A Case Report of Disseminated Blastomycosis and Adult Respiratory Distress Syndrome

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Blastomycosis is a fungal disease endemic to the midwestern and southeastern United States. This is a case report of a 29-year-old woman who presented with weight loss, fever, fatigue, and pneumonia. She developed disseminated blastomycosis, adult respiratory distress syndrome (ARDS), and ulcerative skin lesions, requiring mechanical ventilation, amphotericin B, and multiple surgeries. Blastomycosis is endemic to a large portion of the United States. Family physicians should consider fungal infection in the differential diagnosis of an unresolving pneumonia.

Key words. Blastomycosis; respiratory distress syndrome, adult (ARDS). (*J Fam Pract 1995; 40:597-600*)

Blastomycosis is a fungal disease endemic to the midwestern and southeastern United States. Large outbreaks of blastomycosis were documented in Grifton, North Carolina, in 1955[1] and Eagle River, Wisconsin, in 1986.[2] The typical patient presents with weight loss, fever, fatigue, and a pneumonia with an alveolar pattern as revealed by chest radiograph. Patients may also present with ulcerative skin lesions, bone lesions, central nervous system involvement, or a combination of these factors. Although tissue identification or culture of *Blastomyces* is the accepted standard for diagnosis, an enzyme immunoassay (EIA)[3] and the Western immunoblot assay[4] have been developed with excellent sensitivity and specificity. In patients with life-threatening disease or central nervous system involvement, amphotericin B is the treatment of choice.[5] Patients who are less ill can be treated with ketoconazole or itraconazole.[5]

There are few reports of pulmonary blastomycosis infection progressing to adult respiratory distress syndrome (ARDS). In the literature, including this case, there have been 29 cases of blastomycosis with known or suspected ARDS with only 13 survivors.[6–21] Nine of the 29 patients either had no underlying disease or were thought to have been healthy, and 13 of the patients had a chronic medical condition or were immunosuppressed. The medical status of 7 patients was not reported.

Case History

A 29-year-old, previously healthy black woman initially presented to her family physician with fever, chills, cough, hemoptysis, and right-sided pleuritic chest pain. On chest radiograph, she was found to have pneumonia in the right lower lobe and was treated on an outpatient basis with antibiotics. Following unsuccessful outpatient treatment, she was hospitalized for 4 days, treated with intravenous (IV) antibiotics, and seemed to improve. After discharge, there was no fever, pain, or hemoptysis, but her cough persisted, especially at night.

A chest radiograph 1 month later, however, showed progression of the disease in the right lower lobe. A diagnostic bronchoscopy was normal and the bronchial washing culture grew *Aspergillus* sp. Since the patient had previously been treated with four different antibiotics, the decision was made to treat the presumed fungal pneumonia with fluconazole for 1 month. She was scheduled for a computed tomography (CT)–guided biopsy of her persistent right lung infiltrate, but she did not keep her appointments and was lost to follow-up until 2 months later.

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At that time, the patient saw her family physician for what was considered to be an infected sebaceous cyst on her occiput, which was incised and drained but not cultured. Four days later she returned with persistent right ankle pain 2 weeks after injuring her ankle. On referral to an orthopedist, she was hospitalized for suspected right ankle cellulitis and a lung biopsy.

In the hospital, she developed a small cyst on her forehead while still being treated intravenously with antibiotics. The CT-guided biopsy of the right lung showed chronic inflammation, and the bacterial, fungal, and acid-fast cultures were all negative, but the acid-fast stain of the tissue was positive. A chest radiograph at that time also showed progression of the lung disease to a miliary pattern. The patient was nonreactive to a purified-protein derivative (PPD) of *Mycobacterium tuberculosis* with reactive-appropriate controls. Since she had recently been exposed to tuberculosis, treatment with rifampin, pyrazinamide, and ethambutol hydrochloride was empirically started for suspected tuberculosis. Cellulitis of the right ankle continued to worsen, despite treatment with IV antibiotics, necessitating surgical drainage. A human immunodeficiency virus (HIV) test was negative.

Despite therapy, multiple skin abscesses developed on her abdomen and legs, and cellulitis of the right ankle continued to progress, requiring a second surgical drainage. A repeat bacterial culture of the abscess on the right ankle grew *Staphylococcus aureus*, and because of concern about bacterial superfection, vancomycin hydrochloride was started. A right pleural effusion developed with respiratory distress, and a ventilation/perfusion scan showed matching defects. Because of the patient's progressive pulmonary failure, she was transferred to our institution, where a therapeutic thoracentesis was performed to remove 750 mL of fluid from the right pleural space.

Initially, it was thought that the findings were consistent with progressive miliary tuberculosis, and the patient was treated with isoniazid, rifampin, pyrazinamide, amikacin sulfate, and pyridoxine hydrochloride. Because of impending respiratory failure, mechanical ventilation was initiated (Figure 1). The skin abscesses were drained and cultured, and a skin biopsy of the forehead lesion was performed. Vancomycin therapy was continued for the abscess on her right ankle.

Thirty-six hours after admission, the forehead lesion showed broad-based budding yeast consistent with blastomycosis (Figure 2), and the patient was given 25 mg of amphotericin B after a 1-mg test dose. The next day, her daily amphotericin B dose was increased to 50 mg. Because her PPD remained negative with positive controls, her antituberculosis medications were discontinued.

Ten days later, the right ankle was once again surgically drained, followed by debridement and skin grafting.

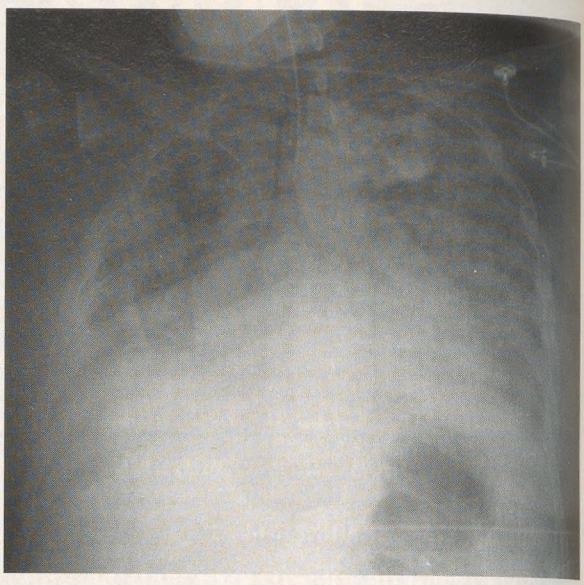

Figure 1. Chest radiograph 8 hours after admission showing diffuse airspace disease and a right pleural effusion.

After 2 weeks, she was weaned from the ventilator and subsequently transferred to a regular medical floor. Following a total dose of 1375 mg of amphotericin B, oral itraconazole was begun. Pulmonary function tests performed before discharge were consistent with restrictive lung disease. The patient was discharged to her home on the 33rd hospital day and was treated with itraconazole 200 mg once a day for 1 year. Figure 3 shows a radiograph of her chest 2 months after discharge.

Discussion

Blastomycosis is a fungal infection caused by the organism *Blastomyces dermatitides*. It occurs in healthy people and is endemic to the Southeast and Midwest of the United States. Two previously reported epidemics have occurred, one in North Carolina[1] and one in Wisconsin.[2]

In humans, *Blastomyces* is found as a thick-walled, round yeast with daughter cells forming from a broad-based bud. In vitro, the organism is dimorphic, growing as a mycelium at 25°C and as a yeast at 37°C.

Clinically, patients can present with an acute pneumonia with fever and a productive cough that does not respond to antibiotics, or with a chronic pneumonia with weight loss, night sweats, and hemoptysis of several months' duration. Radiographically, blastomycosis can appear as a consolidation, a miliary pattern,[7,13,22] or even as a lung mass.[23,24] Often the patient is treated for presumed bacterial pneumonia,[5–8,11,16] and the presence of the miliary pattern can lead to a misdiagnosis of tubercu-

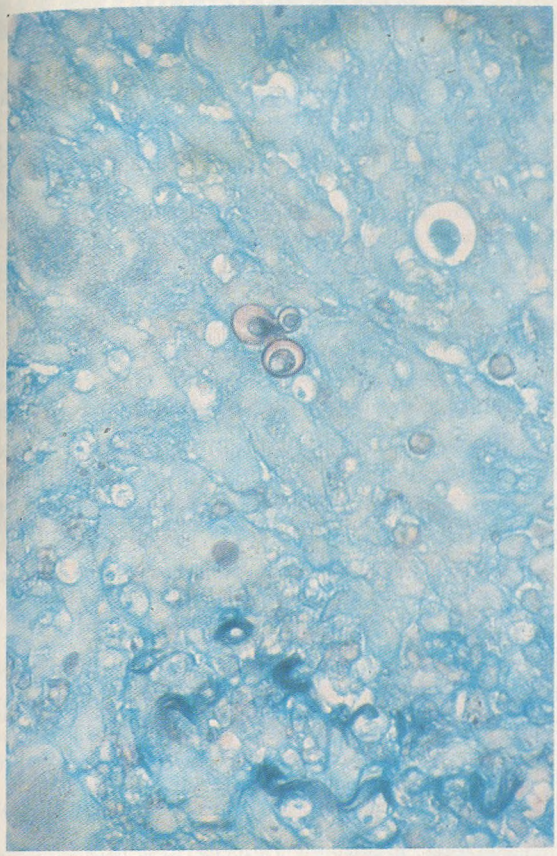

Figure 2. Skin biopsy of the forehead lesions showing broad-based budding yeast consistent with blastomycosis (×100 Gram stain).

losis.[7,13,15,22] Our patient was treated for both during her 6-month illness.

Occasionally, the patient can progress to severe infection with respiratory failure. Of the 29 cases of ARDS related to blastomycosis, only 13 have survived.[6–21] Patients can also present with verrucous or ulcerative skin lesions, the second most common sign of blastomycosis.[5] Bone, genitourinary, and central nervous system involvement are less commonly involved in blastomycosis.[5]

The accepted standard for diagnosis of blastomycosis is by direct microscopic examination of infected tissue or fungal culture. Serologic tests have long been considered unreliable for diagnosing blastomycosis. A recently developed EIA for blastomycosis,[3] based on antigen capture, is 88% sensitive with a specificity approaching 100%. The Western immunoblot assay,[4] which uses a specific extracellular antigen of *Blastomyces dermatitidis,* has been shown to be 91% sensitive and 94% specific. In our patient, the diagnosis was made by light microscopy of infected tissue, followed by positive fungal cultures of sputum, skin, and bone.

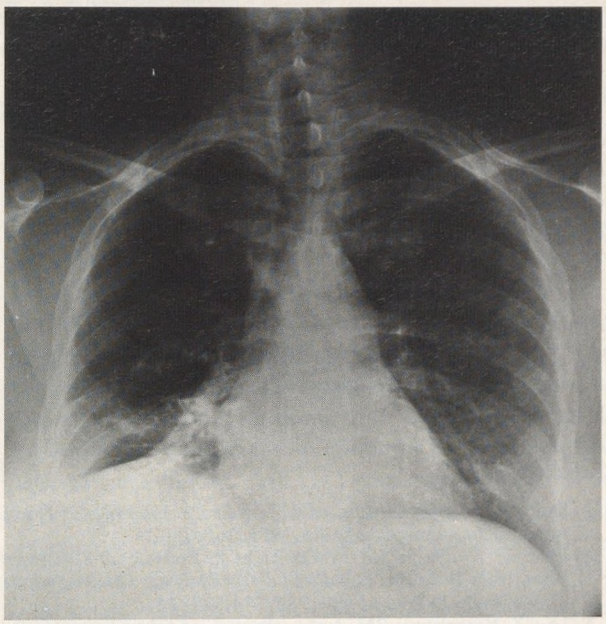

Figure 3. Chest radiograph 2 months after discharge showing persistent disease with a pleural effusion in the right lower lobe. The patient continues to receive oral itraconazole.

Before the development of the triazoles the treatment of choice was with amphotericin B, which is associated with renal toxicity, anemia, thrombocytopenia, hypokalemia, and nausea. In the immunocompromised patient, eg, one with a life-threatening disease or central nervous system involvement, amphotericin B is still the treatment of choice.[2] Less-ill patients can be treated with ketoconazole or, more recently, itraconazole.[25] Since itraconazole appears to be better tolerated and has efficacy rates as high as or higher than that of ketoconazole,[26] it will likely replace ketoconazole as the antifungal therapy for immunocompetent patients with mild disease. The usual dose of itraconazole is 200 mg a day for at least 3 months.[25]

Blastomycosis has been reported in North Carolina,[1,27] Wisconsin,[6,9,10,20] Mississippi,[16] Virginia,[17] Massachusetts,[21] Illinois,[19] Tennessee,[13,15] Kentucky,[28] Louisiana,[12,29] Ohio,[7] Michigan,[8] and Minnesota.[11,14,18] Because the signs and symptoms of blastomycosis mimic other respiratory diseases, family physicians, especially those in the southeastern and midwestern United States, should include blastomycosis in their differential diagnosis of an unresolving pneumonia. If routine sputum tests or bronchial washings for bacteria fail to provide an organism seemingly responsible for a clinical state, further samples should be submitted to test for fungal and acid-fast organisms. Biopsy should be considered for suspect skin lesions that do not improve with appropriate treat-

ment. Open lung biopsy for a diagnosis of blastomycosis has been reported[7,9,11] and may be appropriate when bronchoscopy findings are negative.

Undiagnosed blastomycosis can progress to ARDS and is associated with significant mortality. Our patient's clinical course highlights the need for primary care physicians to maintain a high index of suspicion for blastomycosis in endemic regions of the United States.

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