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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.[1] 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.

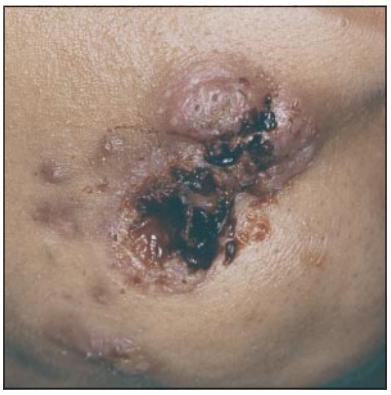

Figure 1.

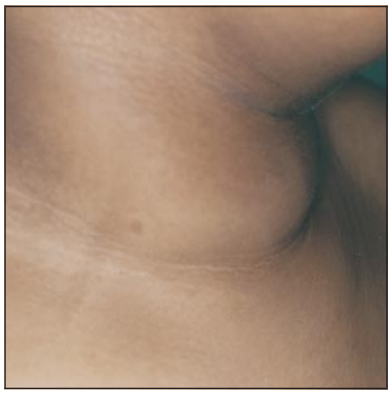

Figure 2.

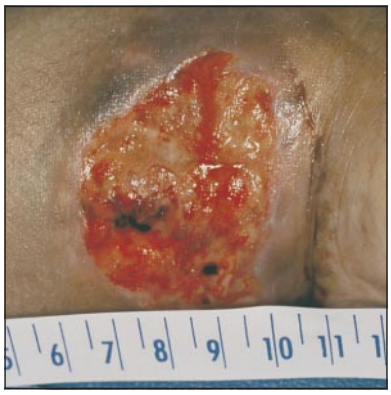

Figure 3.

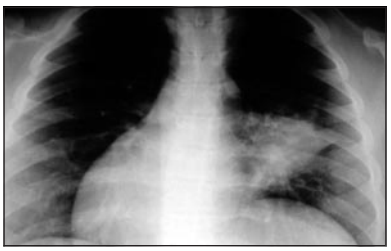

Figure 4.

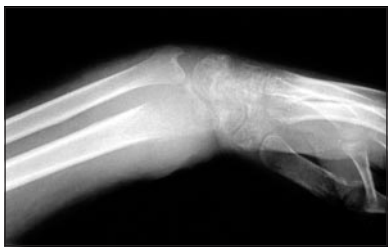

Figure 5.

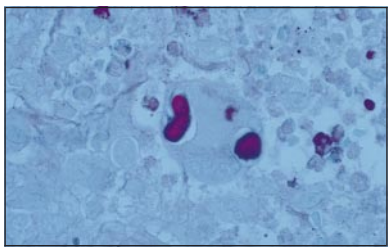

Figure 6.

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).*

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.[1,2] The US endemic area includes the Ohio and Mississippi River valleys as well as the south-central and southeastern portions of the United States.[1,3] 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.[1,4,5] The primary site of infection is the lungs after inhalation of spores from soil.[2,6] The larger spores are more resistant to phagocytosis and can succeed in transitioning to the yeast phase.[5] Over the next 4 to 8 weeks, the yeast forms proliferate, leading to an influenzalike illness.[5] Roughly 50% of infected children will develop symptomatic illness.[5]

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

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.[2] Findings from skin lesions reveal papillomatosis and downward proliferation of the epidermis with intraepidermal abscesses.[1] Hyperplasia and acanthosis suggest a diagnosis of cancer.[1] Osteomyelitis occurs in up to 25% of extrapulmonary cases with involvement of the vertebrae, pelvis, sacrum, skull, ribs, and long bones.[1] Radiographs of osteomyelitis are nonspecific and cannot be differentiated from other forms of osteomyelitis.[1] Prostatitis and epididymo-orchitis are the most common genitourinary manifestations.[1] Meningitis and epidural or cranial abscesses are the forms of central nervous system involvement.[1] Other areas of involvement include the liver, spleen, heart, lymph nodes, psoas muscle, kidney, middle ear, and adrenal and thyroid glands.[5,6]

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

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.[1] If therapy is withheld, patients must be followed carefully for evidence of reactivation or dissemination.[6] Pleural disease or extrapulmonary manifestations require antifungal therapy.[1] Amphotericin has the greatest proven efficacy, but it is associated with toxic effects.[2] Oral ketoconazole and itraconazole are only slightly less effective but have lower toxic effects and easier administration.[2] Itraconazole has replaced amphotericin as the agent of choice to treat less than life-threatening blastomycosis in adults.[4] 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.[1,4] 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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