Blastomycosis in Africa: Clinical Features, Diagnosis, and Treatment


Four cases of blastomycosis seen in two acute care hospitals in Harare, Zimbabwe, are described. All patients had symptoms of at least 2 months' duration before presentation, and all had radiographic evidence of pulmonary consolidation. Three patients had confirmed bone involvement, and two had chronic discharging sinuses. The features of blastomycosis in Africa are reviewed, and problems of diagnosis and treatment are discussed. It is concluded that blastomycosis in Africa may often be misdiagnosed as tuberculosis or pyogenic infection in the absence of adequate facilities for mycologic investigation.

Blastomycosis is a systemic infection caused by the dimorphic fungus *Blastomyces dermatitidis* and most commonly affecting the lungs, skin, and bone. Originally named North American blastomycosis, the disease was believed to be restricted to the United States and Canada until 1952, when the first African case was reported from Tunisia [1]. A number of reports followed, so that by 1973 Bregant et al. [2] knew of 40 African cases. Blastomycosis has now been reported from at least 17 countries in all the major regions of Africa [3]. By far the greatest concentration of cases, however, has been in southern Africa, with 20 cases from South Africa [4] and (the present series included) 31 cases from Zimbabwe [5-7]. Many reported cases believed to have been acquired in Africa have been diagnosed elsewhere [8-10]; thus the disease appears to be underreported within Africa. Although a few isolated reports exist, blastomycosis appears to be extremely uncommon outside the North American and African continents [3].

Involvement of bone and chronic discharging sinuses have been particularly frequent features of African cases of blastomycosis [5]. The differential diagnosis of such cases includes tuberculosis, nocardiosis, and actinomycosis; since these diseases require quite different specific therapies, an accurate diagnosis is essential. No serologic test is of value in the diagnosis of blastomycosis in Africa, so the organism must be demonstrated by microscopy, by culture, or in histologic sections. Many cases of blastomycosis in Africa probably go unrecognized because of inadequacies in the special laboratory facilities required for microbiologic diagnosis and lack of awareness of the disease. We present our recent experience with blastomycosis in order to draw attention to the features of this condition in Africa and to describe the laboratory techniques that we have found appropriate in its diagnosis.

**Laboratory Methods**

Whenever possible, a representative from the mycology laboratory was present when specimens were obtained from patients with suspected deep fungal infections; the goal was to process material as quickly as possible. Wet preparations were made by direct transfer of pus from a draining abscess into a drop of saline on a microscope slide with a syringe or capillary tube. These preparations were examined immediately. If yeast cells were seen, the coverslip was sealed with petroleum jelly and the slides were incubated at 25°C for 1-4 days. The visualization of hyphae emerging from the yeast cells confirmed the dimorphic nature of the organism (figure 1). In addition, pus was inoculated immediately onto a range of media, including Sabouraud dextrose agar, brain-heart infusion (BHI) agar with chloramphenicol (50 mg/L), BHI agar with both cycloheximide (500 mg/L) and chloramphenicol, and niger seed agar. Biopsied specimens were macerated with scalpel blades and inoculated into the same media. BHI agar with cycloheximide and chloramphenicol was incubated at 25°C, Sabouraud dextrose agar at 25°C and 37°C, BHI agar with chloramphenicol at 25°C and 37°C, and niger seed agar at 37°C. Smears were made from pus and macerated biopsies and were stained with gram and periodic acid-Schiff agents. Sputum samples were examined under direct microscopy in potassium hydroxide preparations and with gram staining and were cultured in a manner similar to that described for pus.

Cells of *B. dermatitidis* were readily identified on microscopy by their distinctive single broad-based buds, their size, their thick wall, and their multinucleate structure. The mycelial phase grew in cultures on a variety of standard fungal media at 25°C within 10-18 days and was transformed to the yeast phase by subculture on enriched media (e.g., BHI agar) at 37°C for identification.

**Case Reports**

**Case 1.** A 29-year-old man presented with a 12-month history of multiple chronic discharging sinuses, initially on both feet and later around the right knee and on the left chest wall. Shortly before presentation he developed night sweats and a
Case 2. A 33-year-old man presented with a long history of discharging sinuses over the chest. Six weeks before presentation there was a sudden onset of bilateral chest pain. Four days later the patient noticed numbness in both legs and constipation alternating with diarrhea. On examination he was found to have a paraparesis as well as discharging sinuses on the anterior and right portions of the chest wall (figure 2). Radiography revealed the erosion of one rib under the site of one of the sinuses (figure 3) as well as a collapsed mid-thoracic vertebra. *B. dermatitidis* was identified by direct microscopic examination of pus discharging from the chest wall, and this identification was confirmed by culture. The patient was treated with ketoconazole (200 mg twice daily) and was discharged in markedly improved condition after 6 weeks of therapy.

Case 3. A 12-year-old boy was referred from a district hospital with a 2-month history of neck pain, weight loss, productive cough and noticed a fleshy lesion developing on his nose. Examination revealed signs of consolidation in his left upper pulmonary lobe, and this finding was confirmed by radiography, which also showed erosion of the third, fourth, and fifth ribs. *B. dermatitidis* was identified by direct microscopic examination of pus discharging from the chest wall, and this identification was confirmed by culture. The patient was treated with ketoconazole (200 mg twice daily) and was discharged in markedly improved condition after 6 weeks of therapy.
Figure 4. Blastomycosis affecting the lower cervical vertebrae (case 3).

and deformity of the posterior aspect of his neck. Chest radiography showed consolidation in the right lower zone. Radiography of his cervical spine showed collapse of the body of C7 and sclerosis of the adjacent vertebrae, suggesting chronic infection (figure 4).

The patient’s condition failed to improve during a prolonged course of empiric antituberculous chemotherapy. Surgical exploration showed the anterior longitudinal ligament to be pushed well forward by a fluctuant mass containing yellow fibrinous material. Histologic study of a tissue specimen from this site revealed the large yeast cells with single broad-based buds typical of \( B. dermatitidis \). The boy was treated with amphotericin B and made a satisfactory recovery.

Case 4. A 38-year-old Mozambican woman complained of cough, thoracic back pain, and weight loss over the previous 3 months. She had received 1 month of treatment for tuberculosis in Mozambique, without benefit, before referral to Harare. She was found to be cachectic and tachypneic, with widespread crackles on chest auscultation. There was tenderness over the upper thoracic spine but no deformity or neurologic impairment. A chest radiograph confirmed widespread consolidation with cavitation compatible with tuberculosis (figure 5).

Antituberculous chemotherapy was continued during further investigation. \( B. dermatitidis \) was seen in sputum by direct microscopic examination on the fifth day of hospitalization, and its identity was later confirmed by culture. The patient died before antifungal therapy could be instituted.

Figure 5. Widespread pulmonary consolidation due to blastomycosis (case 4).

Discussion

The clinical features and natural history of blastomycosis in North America have been described in some detail. Features of the chronic syndrome include suppurative or granulomatous pulmonary disease that often resembles tuberculosis, localized granulomatous skin lesions, bone involvement, and subcutaneous suppuration with discharging sinuses [11]. More recently, acute pneumonia has been recognized and may in fact be the most common clinical manifestation. There is nothing distinctive about this acute illness, which is associated with a variety of radiographic changes, including segmental consolidation, diffuse patchy shadowing, and solitary coin lesions [12]. Most such cases appear to resolve completely without specific treatment [13]. Unlike other deep mycoses, blastomycosis is rarely opportunistic.

There is evidence that African strains of \( B. dermatitidis \) differ from North American strains [14]. In particular, antigen A—the most specific antigen detected in immunodiffusion experiments with North American isolates—is absent from African strains [15]. The pattern of clinical manifestations in African cases also differs from the North American experience. Only chronic disease has been reported in Africa. Bone involvement has been a frequent feature, occurring in 15 of the 21 cases reviewed by Ross and Gelfand [5], with vertebral disease (including paraplegia) particularly prominent. Subcutaneous suppuration, usually on the chest wall or the legs, is also common and purely cutaneous granulomatous disease rather less common. The present series conforms to this pattern, with three cases of confirmed bone disease, including two with vertebral involvement. In addition, all of our cases had evidence of pulmonary disease—none of the commonest features both in North American cases and in those African cases that have been described in detail. None of the
manifestations described in Africans falls outside the known spectrum of blastomycosis in North America, and, despite differences in the prevalent strains of *B. dermatitidis*, it is not clear whether the natural history of the disease is significantly different on the two continents. The apparent excess of bone disease and cutaneous sinuses in the reported African cases may reflect late presentation in Africa or less awareness of some of the other presentations of blastomycosis.

The two acute care hospitals in Harare have had more experience with blastomycosis than most centers in Africa. Nevertheless, in only two of the four cases described herein (cases 1 and 2) was blastomycosis the initial clinical diagnosis. Multiple discharging sinuses suggest the possibility of fungal infection to most physicians, whereas chronic pulmonary disease, granulomatous skin lesions, and isolated bone lesions are more likely to be attributed to tuberculosis or pyogenic bacterial infection. Blastomycosis will not be recognized in cases with the latter manifestations unless an appropriate search for the organism is undertaken. We have found simple techniques of direct microscopy to be useful in identifying *B. dermatitidis*. Because of its characteristic appearance, this organism is unlikely to be confused with any other fungal pathogen.

When few organisms are present (as in chronic granulomatous skin lesions), differentiation from tuberculosis may be particularly difficult. Problems are also encountered (as in case 3) when the site of infection is not readily accessible. The common practice in developing countries of treating spinal disease as tuberculosis on the grounds of radiographic evidence only, while no doubt often justified as a practical expedient, inevitably results in the overlooking of other chronic infections. If a patient’s progress during empiric antituberculous therapy is not satisfactory, there is no alternative to obtaining diagnostic material directly from the site of disease. In our experience, erosion of adjacent transverse processes, pedicles, and ribs as well as severe erosion of cortical surfaces of the vertebral bodies, with cavity formation and surrounding increased density, may provide a clue to the fungal etiology of vertebral disease.

The efficacy of amphotericin B in blastomycosis is well established; because of the toxicity, discomfort, and expense associated with this agent, however, newer drugs have also been assessed. Particularly in Africa, the complexities of administering amphotericin B are daunting, and the supply of the drug is likely to be limited. Thus the incentive to use other drugs is strong. Ketoconazole in doses of at least 400 mg/d is effective in 75%–80% of cases [16, 17] if given for 6 months. There have been several reports of failure with ketoconazole, however [18, 19], and amphotericin B remains the drug of choice for life-threatening infections and in cases with bone involvement. Failure to administer amphotericin B immediately as the first line of treatment may well have contributed to the poor outcome of case 2. Itraconazole has not yet been fully assessed in blastomycosis, but first reports suggest that it may be effective [20–23].

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References