Treatment of Primary Aspergilloma of the Central Nervous System in a Diabetic Immunocompetent Patient with Surgical Resection and Voriconazole: A Case Report and Review of the Literature

ABSTRACT

Fungal infections of the central nervous system (CNS) are uncommon and occur mainly in immunocompromised patients. We describe a case of central nervous system aspergilloma without any evidence of systemic or paranasal foci in a diabetic but otherwise immunocompetent 71-year-old female treated successfully with surgical resection and medical therapy with voriconazole. Magnetic resonance imaging (MRI) after 6 months of voriconazole showed improvement and no evidence of residual or recurrent disease. Given its good CNS penetration, voriconazole along with surgical resection appears to be promising in treatment of these infections. Our case also demonstrates the importance of surgical intervention in the diagnosis and management of these atypical cases.

KEYWORDS: Aspergillus, Central nervous system, Voriconazole

INTRODUCTION

Aspergillus is a common fungus that lives in the soil and decaying vegetation and is ubiquitous throughout the world (2). In general, these fungi are organisms of low pathogenicity, emerging as opportunistic organisms in a compromised host, however, infections in immunocompetent hosts have also been described (11).

The primary sites of infection are the lungs and the paranasal sinuses in immunosuppressed subjects though gastrointestinal and skin infection can occur. More rarely a central nervous system (CNS) primary infection can occur without an extracranial source with involvement of the cerebral parenchyma, the meninges or the vascular system (17).

Here we present a case of CNS aspergillosis in a diabetic but otherwise immunocompetent person with no other obvious extra cranial source, which was successfully treated with voriconazole after undergoing partial resection. This case illustrates the importance of obtaining biopsy specimens and surgical resection in conjunction with voriconazole in the management of these difficult to diagnose cases.

CASE REPORT

A 71-year-old Pakistani female was admitted to our hospital with new onset of seizures and headache. Her history...
included type 2 diabetes mellitus, which was well controlled prior to admission. Examination was unrevealing with no focal deficits. Magnetic resonance imaging (MRI) of the brain showed a 3 cm right temporal enhancing mass (Figure 1,2). She underwent a stereotactic biopsy of the lesion. Pathology revealed fungal organisms with branching septate hyphae consistent with Aspergillus, cultures however remained negative. Voriconazole was started. Subsequently, she underwent partial resection of the lesion. Her workup for extra cranial source including CT and MRIs of sinuses, CT chest, a 2-dimensional echocardiogram and fungal blood cultures were negative. She was HIV negative and other than her diabetes had no immune compromise. She was treated with a 6-month course of voriconazole orally.

**Figure 1:** Coronal Post Gadolinium T1 weighted MRI showing Right temporal lobe lesion and surrounding edema.

**Figure 2:** Axial Flare T2 weighted MRI with water suppression showing Right basal ganglia/temporal lobe lesion

**Figure 3:** Axial flare T2 weighted MRI with water suppression 3 months into treatment showing improved Right basal ganglia/temporal lobe lesion.

**Figure 4:** Coronal Post Gadolinium T1 weighted MRI 3 months into treatment demonstrating improved Right temporal lobe lesion.
DISCUSSION

Central nervous system aspergillosis is an uncommon infection mainly occurring in the immunocompromised. It accounts for 5% of all intracranial fungal infections (24). It can manifest with acute onset of focal neurologic deficits. In those with paranasal disease, orbital involvement can be seen. Presenting symptoms include convulsions, fever, hemiparesis, cranial nerve deficits, paralysis and sensory impairment. Features of meningitis and subarachnoid hemorrhage resulting from mycotic aneurysms may occur (11,26).

Of late a newer class of patients have been recognized, those who are apparently immunocompetent, harboring CNS fungal infections. Case reports of atypical cases of aspergillosis in immunocompetent patients include vertebral osteomyelitis (26), skull base osteomyelitis (23), and infections of vascular grafts, have also been described (4).

Cranio-cerebral aspergillosis in immunocompetent hosts has been reported mainly from Pakistan, India, Saudi Arabia, Sudan, and other African countries (1,3,14,19). This prevalence in immunocompetent hosts is thought to be related to tropical hot and dry conditions, bad hygiene, and poor socioeconomic status (1,3,15). The mechanism causing invasiveness of aspergillosis in immunologically competent hosts remains unclear, but is thought to be unrecognized or poorly characterized qualitative cellular or sub cellular immunodeficiency (24). These cases present an interesting diagnostic dilemma for physicians and surgeons as the patient being immunocompetent, the possibility of fungal infection is considered low on the list of differentials. Surgical biopsy is therefore very important in establishing diagnosis.

The diagnosis of CNS aspergillosis can be aided by the use of cultures and neuroradiology. The characteristic findings of CNS disease are multiple infarctions or hemorrhages due to the angio-invasive nature of the fungus, particularly in immunocompromised patients. In immunocompetent individuals, the usual finding is a mass lesion with a thick irregular wall. The characteristic branching septate hyphae and conidia of Aspergillus species are seen on pathology (11).

Clinical outcomes in cranio-cerebral aspergillosis depend on the severity of the infective process and immune status of the patient (7,16). Mortality remains high and a case series from Pakistan of twenty-five immunocompetent patients with CNS aspergillosis showed an overall mortality of 28% when treated with itraconazole (22). Most case series recommend radical surgical excision followed by aggressive antifungal chemotherapy (1,7,19,25). In our patient, medical therapy in conjunction with surgical resection using voriconazole was successfully attempted.

Voriconazole is a broad-spectrum triazole that is active in vitro against various yeasts and molds, including Aspergillus species (9). Other antifungal agents including itraconazole, and caspofungin show negligible levels in cerebrospinal fluid or brain tissue (5,6,10,13). However, voriconazole has shown good penetration into the central nervous system in humans with a cerebrospinal fluid-to-plasma ratio of 0.22 to 1. In addition, high voriconazole brain tissue levels were found at autopsy in two patients with pulmonary aspergillosis, indicating that voriconazole is enriched in brain tissue (18). In a large randomized trial, initial therapy with voriconazole has shown superior efficacy compared to that with amphotericin B in all forms of invasive aspergillosis (12). Moreover, voriconazole has been used successfully in a few patients with CNS aspergillosis (8,20,21).

In immunocompetent hosts, mortality ranges from 40-80% (24). Patients with mainly sinonasal disease carry a good prognosis with mortality less than 20% and outcomes in extradural aspergillosis are better than intracerebral involvement (24).

To our knowledge this is one of the few documented cases of successful treatment of CNS aspergillosis in an otherwise immunocompetent patient with oral voriconazole after surgical resection. CNS aspergillosis should be considered a part of the differential in otherwise immunocompetent patients particularly from the tropical regions presenting with CNS lesions. Obtaining a biopsy is essential to diagnose these atypical cases. Our case also illustrates the importance of surgical resection in the treatment of these cases. Given its good CNS penetration, voriconazole therapy appears to be promising in treatment of these infections.

REFERENCES

Koshy R and Malhotra P: Treatment of Primary Aspergilloma of the Central Nervous System