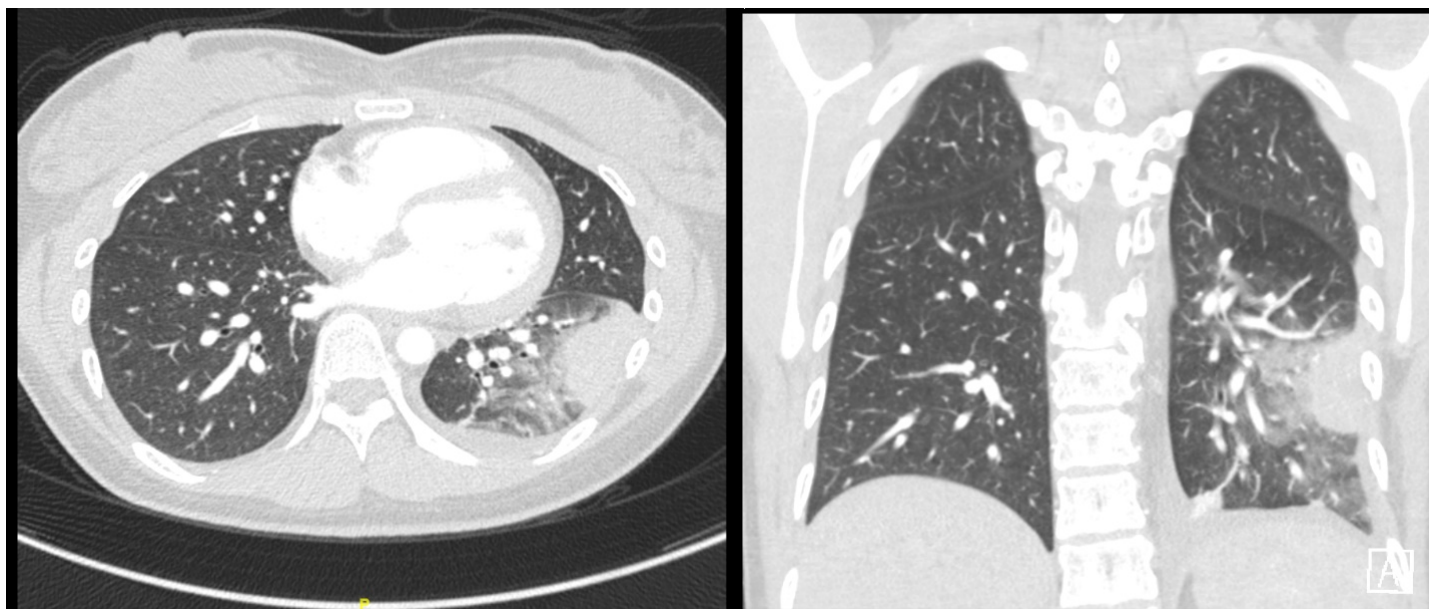


Figure 1. Admission CT chest with contrast demonstrating dense consolidation with air bronchograms in the apical segment of the left lower lobe and trace left pleural effusion.

A lumbar puncture was performed to rule out central nervous system (CNS) involvement. Non-contrast enhanced computed tomography (CT) scan of the head prior to lumbar puncture did not show any significant space occupying lesions. The lumbar puncture had an opening pressure of 16mmHg and cerebrospinal fluid (CSF) studies showed one nucleated cell, normal glucose and protein levels and negative CrAg. She was started on oral fluconazole therapy as there was no evidence of CNS involvement with plan for a 12-month course. Three weeks after discharge, the patient was seen in rheumatology and reported significant improvement in her dyspnea and pleuritic chest pain. Repeat CT scan four months after initial diagnosis showed significant improvement of left lower lobe airspace consolidation with residual subpleural triangular soft tissue density consistent with resolving cryptococcal pneumonia.

Discussion

In immunocompromised patients, most cryptococcal infections are caused by *Cryptococcus neoformans*. In contrast, infections in immunocompetent patients are largely secondary to *Cryptococcus gattii*. A large proportion of the population has been exposed to *Cryptococcus neoformans* by inhalation of spores or encapsulated yeast. The organism is found abundantly in the environment, especially in soil and droppings of certain animals.

Cryptococcus predominantly causes infection in the lungs and may disseminate to the central nervous system. Most *Cryptococcus neoformans* infections are asymptomatic. The vast majority of patients who develop symptoms are immunocompromised. These include patients with history of HIV, organ transplantation, malignancy, or treatment with steroids and immunosuppressive therapy. Both the innate and adaptive immune systems are thought to be important host defenses against cryptococcal infection. Alveolar macrophages eliminate cryptococcal cells in most immunocompetent patients by forming granulomas that resolve over weeks to months. In patients with compromised immune systems, cryptococcus may survive in granulomas and establish latent infection or colonize the respiratory tract. The T-cell response is critical to controlling the infection, and a low CD4 count is a significant risk factor for dissemination and development of cryptococcal meningitis.¹

The most common presenting symptoms of cryptococcal pneumonia are fever, cough, chest pain and dyspnea. Pulmonary nodules are the most common radiographic finding in immunocompetent hosts. Immunocompromised patients display a wide range of radiographic findings including single or multiple nodules, consolidation (as seen in our patient), and cavitary or mass lesions.² The diagnosis of pulmonary cryptococcus is established by clinical suspicion, radiographic findings, and confirmation with laboratory data including culture, histopathology of respiratory samples, and/or presence of serum cryptococcal antigens. The sensitivity of cryptococcal antigen testing is near 100% in HIV patients and 56 to 70% in other immunocompromised patients.³

Once the diagnosis of cryptococcal infection is made, lumbar puncture to rule out CNS involvement must be considered. The most recent guidelines by the Infectious Disease Society of America (IDSA), recommends lumbar puncture for CSF examination in any immunosuppressed patient diagnosed with a cryptococcal infection. The presence of disseminated disease in the CNS drastically alters the choice and duration of therapy.⁴ Patients with CNS involvement require induction therapy and monitoring of intracranial pressures. When performing LPs, an opening pressure, CSF culture and CSF cryptococcal antigen should be obtained. In patients with altered mentation or focal neurologic deficits, head imaging may be pursued to rule out a space occupying lesion, though this is rarely found. Patients who are immunocompetent have low risk of dissemination and CSF involvement. The decision for lumbar puncture is a clinical one. Lumbar puncture may be deferred in immunocompetent patients with low or negative CrAg in the blood, are free of neurologic symptoms, and do not have risk factors for dissemination. Braddley et al noted that the presence of cirrhosis, fever, altered mental status, and high dose steroid usage was positively associated with dissemination in patients without HIV.⁵

Our patient's initial presentation with rapid onset of fevers, pleuritic chest pain and consolidation on imaging led to a preliminary diagnosis of community acquired pneumonia. Non-infectious causes such as pulmonary embolism and pleurisy were also considered given the history of autoimmune disease. A high index of suspicion is required to diagnose cryptococcal pneumonia given the similarity of presenting symptoms and radiographic appearance to more typical bacterial infections, especially in immunocompromised patients. Fortunately, our patient was diagnosed prior to extra-pulmonary dissemination. IDSA guidelines recommend 6 to 12 months of therapy with fluconazole for mild to moderate isolated pulmonary cryptococcal infection without diffuse infiltrates. The patient had near resolution of symptoms and near radiographic resolution of pneumonia after 4 weeks of treatment with fluconazole.

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