Case Report

**Intracranial blastomycotic abscess mimicking malignant brain neoplasm: Successful treatment with voriconazole and surgery**

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Received: 01 July 15  Accepted: 09 September 15  Published: 20 November 15

**Abstract**

**Background:** Cerebral blastomycosis is a rarely reported disease, and in the absence of associated, underlying systemic infection, poses a great diagnostic difficulty. Magnetic resonance imaging can sometimes provide equivocal information when trying to pinpoint a diagnosis. Classically, cerebral blastomycosis has been treated with amphotericin B. Voriconazole is a newer triazole antifungal with potential as a follow-up treatment of blastomycosis of the central nervous system after initial therapy with amphotericin B.

**Case Description:** We describe one such case of a cerebral blastomycotic abscess, presenting in the absence of any systemic disease, which was initially thought to be a neoplasm. It was successfully treated by surgical resection followed by sequential amphotericin B and voriconazole. The patient did well with voriconazole therapy and was followed for voriconazole tolerance with liver function tests, which continued to be stable at 8 months past the initiation of therapy. At 12 months postoperatively, the patient was doing well and showed gradual improvement in a visual field cut, with no sign of recurrent infection.

**Conclusions:** Isolated cerebral blastomycosis can present a diagnostic challenge. In the absence of systemic infection, surgical resection followed by antifungal therapy is a logical treatment plan.

**Key Words:** Blastomycotic abscess, cerebral blastomycosis, voriconazole

**INTRODUCTION**

Blastomycosis is an uncommon but often serious mycosis, endemic in the Southeastern and the Central United States. Approximately, 800 hospitalizations occur annually in the United States for blastomycosis, of which 6% result in death.[1] It is primarily a disease of the lung and is characterized by suppurative and granulomatous lesions in the lungs, skin, bones, and genito-urinary tract.[9,12,15,16] Central nervous system (CNS) involvement is rare, reported in about 4–10% of cases.[9] When present, it is almost invariably associated with the involvement of other organs, and it is often the result of hematogenous dissemination from a pulmonary source.[15,17] Cases presenting with solitary or multiple intracranial mass...
lesions in the absence of systemic infection are extremely rare, though they have been documented and have often been mistaken for brain neoplasms.\(^2\),\(^3\),\(^15\),\(^19\)

Once diagnosed, intracranial blastomycosis has classically been treated with amphotericin B deoxycholate or lipid formulations of amphotericin B.\(^18\) Voriconazole, an azole antifungal, has shown promise as a treatment option for CNS blastomycosis. Clinical experience with voriconazole as a part of the treatment regimen for CNS blastomycosis is limited.\(^1\),\(^2\),\(^4\),\(^8\),\(^14\)

This report discusses a case of a 37 year old, otherwise healthy, nondiabetic, and immunocompetent, white man presenting with an isolated left temporo-occipital mass lesion, identified as *Blastomyces dermatitidis*, and successfully treated with surgical resection, followed by the sequential use of amphotericin B and voriconazole.

**HISTORY**

A 37-year-old, ambidextrous taxidermist presented to ophthalmology clinic at the University of Alabama at Birmingham Hospital with a several year history of visual floaters of the right eye and intermittent decreased hearing on the left. He complained of worsening symptoms over the previous 8 months with intermittent sensations of pressure behind the right eye, difficulty with balance and ambulation, difficulty reading, and mild headaches. He also described poorly defined problems with cognition. He did not report the impairment of speech, language, or comprehension. His past medical and surgical histories were unremarkable. He denied the use of tobacco or intravenous drugs and indicated infrequent alcohol use.

**Examination**

On physical examination, significant findings included a small right inferior quadrantanopia to confrontational examination. Automated visual fields documented the presence of a congruous inferior quadrantanopia. His neurologic examination was otherwise normal. No abnormal skin findings were present.

**Work-up**

An magnetic resonance imaging (MRI) of the brain was obtained and revealed two closely associated large, heterogeneous, left temporo-occipital lesions with mass effect. The lesions were heterogeneously enhancing on T1-weighted images, and T2-weighted images showed changes consistent with edema extending through the temporal and occipital lobes. Diffusion-weighted imaging demonstrated equivocal increased signal intensity within the lesions. A low apparent diffusion coefficient (ADC) was not seen on the ADC map, as is typical with a cerebral abscess. While closely associated with the convexity dura and the tentorium, the masses appeared to be intra-axial, and were interpreted as most consistent with malignant glioma or metastatic lesion [Figure 1]. Of note, his blood profile indicated mild leukocytosis (12 × 10\(^3\)/mm\(^3\)) and predominantly neutrophilic (74%). Lumbar puncture was deferred because of intracranial mass effect. Body imaging did not reveal extracranial lesions and urine cultures were negative.

**Operation and initial treatment**

For diagnosis and therapy, the patient was taken to the operating room for a neuronavigation-guided resection of the mass via a temporo-occipital craniotomy with ultrasound assistance in delineating the borders of the lesion. The intra-operative specimen appeared to be a fungal abscess on frozen section evaluation. The abscess was resected [Figure 2] and the patient was started on intravenous lipid complex amphotericin B and flucytosine, which he received for approximately 3 weeks. The microbiology cultures demonstrated *B. dermatitidis*. The amphotericin B and flucytosine were stopped and the patient was electively prescribed oral voriconazole 200 mg twice a day.

**Neuropathology**

Histopathology revealed a granulomatous process with encapsulated yeast forms. Numerous multinucleated giant cells were present, some of which contained fungal organisms, which were small, refractile, and variably-sized. A CD163 stain demonstrated abundant macrophages, and also highlighted the larger, multinucleated histiocytic giant cells [Figure 3]. The fungal organisms were positive for both periodic acid-Schiff and Gomori’s methenamine silver [Figure 4] stains. There was an abundance of T cells, with a slight predominance of the CD4 helper/inducer subset as compared to the CD8 cytotoxic/suppressor subset [Figure 5]. Natural killer...
cells were rarely present [Figure 6]. The abscess displayed a sharp border with the underlying gliotic brain tissue.

Follow-up
The patient did well with voriconazole therapy and was followed up for possible voriconazole toxicity with liver function tests, which continued to be stable at 8 months past the initiation of therapy. Due to the development of photosensitivity and some areas of cutaneous erythema, voriconazole was stopped after 7 months of therapy and switched to oral fluconazole 800 mg daily. This was continued for 3 months. At 12 months postoperatively, the patient was doing well and showed gradual improvement in his visual field deficit. His MRI at this time showed small lobulated areas of enhancement that were interpreted as postsurgical change and not a recurrence of the abscess [Figure 7]. All antifungal therapy was stopped. The patient has continued to do well at 2½ years postoperatively with a stable right inferior quadrantanopia on ophthalmologic examination.

DISCUSSION
Blastomycosis is a systemic fungal infection caused by a dimorphic fungus B. dermatitidis. A disease of worldwide distribution, it is found to be endemic in the Ohio and Mississippi river valleys of the United States, as well as Central Canada.

It is primarily a disease of the lung, though secondary dissemination to skin, bones genito-urinary tract, and rarely CNS has been documented.6,13,15 CNS involvement is most frequently secondary to systemic blastomycosis and may manifest as acute or chronic meningitis, spinal masses, and intracranial mass lesions, which are usually multiple.2,9,12,15,16 Solitary lesions without systemic disease as described in this case report have been rarely described in the literature.2,3,19 Solitary, or in this case, multiple-enhancing brain lesions are difficult or impossible to diagnose without direct examination of the tissue and warrant surgical excision since skin tests are unreliable and attempts to culture the organism from spinal fluid are futile.10,12 Diagnosis of the fungal species by culture may take 3–4 weeks.

The guidelines published by the Mycosis Study Group under the auspices of the Infectious Disease Society of America in 2008 recommend the intravenous amphotericin B lipid formulations as first line treatment for CNS blastomycosis.5 The use of amphotericin...
B is often limited by nephrotoxicity with prolonged use; therefore follow-up with another class of antifungals - the azoles (fluconazole, itraconazole, and voriconazole) - after initial therapy with amphotericin B is also recommended. Voriconazole is a broad-spectrum triazole antifungal, which has excellent blood-brain penetration independent of meningeal inflammation. It has emerged as a potential first line treatment option for CNS blastomycosis. The clinical experience with voriconazole in treating CNS blastomycosis in humans is limited. Review of the literature revealed that many were cases of systemic blastomycosis with secondary CNS involvement, which had been treated with amphotericin B and other azoles on multiple occasions before initiating treatment with voriconazole. Furthermore, most involved only medical management and surgical excision was not the part of the treatment plan. Our patient, electively started on voriconazole after surgical excision and a course of amphotericin B, showed a favorable response and continued to improve 12 months postoperatively.

While an isolated visual field deficit can be difficult to detect if it is subtle, this case report emphasizes the importance of full visual field examination as part of a neurological examination. While we do not believe that the abscess was related to some of the patient’s initial complaints, such as the visual floaters and decreased hearing on the left, we are certain that the lesion does explain the visual field deficits found on examination. A congruous and right sided quadrantanopia fits with a lesion in the left occipital lobe, which was the location of our patient’s abscess. Furthermore, our patient had improvement in visual fields after the resection of the abscess. MRI evaluation of blastomycosis can be difficult, and these lesions can appear consistent with intracranial malignancies or other infectious conditions. In addition, it is rare, but possible, to have an intracranial fungal abscess without systemic disease. Our patient had no risk factors for infection nor any evidence of any systemic malignancy and thus surgical treatment was the logical approach to both diagnosis and treatment.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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