

SECTION EDITOR: ENID GILBERT-BARNES, MD

## Pathological Case of the Month

Mary Ann DeLeon, MD; Alan Johnson, MD

**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.

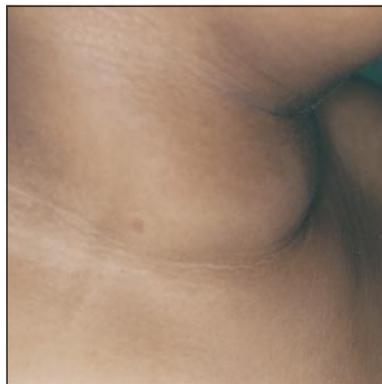


Figure 2.



Figure 3.



Figure 4.



Figure 5.

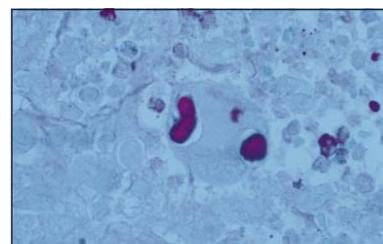


Figure 6.

# 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  $\times 400$ ).

Microscopic 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.

Accepted for publication January 1, 1999.

Reprints: Mary Ann DeLeon, MD, Children's Memorial Hospital, 2300 Children's Plaza, Chicago, IL 60614.

## REFERENCES

1. Bradsher RW. Histoplasmosis and blastomycosis. *Clin Infect Dis*. 1996;22 (suppl 2):S102-S111.
2. Kuzo RS, Goodman LR. Blastomycosis. *Semin Roentgenol*. 1996;31:45-51.
3. Lowry PW, Kelso KY, McFarland LM. Blastomycosis in Washington Parish, Louisiana, 1976-1985. *Am J Epidemiol*. 1989;130:151-159.
4. Schutze GE, Hickerson SL, Fortin EM, et al. Blastomycosis in children. *Clin Infect Dis*. 1996;22:496-502.
5. Bradsher RW. Blastomycosis. *Clin Infect Dis*. 1996;14(suppl 1):S82-S90.
6. Schutze GE. Blastomycosis. In: Feigin RD, Cherry JD, eds. *Textbook of Pediatric Infectious Diseases*. Philadelphia, Pa: WB Saunders Co; 1998.