A 19-Year-Old Man With Nonresolving Pneumonia*

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A 19-year-old white man was referred to the pulmonary clinic with a 2-month history of refractory cough, low-grade fevers, night sweats, and 30-lb weight loss. He had right-sided pleuritic pain and episodic scant hemoptysis. He denied smoking and using illicit drugs. He was single and had protected sex with two female partners over the past several years. He worked as a pipe fitter and denied any unusual hobbies, hunting, or recent travel. He would frequently go on camping and fishing trips near his hometown lake in southern Indiana. Chest radiographs and CT scans over 2 months showed progressive right upper lobe consolidation. He had negative findings on purified protein derivative and HIV screening. He had undergone bronchoscopy with normal results, and BAL specimens and brushes were culture negative for acid-fast bacilli, fungi, and cytology. He had been treated with multiple antibiotics, including amoxicillin, azithromycin, ciprofloxacin, clindamycin, and cephalaxin.

Physical Examination

In the clinic, his physical examination revealed a heart rate of 116 beats/min, BP of 108/58 mm Hg, temperature of 37.5°C, and a room air oxygen saturation of 94%. There was no cervical, axillary, or inguinal lymphadenopathy. Chest examination revealed bronchial breath sounds in the right upper lobe. Cardiac examination revealed tachycardia without gallops or murmurs. Abdomen was nontender without hepatosplenomegaly. Extremities were free of cyanosis, edema, and clubbing. There were no skin lesions.

Laboratory Data

Laboratory data showed the following: hemoglobin, 11.5 g/dL, WBC count, 14,500/µL, with 85% neutrophils, 7% lymphocytes, and 6% monocytes, and platelet count of 58,900/µL. Serum electrolytes, renal functions, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, and glucose levels were within normal limits. Urinalysis did not reveal hematuria. Erythrocyte sedimentation rate was 98 mm/h. Histoplasma complement fixation test and fungal gel immunodiffusion findings for Histoplasma capsulatum, Coccidioides immitis, and Blastomyces dermatitidis were negative. Other serologic findings, which were negative, included antinuclear antibody, classic-pattern antineutrophil cytoplasmic antibody, and perinuclear-antineutrophil cytoplasmic antibodies. A chest radiograph revealed airspace disease with cystic lucencies involving the posterior segment of the right upper lobe and superior segment of the right lower lobe (Fig 1). Chest CT showed dense consolidation with multiple cavities involving the posterior segment of the right upper lobe and the superior segment of the right lower lobe (Fig 2). The patient underwent fiberoptic bronchoscopy with BAL, protected specimen brushings, and transbronchial biopsies of the right upper lobe. Papanicolaou stain of the BAL specimen is shown in Figure 3.

What is the likely diagnosis?
FIGURE 1. Chest radiograph showing right upper lobe consolidation.

FIGURE 2. Chest CT showing consolidation with areas of cavitation involving the posterior segment of the right upper lobe.

FIGURE 3. Papanicolaou stain of BAL specimen demonstrating *B dermatitidis* (arrow) [original × 200].
Panpanicolau staining of BAL specimen revealed numerous yeasts with thick, refractile cell walls characteristic of *B dermatitidis*. Blastomycosis is the least common of all the endemic mycoses and is caused by a dimorphic fungi *B dermatitidis*. Blastomycosis is endemic in central and southeastern United States, including the Mississippi and Ohio River Valleys, the Great Lakes, an area in New York along the St. Lawrence River, and the Canadian provinces of Ontario and Manitoba. The states with the highest prevalence of blastomycosis are Wisconsin, Mississippi, Arkansas, Kentucky, and North Carolina. Due to lack of a reliable diagnostic test, epidemiology of blastomycosis is dependent on case reports of sporadic cases and studies of point source outbreaks. The incidence of blastomycosis in the United States is estimated to be 0.6/100,000/yr. It may be as high as 40/100,000/yr in endemic areas.

Fungal growth occurs in nitrogen-rich soil containing decaying vegetation around lakes and rivers and is facilitated by heat and humidity. Though most cases of blastomycosis are sporadic and can be linked to outdoor activities, many of them may not have a history of recreational or occupational exposure to waterways and woods. Except for rare instances of direct inoculation, the infection primarily occurs by inhalation of conidia of *B dermatitidis* from the soil, which transforms to the yeast form in the distal airways. Person-to-person transmission does not occur. In endemic areas, a good history will often help identify the source of infection in majority (80%) of cases.

Blastomycosis presents with varying degrees of pulmonary or extrapulmonary manifestations. While 30% of patients have disseminated disease, 70% present with isolated pulmonary involvement. Acute pulmonary blastomycosis is often diagnosed following a point source outbreak, and symptoms tend to occur 6 weeks following the exposure (range, 21 to 106 days). The illness often resembles influenza or an acute bacterial pneumonia, in which case chest radiographs demonstrate segmental or lobar consolidation. Most cases presenting with mild disease without respiratory compromise resolve spontaneously over a month without antifungal therapy. Rarely, blastomycosis presents with ARDS and is associated with a high mortality.

Patients with chronic pulmonary blastomycosis often present with a 3- to 6-month history of productive cough, low-grade fevers, night sweats, and weight loss. Radiographic findings are highly variable and may demonstrate mass-like lesions, nodules, or alveolar infiltrates. The disease is often mistaken for malignancy or tuberculosis. Pleural effusion, mediastinal lymphadenopathy, and cavitation are uncommon.

Diagnosis of blastomycosis requires demonstration of the fungus by direct visualization or culture of sputum, tissue, or other infected body fluid. The simplest method for rapid diagnosis is by examination of fresh sputum or bronchial washings digested with 10% potassium hydroxide under a microscope. The yeast is 8 to 20 μm in size, and has a characteristic thick, double, refractile cell wall with multiple nuclei and a broad-based budding. Panpanicolau staining of sputum or bronchoscopy specimens has been shown to have a high diagnostic yield (93%), and in reliable hands can reduce the need for invasive procedures in patients with suspected pulmonary blastomycosis. The organism appears refractile and stains pale blue-green with Panpanicolau stain. Identification of *B dermatitidis* in hematoxylin-eosin–stained histopathologic specimens is often difficult; therefore, special stains, such as Gomori methenamine-silver or periodic acid-Schiff stains are often required. Identification of the fungus by culture is slow and takes 3 to 4 weeks. However, newer exoantigen testing and DNA probes can significantly shorten the diagnostic time. Available serologic tests such as complement fixation and immunodiffusion have poor sensitivities (16% and 40%, respectively), although the enzyme immunoassay for antibodies to the A antigen of *B dermatitidis* appears to be better with a sensitivity of approximately 80%. A positive test result in the appropriate clinical setting raises the possibility of blastomycosis. If sputum and bronchoscopy are nondiagnostic, thoracocopy or thoracotomy may be required to obtain a diagnosis.

Patients with mild acute pulmonary blastomycosis can be closely monitored without therapy. In con-
In the present patient, transbronchial biopsies showed necrotizing granulomas with giant cells, plasma cells, eosinophils, and neutrophils, along with fungal organisms. Gomori methenamine-silver stains confirmed the presence of fungal organisms, some of them demonstrating broad-based budding consistent with *B dermatitidis* (Fig 4). The patient probably contracted the disease during his fishing and camping trips around his hometown lake in southern Indiana. He began itraconazole treatment, and at 2-month follow-up was asymptomatic with near-complete resolution on the chest radiograph (Fig 5).

**Clinical Pearls**

1. Blastomycosis should be considered in patients with nonresolving pneumonia, especially if they have a history of recreational or occupational outdoor activities.

2. Analysis of sputum and bronchial washing specimens with 10% potassium hydroxide and Papnicolaou stain provide rapid and reliable diagnosis of *B dermatitidis*.

3. Available serologic tests such as complement fixation and immunodiffusion have poor sensitivity. However, a positive test result in the appropriate clinical setting raises the possibility of blastomycosis.

4. Patients with progressive pulmonary blastomycosis without evidence of life-threatening disease or CNS involvement require 400 mg/d of itraconazole for at least 6 months.

**Suggested Reading**


Lemos LL, Baliga M, Guo M. Blastomycosis: the great pretender can also be an opportunist: initial clinical diagnosis and underlying diseases in 123 patients. Ann Diagn Pathol 2002; 6:194–203


Trumbull ML, Chesney TM. The cytological diagnosis of pulmonary blastomycosis. JAMA 1981; 245:830–838


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*Figure 5. Chest radiograph showing near-complete resolution of right upper lobe consolidation.*

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