apparent infection is much more likely. Ultimately, the T lymphocyte response—specifically, a T_H1 response—is the primary factor in limiting infection and dissemination. Moreover, yeast-phase conversion results in the expression of yeast phase–specific proteins such as the 120-kDa glycoprotein adhesin BAD-1 and the *Blastomyces* yeast phase–specific protein 1 (BYS1). BAD-1 has been well characterized as a virulence factor and is the major epitope for humoral and cellular immunity. The role of BYS1, putatively identified as a signal peptide, has not been determined.

APPROACH TO THE PATIENT: Blastomycosis

Blastomycosis most commonly presents as acute or chronic pneumonia that has been refractory to therapy with antibacterial drugs. Whether acute or chronic, blastomycosis may mimic many other disease processes. For example, acute pulmonary blastomycosis may present with signs and symptoms indistinguishable from those of bacterial pneumonia or influenza, and chronic pulmonary blastomycosis may mimic malignancy or tuberculosis. Skin lesions are often misdiagnosed as basal cell or squamous cell carcinoma, pyoderma gangrenosum, or keratoacanthoma. Laryngeal lesions are frequently mistaken for squamous cell carcinoma. Thus, the clinician must maintain a high index of suspicion and ensure that secretions or biopsy materials from patients who live in or have visited regions endemic for blastomycosis are subjected to careful histologic evaluation. This diligence is especially important in caring for individuals with pneumonia who fail to respond to treatment with antibacterial agents.

CLINICAL MANIFESTATIONS

Acute pulmonary infection is often diagnosed in association with point-source outbreaks. Typical symptoms include the abrupt onset of fever, chills, pleuritic chest pain, arthralgias, and myalgias. Cough is initially nonproductive but frequently becomes purulent as disease progresses. Chest radiographs usually reveal alveolar infiltrates with consolidation. Pleural effusions and hilar adenopathy are uncommon. Most patients diagnosed with pulmonary blastomycosis have chronic indolent pneumonia with signs and symptoms of fever, weight loss, productive cough, and hemoptysis. The most common radiologic findings are alveolar infiltrates with or without cavitation, mass lesions that mimic bronchogenic carcinoma, and fibronodular infiltrates. Hematogenous dissemination to the skin, bones, and genitourinary tract occurs most often in association with chronic pulmonary disease. Although blastomycosis is not considered an opportunistic infection, immunosuppression has been recognized as a risk factor for more serious pulmonary involvement, including respiratory failure (adult respiratory distress syndrome) associated with miliary disease or diffuse pulmonary infiltrates. In the late stages of AIDS, mortality rates of ≥50% have been documented. Most deaths occur within the first few days of therapy. Solid-organ transplant recipients with endemic fungal infections, including both histoplasmosis and blastomycosis, frequently have more severe pulmonary disease as well as dissemination. Blastomycosis has been associated with a mortality rate of 36% in these patients.

In Africa, pulmonary cases typically include bony involvement (frequently of the vertebrae), with subcutaneous abscesses of the chest wall or legs. All of the manifestations seen in African patients fall within the spectrum of blastomycosis observed in North America. The increased prevalence of chronic and disseminated bone disease in these patients may reflect a delay in diagnosis in regions where spinal disease is often treated empirically as tuberculosis.

Skin disease is the most common extrapulmonary manifestation of blastomycosis. Two types of skin lesions occur: verrucous (more common) and ulcerative. Osteomyelitis occurs in as many as one-fourth of *B. dermatitidis* infections. The vertebrae, pelvis, sacrum, skull, ribs, and long bones are most frequently involved. Patients with *B. dermatitidis* osteomyelitis often present with contiguous soft-tissue abscesses or chronic draining sinuses. In men, blastomycosis may involve the prostate and epididymis. Central nervous system (CNS) disease occurs in fewer than 5% of immunocompetent patients with blastomycosis. A recent multicenter review identified 22 patients with CNS disease, of whom 12 (54%) met at least one criterion for immunosuppression; although most cases of CNS blastomycosis are associated with infection at other sites, 22.7% of the reviewed cases had only CNS involvement. CNS disease, usually presenting as a brain abscess, has been reported in ~40% of cases in patients with AIDS. Less common forms of CNS disease are cranial or spinal epidural abscess and meningitis.

DIAGNOSIS

Definitive diagnosis of blastomycosis requires growth of the organism from sputum, bronchial washings, pus, or biopsy material. Specimens should be inoculated onto a fungal medium such as Sabouraud dextrose agar, with or without chloramphenicol. *B. dermatitidis* is generally visible in 5–10 days but may require incubation for up to 30 days if only a few organisms are present in the specimen. A presumptive diagnosis may be based on demonstration of the characteristic broad-based budding yeast by microscopic examination of wet preps of sputum in pneumonia or of skin-lesion scrapings. Serologic testing for antibodies to *B. dermatitidis* by complement fixation, immunodiffusion, or enzyme immunoassay is of little value for diagnosis because of limited sensitivity and specificity as well as cross-reactivity with other fungal antigens.

A *Blastomyces* antigen assay that detects antigen in urine and serum is commercially available and is reasonably sensitive and specific (MiraVista Diagnostics, Indianapolis, IN). Antigen detection appears to be more sensitive in urine than in serum. This antigen test may be useful for monitoring of patients during therapy or for early detection of relapse. Chemiluminescent DNA probes (AccuProbe; GenProbe Inc., San Diego, CA) are commonly used to confirm identification of *B. dermatitidis* once growth has been detected in culture. Repetitive sequence–based PCR is available (DiversiLab System; bioMérieux, Durham, NC). Molecular identification techniques are currently used only to supplement traditional diagnostic methods.

TREATMENT BLASTOMYCOSIS

The Infectious Diseases Society of America has published guidelines for the treatment of blastomycosis. Selection of an appropriate therapeutic regimen must be based on the clinical form and severity of the disease, the immune status of the patient, and the toxicity of the antifungal agent **(Table 238-1)**. Although spontaneous cures of acute pulmonary infection are well documented, there are no criteria by which to distinguish patients whose disease will progress or resolve without treatment. Thus all patients with blastomycosis should be treated.

Itraconazole is the agent of choice for immunocompetent patients with mild to moderate pulmonary or non-CNS extrapulmonary disease. Therapy is continued for 6–12 months. Amphotericin B (AmB) is the preferred initial treatment for patients who are severely immunocompromised, who have life-threatening disease or CNS disease, or whose disease progresses during treatment with itraconazole. Although not rigorously studied, lipid formulations of AmB provide an alternative for patients who cannot tolerate AmB deoxycholate. Most patients with non-CNS disease whose clinical condition improves after an initial course of AmB (usually 2 weeks in duration) can be switched to itraconazole to complete 6–12 months of therapy. Fluconazole, because of its excellent penetration of the CNS, is useful in the treatment of patients with brain abscess or meningitis after an initial course of AmB.

Voriconazole has been used successfully to treat refractory blastomycosis, blastomycosis in immunosuppressed patients, and—given