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DISSEMINATED BLASTOMYCOSIS IN A TEENAGER PRESENTING WITH PLEURAL EFFUSION AND SPLENOMEGALY

John Teijido, MD* and Amy L. Drendel, DO, MS*†

*Medical College of Wisconsin, Milwaukee, Wisconsin and †Children's Hospital of Wisconsin, Milwaukee, Wisconsin
Reprint Address: John Teijido, MD, Medical College of Wisconsin, 8701 W. Watertown Plank Rd., Milwaukee, WI 53226

□ **Abstract—Background: Blastomycosis is caused by a fungus endemic to states and providences bordering the Lawrence Rivers and the Great Lakes. It can lead to significant pathology in both immunocompetent and immunocompromised hosts. This case report describes disseminated blastomycosis in an otherwise healthy 16-year-old patient. Case Report: A 16-year-old male presented with a chief complaint of flank pain. In the Emergency Department he described additional symptoms of emesis, cough, and weight loss. His vitals were appropriate; however, he had absent lung sounds in the left lower lung field, splenomegaly, a left thigh abscess, and lower-extremity edema. Imaging studies showed a left pleural effusion, mediastinal shift to the right, splenomegaly, a left psoas abscess, and undifferentiated bony involvement of L1 transverse process and the left 12th rib. Abscess cultures grew *Blastomyces dermatitides*. He was treated with amphotericin B, demonstrated clinical improvement, and was discharged on itraconazole. Why Should an Emergency Physician Be Aware of This?: The case fatality rate of blastomycosis is estimated at between 4.3% and 6.4%. Patients with solid organ transplant and associated immune suppression had a mortality of 33–38%. Given the nonspecific nature of this condition, a high level of suspicion is required for diagnosis, and early diagnosis is essential, as end organ damage in disseminated disease can include high-severity illness, including acute respiratory distress syndrome and central nervous system dysfunction. If any patient presents with symptomatology involving both skin and pulmonary systems, blastomycosis must be entertained as a possible diagnosis. Prompt diagnosis and treatment will significantly improve morbidity and mortality.** © **2018 Elsevier Inc. All rights reserved.**

□ **Keywords—blastomyces; blastomycosis; pleural effusion; splenomegaly**

INTRODUCTION

Blastomycosis is caused by a fungus endemic to states and providences bordering the Mississippi, Ohio, and St. Lawrence Rivers, and the Great Lakes (1). This organism can cause invasive disease in immunocompetent hosts, as well as more severe disease in immunocompromised patients. Clinical manifestations of blastomycosis range broadly, as it has been called "the great pretender" (2). Most commonly it presents with pulmonary and dermatologic findings. This report describes a case of blastomycosis in an otherwise healthy 16-year-old patient. The case is followed by a review of the organism's epidemiology, clinical manifestation, diagnostic options, treatment, and prognosis.

CASE REPORT

The patient was a 16-year-old male with no past medical history presenting with a chief complaint of nausea and flank pain. At school on the day of presentation, the patient had acute onset of nausea when bending down to drink water. He went to the nurse's office, sat down, and fell asleep. The school notified his mother, who was concerned and brought him to the Emergency Department.

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Review of systems revealed daily emesis for the past several weeks, left-sided flank pain for the past 1–2 weeks, and an infrequent, wet, productive cough for the past 3 months. During the past 3 years he had some weight loss, but he could not quantify how much. He had no sick contacts, pets at home, animal exposures, or recent travel. He lived with his mother in an urban Midwest neighborhood.

His mother brought him from school to a community hospital, where he was noted to have normal vital signs with a normal examination except for decreased lung sounds on his left side and pitting edema in both lower extremities. He was transferred to the tertiary care children's hospital for further work-up. On initial presentation he was well appearing and in no distress. His vital signs were: temperature 37.6°C, heart rate 95 beats/min, respiratory rate 18 breaths/min, blood pressure 148/79 mm Hg, and oxygen saturation 99% on room air. His examination was confirmed to be normal except that he had no lung sounds in the left lower lung field, diminished lung sounds in the left upper lung field, and bilateral lower-extremity pitting edema up to his knees. A left thigh abscess that was 2 × 2 cm in size was also incidentally noted.

Chest x-ray study showed a large left-sided pleural effusion with mediastinal shift to the right (Figure 1). Laboratory tests showed normal electrolytes, renal function, and liver function. He had a leukocytosis to 13, normal hemoglobin, and normal platelets. He had a negative Monospot, erythrocyte sedimentation rate of 84, and C-reactive protein of 8.1. A chest tube was placed on the left and 1100 mL of exudative fluid was sent for further studies. Computed tomography of his abdomen and pelvis showed splenomegaly and a left psoas abscess (Figure 2). The patient was admitted to the hospital for ongoing work-up and care.

During his hospitalization, sputum mycobacterial cultures were negative, purified protein derivative was negative, and QuantiFERON-TB Gold (Qiagen, Germantown, MD) returned negative. A drain was placed into the left psoas abscess and fluid culture grew broad budding yeast. The left thigh abscess was also incised, drained, and cultured.

Both abscess fungal cultures grew *Blastomyces dermatitides*. Mycobacterial cultures were negative. The patient was started on amphotericin B for disseminated blastomycosis. Evaluation to determine the extent of disease was pursued. Brain magnetic resonance imaging (MRI) was normal and a bone scan showed possible involvement at the posterior aspect of the left 12th rib and left L1 transverse process (no tissue samples of these locations were done). Pleural fluid fungal studies and cytology were negative.

The patient responded well to amphotericin, with overall clinical improvement and reduction in the C-reactive protein. He was transitioned to twice-daily itraconazole on Day 10. Oncology was consulted to evaluate for the possibility of unrecognized malignancy, but none was found. He was discharged home in improved condition 14 days after admission.

DISCUSSION

Blastomyces dermatitidis and *Blastomyces gilchristii* are the causative agents of blastomycosis. It is a fungus endemic to North America, particularly states and

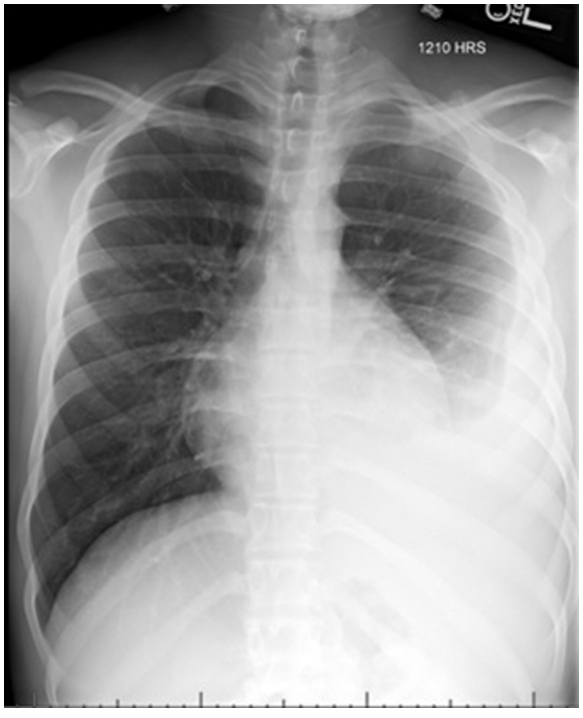

Figure 1. Initial chest x-ray study showing large left-sided pleural effusion with mediastinal shift.

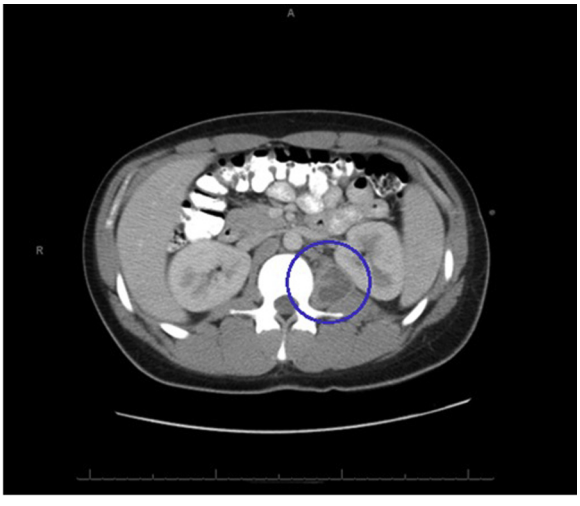

Figure 2. Computed tomography of the abdomen with psoas abscess indicated by the blue circle.

providences bordering the Mississippi, Ohio, and St. Lawrence Rivers, and the Great Lakes (1). Blastomyces inhabits sandy soils with an acidic pH, decaying vegetation, organic material, and rotting wood near water sources (3). Most infections are sporadic, but occasionally there are infections secondary to occupational or recreational activities that disrupt soil such as construction, hunting, or boating (3,4). Most blastomycosis cases occur in adults. About 13% of cases occur in the pediatric population. Overall, there is a slight male predominance (4). This organism can cause invasive disease in immunocompetent hosts, but patients who are immunocompromised by solid organ transplant, tumor necrosis factor α inhibitors, malignancy, or human immunodeficiency virus can develop more severe disease. There is a higher incidence of blastomycosis in some ethnic groups, including aboriginal ethnicity in Canada and Hmong populations in Wisconsin (5).

The clinical manifestations of blastomycosis range from asymptomatic infection to pneumonia and acute respiratory distress syndrome. It has been described as "the great pretender" due to its variable presentation, but it more commonly involves pulmonary and dermatologic findings (2). Only 54% of patients have fever on presentation. Inoculation typically occurs via the lungs. Onset of symptoms occurs between 3 weeks and 3.5 months after inhalation of mycelial fragments or spores. Chest radiography may show masses, nodules, or cavitations, often in the upper lobes. For 25% to 40% of patients, extrapulmonary dissemination at the skin, bones, genitourinary tract, and central nervous system (CNS) may be the initial symptoms; although any organ can be affected (4). Extrapulmonary blastomycosis should be treated like disseminated disease. The most common site of infection outside of the lungs is the skin. Patients develop a papulopustular lesion that progresses to a verrucous, crusted lesion. Abscesses may develop as well (6). After skin, the bone is the second most common extrapulmonary site of disseminated disease. Osseous lesions are painful and often associated with soft tissue abscesses similar to this patient (7). Genitourinary involvement has been reported in 20–30% of cases, although these data come from case series from the 1950s. In men, the most common sites are the prostate and epididymis, whereas in women blastomycosis can cause tubo-ovarian abscess, endometritis, and salpingitis (8). CNS blastomycosis is less common in immunocompetent patients and can manifest as meningitis, epidural abscess, or brain abscess (9).

Given the nonspecific nature of the clinical presentation often seen in patients infected with blastomyces species, a high level of suspicion is needed for prompt diagnosis. In patients with pneumonia, providers should inquire about medical history, place of residence, travel, outdoor activities, hobbies, recent construction done on the home, wood burning stove use, a community compost pile, or exposure to road construction. Further, any patient with disease of both the pulmonary and dermatologic systems must have the diagnosis of blastomycosis entertained.

The discovery of yeast forms with broad-based budding, and double refractile cell wall is a clue that can lead to a presumptive diagnosis of blastomycosis. Current serologic testing has poor sensitivity and specificity, and for that reason, has little role in diagnosis. Additionally, serologic tests have significant cross-reactivity with other dimorphic fungi such as *Histoplasma capsulatum*. A newer enzyme immunoassay that uses microplates coated with BAD1 protein has enhanced sensitivity and specificity with less cross-reactivity with *H. capsulatum*; however, it is not yet commercially available. Real-time polymerase chain reaction is also in development. One assay demonstrated 100% specificity and sensitivity with culture isolates, and another assay detecting the BAD1 gene promoter also has very high specificity and sensitivity. These polymerase chain reaction tests have no cross-reactivity with *H. capsulatum*, and have a result time of 4 to 5 h (1,10). Fungal culture remains the definitive method of diagnosis. For pulmonary blastomycosis, bronchoscopic culture showed a 92% diagnostic yield, whereas sputum samples, tracheal secretions, and gastric washings showed a yield of 86% (11). Blastomyces grows slowly in culture, and fungal colonies take 5 to 14 days to be visualized (10).

Treatment recommendations are based on severity of symptoms, site of infection, and immune status of the patient. Regardless of clinical symptoms, all patients should be treated with antifungals. This is in contrast to other fungal illnesses, such as acute histoplasmosis, for which treatment is not always needed. Prior to therapy, baseline hepatic function, renal function, and hematologic testing should be obtained. A baseline electrocardiogram with QT interval should be obtained because azole antifungals can lengthen this interval; especially when co-administered with other QT-prolonging agents. The typical initial therapy includes amphotericin B or itraconazole, depending on severity of illness and patient-specific risk factors. Pregnant patients should not be treated with azoles due to teratogenic effects. Immunocompromised patients, newborns, and patients with CNS disease should be treated with amphotericin B. Often, patients can be transitioned to an azole such as itraconazole, fluconazole, or voriconazole as step-down therapy, which is often continued for 6 to 12 months (12,13).

WHY SHOULD EMERGENCY PHYSICIANS BE AWARE OF THIS?

The case fatality rate of blastomycosis is estimated at between 4.3% and 6.4%. A shorter duration of symptoms

has been associated with increased mortality, which suggests a more fulminant presentation (14). Patients with acquired immune deficiency syndrome had an estimated mortality of 40% with blastomycosis infection, and patients with solid organ transplant and associated immune suppression had a mortality of 33–38% (15,16).

Given the nonspecific nature of this condition, a high level of suspicion is required for diagnosis. Early diagnosis is essential to avoid disseminated disease and end organ damage such as acute respiratory distress syndrome or CNS dysfunction. As mentioned, any patient presenting with symptoms involving both the pulmonary system and the skin should have this diagnosis entertained. This case report is an excellent example of the vague presentation of blastomycosis in a patient with simultaneous multiorgan pathology. Therefore, prompt diagnosis and treatment will significantly improve morbidity and mortality.

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