

SECTION EDITOR: ENID GILBERT-BARNES, MD

## Pathological Case of the Month

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**A** 15-YEAR-OLD male had a 4-month history of cough productive of blood-tinged sputum, low-grade fevers, night sweats, progressive left wrist pain, and a 40-lb weight loss.<sup>1</sup> Symptoms and radiographic findings of a right middle lobe pneumonia persisted despite multiple courses of antibiotics, including erythromycin, bactrim, and ciprofloxacin over the next 4 months. He was thought to have an asthmatic component to his respiratory symptoms and was prescribed a course of prednisone and albuterol without improvement. He developed worsening left wrist pain, stiffness, swelling, and dysfunction. Social and travel history was notable only for a brief visit to central Wisconsin 14

months prior to the development of symptoms. Findings from physical examination revealed a cooperative male in no distress. His temperature was 39°C with a respiratory rate of 24, heart rate of 96, and blood pressure of 139/96 mm Hg. He had multiple verrucous and ulcerating lesions on his face, scalp, arms, and back (**Figure 1**). He had a 16-cm symmetric goiter that was not nodular, tender, or warm (**Figure 2**). His lungs had decreased aeration in the right middle lung field. His left wrist was contracted, and he had a 4×5-cm friable purulent wound on the volar aspect (**Figure 3**). A chest radiograph revealed a right middle lobe consolidation (**Figure 4**) and a radiograph of his left wrist revealed an extensive destructive lesion involving the distal radius (**Figure 5**). He underwent a diagnostic procedure. Skin and bone specimens were collected for biopsy (**Figure 6**).

From the Children's Memorial Hospital, Chicago, Ill.



Figure 1.

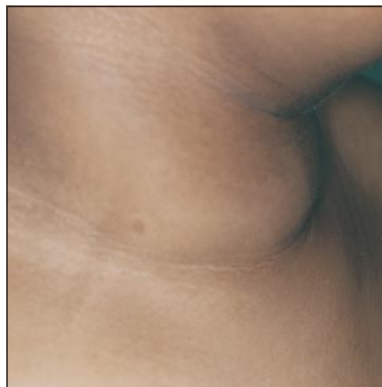


Figure 2.



Figure 3.



Figure 4.



Figure 5.

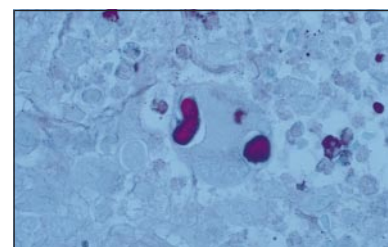


Figure 6.

# Diagnosis and Discussion

## *Blastomyces dermatitidis*

**Figure 1.** *Blastomycosis of the skin.*

**Figure 2.** *Goiter from blastomycosis of the thyroid.*

**Figure 3.** *Extension to the skin from osteomyelitis of the radius.*

**Figure 4.** *Pneumonia due to blastomycosis.*

**Figure 5.** *Osteomyelitis of the radius due to blastomycosis.*

**Figure 6.** *Broad-based budding (hematoxylin-eosin, original magnification ×400).*

**M**icroscopic examination of skin, bone biopsy specimens, and bronchoalveolar lavage specimens revealed *Blastomyces dermatitidis*. He was treated with 250 mg/kg of liposomal amphotericin and 400 mg daily of itraconazole for 8 weeks with resolution of pneumonia, goiter, and systemic symptoms. Surgeries of his left wrist included multiple incision and debridements, external fixator placement, split-thickness skin graft placement, and wrist fusion.

*Blastomyces dermatitidis*, a primary pathogen, is a dimorphic fungus that exists as a thick-walled yeast cell with broad-based budding daughter cells in tissues and in the mycelial form in its environmental reservoir.<sup>1,2</sup> The US endemic area includes the Ohio and Mississippi River valleys as well as the south-central and southeastern portions of the United States.<sup>1,3</sup> Most patients are between age 20 and 70 years with an estimated 3% to 11% of cases occurring in patients younger than age 20 years.<sup>1,4,5</sup> The primary site of infection is the lungs after inhalation of spores from soil.<sup>2,6</sup> The larger spores are more resistant to phagocytosis and can succeed in transitioning to the yeast phase.<sup>5</sup> Over the next 4 to 8 weeks, the yeast forms proliferate, leading to an influenzalike illness.<sup>5</sup> Roughly 50% of infected children will develop symptomatic illness.<sup>5</sup>

Chronic pneumonia usually precedes definitive diagnosis by 2 to 6 months.<sup>1</sup> This pneumonia can resolve or progress to localized pulmonary involvement or extrapulmonary disease.<sup>4</sup> Most patients progressing to adult respiratory distress syndrome die soon thereafter.<sup>1</sup> The most common finding on chest radiography is an alveolar or masslike infiltrate.<sup>1</sup> There may also be interstitial disease with reticulonodular, nodular, or miliary opacities and cavitation.<sup>2</sup> Diagnosis may be delayed because these various patterns can mimic other disease processes such as tuberculosis, bacterial pneumonia, malignant tumors, and sarcoidosis.<sup>5</sup> Hilar and mediastinal adenopathy are rare, however, in contrast to histoplasmosis.<sup>2</sup>

Dissemination occurs months to years after pulmonary infection, and almost any organ site can be involved, including skin, bone, male genitourinary system, and the central nervous system.<sup>2</sup> Findings from skin lesions reveal papillomatosis and downward proliferation of the epidermis with intraepidermal abscesses.<sup>1</sup> Hyperplasia and acanthosis suggest a diagnosis of cancer.<sup>1</sup> Osteomyelitis occurs

in up to 25% of extrapulmonary cases with involvement of the vertebrae, pelvis, sacrum, skull, ribs, and long bones.<sup>1</sup> Radiographs of osteomyelitis are nonspecific and cannot be differentiated from other forms of osteomyelitis.<sup>1</sup> Prostatitis and epididymo-orchitis are the most common genitourinary manifestations.<sup>1</sup> Meningitis and epidural or cranial abscesses are the forms of central nervous system involvement.<sup>1</sup> Other areas of involvement include the liver, spleen, heart, lymph nodes, psoas muscle, kidney, middle ear, and adrenal and thyroid glands.<sup>5,6</sup>

Diagnosis is easily established by recovery of the organism from clinical specimens.<sup>1,4</sup> Examination of bronchoalveolar fluid microscopically in addition to culture is an effective method for diagnosis in adults.<sup>4</sup> In children and adolescents, failure to identify organisms in sputum or bronchoalveolar fluid is common.<sup>4</sup> It is recommended that children and adolescents suspected of having blastomycosis undergo lung biopsy if sputum and bronchoscopy examination are nondiagnostic.<sup>4</sup> Other techniques such as complement fixation, immunodiffusion, or delayed hypersensitivity of skin to blastomycin are unreliable for diagnosis.<sup>1</sup>

The decision to treat requires balancing the severity of illness with the toxic effects of antifungals. Observation should be limited to cases of mild pulmonary blastomycosis.<sup>1</sup> If therapy is withheld, patients must be followed carefully for evidence of reactivation or dissemination.<sup>6</sup> Pleural disease or extrapulmonary manifestations require antifungal therapy.<sup>1</sup> Amphotericin has the greatest proven efficacy, but it is associated with toxic effects.<sup>2</sup> Oral ketoconazole and itraconazole are only slightly less effective but have lower toxic effects and easier administration.<sup>2</sup> Itraconazole has replaced amphotericin as the agent of choice to treat less than life-threatening blastomycosis in adults.<sup>4</sup> Amphotericin is warranted if patients do not clinically respond within 2 to 4 weeks, if serum levels are not adequate, if clinical deterioration is documented, if osteomyelitis or central nervous system involvement is present, or if life-threatening blastomycosis exists.<sup>1,4</sup> A high index of suspicion for blastomycosis is essential. Its symptoms are nonspecific and can mimic other diseases. When there is a persistent pulmonary infiltrate, skin lesions, bone involvement, and a suspicious travel history, blastomycosis must be considered.

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