Recurrent Blastomycosis of the Central Nervous System: Case Report and Review

Although blastomycosis of the central nervous system (CNS) occurs in ~4% of patients with blastomycosis, recurrent CNS blastomycosis is very rare. We review the clinical features, treatment, and outcome of 4 previously reported cases. We also report a case of recurrent CNS blastomycosis successfully treated with surgery and liposomal amphotericin B after an inadequate response to amphotericin B therapy. This treatment may be an alternate approach for management of similar cases.

Recurrent CNS blastomycosis is very rare [1-4] and may present either as meningitis or as a space-occupying lesion. We describe a patient with recurrent CNS blastomycosis that occurred 3 years after the first episode and review the management of recurrent CNS blastomycosis.

In March 1998, a 54-year-old man presented with a 3-week history of gradual weakness and numbness of the left arm and leg. Comorbid conditions included diabetes mellitus, hypertension, hypercholesterolemia, status post myocardial infarction, right hemiparesis, right eye blindness, renal insufficiency, and history of pulmonary blastomycosis treated with itraconazole.

He was treated for a cerebellar blastomyctoma in March 1995 with surgery and amphotericin B (3251 mg). Clinical or radiological recurrence was not noted in the following 18 months.

Physical examination revealed decreased leg strength and visual field neglect on the left. The erythrocyte sedimentation rate was 52 mm/h, WBC count was 10 × 10⁶ cells/L, and HIV serology was negative. Levels of serum electrolytes, albumin, and transaminases were normal. Brain MRI showed a multilocular right cerebral abscess with associated edema (figure 1). Recurrence of CNS blastomycosis was diagnosed, albeit at a different anatomic location.

He was treated with phenytoin and dexamethasone. The following day, 10 mL of purulent material was aspirated; culture from the material yielded Blastomyces dermatitidis. Although he initially regained strength, he developed left-hand clumsiness that did not respond to a higher dose of dexamethasone. The brain abscess was excised when a brain MRI showed that it had increased in size. The cerebral cortex showed chronic inflammation, with giant cells containing B. dermatitidis. No fungi were isolated from cultures of brain, blood, or urine specimens. Treatment was begun with amphotericin B colloidal dispersion (ABCD; Amphotec, Sequus Pharmaceuticals, Menlo Park, CA). Amphotericin B treatment was restarted when no further recurrence was noted clinically or by MRI.

The subsequent hospital stay was uneventful, and the patient was discharged home; thrice weekly amphotericin B was prescribed at discharge. In June 1998, the patient underwent cholecystectomy. B. dermatitidis was not seen in the gallbladder. In November 1998, he was declared dead on arrival at a local hospital. An autopsy was not done. The cause of death, while suspected to be cardiac, is unknown.

Approximately 2.5% of patients with pulmonary or systemic blastomycosis develop CNS involvement [5, 6]. Recurrent CNS blastomycosis is very rare; in addition to the case we describe here, only 4 other cases have been reported [1-4]. These cases are summarized in table 1. All cases had initial pulmonary or skin involvement. The initial episode of CNS blastomycosis was diagnosed after variable intervals and different treatment modalities were used for management. Recurrent CNS blastomycosis presented as meningitis [2-4], cerebral mass [1]; our patient was the only one who developed an abscess in the primary and recurrent episodes of CNS blastomycosis. Two patients died, 1 after suboptimal treatment [3] and the other of presumed cardiac causes.

We reviewed the current data on drug therapy for primary and recurrent CNS blastomycosis. Our review included information from MEDLINE searches (1966-1999), textbooks, individual articles (especially for the years before 1966), and the articles referenced in textbooks and individual articles. The drug of choice for treatment of CNS blastomycosis is amphotericin B [7]. Table 1 demonstrates that CNS blastomycosis can recur despite the use of appropriate doses of amphotericin B, suggesting that it may not be the drug of choice for treating recurrent CNS blastomycosis. Because CNS blastomycosis can occur after azole treatment of pulmonary blastomycosis [1, 2, 8], these agents should not be used to treat CNS blastomycosis. However, because it achieves higher CSF concentrations than other azoles [9], fluconazole may be an exception. But, other than case reports [10, 11], there are insufficient data to suggest that fluconazole is as effective as amphotericin B in treating CNS blastomycosis. Flucytosine also penetrates the CNS well [12], although there is...
only 1 report of its use to treat CNS blastomycosis [11]. Flucytosine and fluconazole should probably be reserved for extraordinary situations.

Following administration of iv amphotericin B, CSF levels of amphotericin B are <1% of plasma levels [13]. Liposomal amphotericin B achieves higher tissue levels [14], and CNS concentrations of amphotericin B in mice are 3 times higher after administration of liposomal amphotericin B than after administration of amphotericin B (Hetty Waskin, The Liposome Company, personal communication). We believed that this patient’s clinical response was poor was due to inadequate CNS penetration of amphotericin B. Given these facts, we chose to start ABCD treatment. Approximately 5 g of amphotericin B was given before 10 g of ABCD; the cumulative dose was tolerated without any deterioration in hematologic or renal status.

Although immunosuppression predisposes to infection, its role in recurrence is unknown. The reason for recurrence of CNS blastomycosis is also unknown. It may be due to reactivation of dormant microfoci of *B. dermatitidis*. Alternately, it may represent new infection, which would imply that low CNS levels of
amphotericin B are adequate to eradicate all viable *B. dermatitidis* when treating primary CNS blastomycosis. PCR analysis of specimens obtained during episodes of CNS blastomycosis could help differentiate between reinfection and reactivation.

On the basis of the recommendations for the treatment of primary CNS blastomycosis that were reported by Ward et al. [15] and the above-mentioned facts, we developed the following management strategy for this patient. First, surgically resect the mass and/or abscess. The initial use of CT-guided aspiration and amphotericin B was inadequate for treating CNS blastomycosis in this case. Second, after surgery, treat with liposomal amphotericin B. An empirical dose would range from 5 to 10 g. Third, continue long-term antifungal therapy with outpatient amphotericin B administration. For our patient, the total amphotericin B dose given was empirically doubled from that given in 1995. Fourth, follow the patient closely with physical examinations and brain scans (CT or MRI) 3 months after therapy is completed and every 6 months thereafter for at least 36 months. Physicians who encounter similar situations could tailor this information to the clinical situation they face.

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References


Peritoneal Coccidioidomy: Case Report and Review

Peritonitis is an unusual extrapulmonary manifestation of coccidioidomy. Peritoneal involvement often has an indolent course and may resolve spontaneously. Optimal management has not been defined; however, fluconazole’s spectrum of activity, pharmacokinetic profile, and efficacy in dialysis-related yeast peritonitis suggest that it may be an effective treatment. To our knowledge, we report the first case of coccidioidal peritonitis treated with fluconazole and review the literature.

Less than 1% of individuals with coccidioidomy will develop extrapulmonary disease, which usually involves the skin, CNS, bones, or joints [1]. Almost any site may be infected; however, gastrointestinal tract involvement is rare. As for other diseases that are not reportable, the true incidence of this entity is probably underestimated. Coccidioidal peritonitis was first reported by Ruddock and Hope [2] in 1939. We identified 25 previously reported cases [2–10] (table 1); most of these patients were treated before the availability of azole antifungal drugs. To our knowledge, we report the first case of coccidioidal peritonitis treated successfully with fluconazole and review the literature.

A 71-year-old white Canadian woman presented in May 1993 with a 2-month history of increasing abdominal girth associated with vaginal prolapse, anorexia, and a 5-lb weight loss. However, she denied abdominal pain, fevers, night sweats, and previous pneumonia. She had been successfully treated with chlorambucil and prednisone in 1991 for low-grade non-Hodgkin’s lymphoma. She had spent the winters in Arizona during the previous 10 years.

Physical examination was notable for peripheral wasting and marked abdominal distension due to ascites. A chest radiograph revealed bilateral pleural effusions but no parenchymal disease. Paracentesis revealed turbid yellow ascitic fluid. Analysis of the fluid revealed the following: lactate dehydrogenase level, 805 U/L; glucose level, 4.6 mmol/L; protein level, 44 g/L;...