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Case Report

Cerebral Mucormycosis in an Immunocompetent Patient: A Case Report

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Abstract :

Mucormycosis is a fungus found in the environment. In an immunocompetent person, it may cause localized infection. Invasive Mucormycosis has a poor prognosis. We describe a case of cerebral mucormycosis in an immune competent patient. A 46-year-old man was admitted with seizures and headaches. Magnetic resonance imaging (MRI) of the brain showed contrast enhancing lesion at the right frontal region. Excision biopsies showed granulomatous reactions, compatible with mucormycosis. Amphotericin B was begun. The results of testing for human immunodeficiency virus (HIV) were negative. Unfortunately the patient died on twenty-fifth postoperative day. Most cases of invasive mucormycosis show that this organism is pathogenic in immuno-compromised patients; however, some case reports show that invasive mucormycosis may not be so rare in immunocompetent patients. In these patients, virulent and drug-resistant forms of mucormycosis may be responsible for the disease, and treatment with antifungal agents are often ineffective, so that surgical excision is required.

Keywords: *Mucormycosis; Brain abscess; Meningitis; Immunocompetence; Mycoses; Voriconazole; Amphotericin B*

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Introduction:

Of all the fungi identified, only 300 may show virulence to humans, and only 10–15% of these could influence the CNS. Clinically relevant fungi being etiological agents of fungal infections of the CNS include yeasts, filamentous fungi, and dimorphic fungi. Mucormycetes are filamentous fungi that cause CNS infection[1]. Rhinocerebral mucormycosis is a life-threatening infection caused by saprophytic fungi belonging to the genera *Mucor*, *Rhizopus* and *Absidia*. All of these

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belong to the order Mucorales and class *Zygomycetes*[2].

Mucormycosis is the third most common invasive fungal infection with high morbidity and mortality. The disease is prevalent in uncontrolled diabetic patients of India, Despite the rise in awareness of the disease, the early diagnosis of mucormycosis remains elusive due to difficulty in sample collection from deep tissues and absence of a biomarker. In recent years polymerase chain reaction (PCR) for early diagnosis of mucormycosis has been evaluated with good results, but no standardized commercial kit is still available for routine use[3].

The most prominent clinical manifestation of mucormycosis is vascular invasion that results in thrombosis, infarction and tissue necrosis. Infarction alone results in hypoxia and acidosis, promoting fungal growth in the tissue. The fungus enters the nasal mucosa and proliferates, invading the paranasal sinuses and the palate[4]. Penetration of pathogen across the blood–brain barrier (BBB) is an essential step for CNS invasion. Three mechanisms have been described for pathogens to cross the BBB: trans-cellular migration, para-cellular migration, and the Trojan Horse Mechanism[1].

The most pathogenic are *Mucor*, *Rhizopus*, *Absidia*, *Cunninghamella* spp., and *Lichtheimia corymbifera*. In a review of 96 mucormycosis cases from literature, the most frequent pathogens were *Rhizopus* spp. (31%), followed by *Mucor* spp.(15%)[5]. Risk factors for *Mucor* infection are hematological malignancies, immunosuppression states, prolonged neutropenia, chronic corticosteroid therapy, hematopoietic stem cell and kidney transplantation, diabetes, renal failure, injectable drug users, trauma, malnutrition, iron overload, and the use of deferoxamine chelation therapy. Uncommonly, mucormycosis can affect immunocompetent subjects, mainly when the skin barrier is affected in wounds and burns[5]. In a review of published cases, rhino-orbital was the predominant site of infection (38.5%, of which 43% also had CNS involvement),followed by disseminated disease (22%)[5].

Isavuconazole, a new antifungal agent has been introduced in managing mucormycosis, but the drug is not available in Indian market. Amphotericin B, oral posaconazole liquid suspension, and occasionally deferasirox are used to treat mucormycosis patients in that country. Total of 107 cases (27.6%) were diagnosed as probable mucormycosis. The male to female ratio was 2.3:1(271:117) and the median age of the patients was 45.5 years (range, 1 month to 85 years)[3].

Case report:

A 46 year old non-hypertensive nondiabetic man was admitted to the Department of

Neurosurgery, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh hospital with generalized tonic clonic seizure starting from the left side body and weakness of left side of the body for 8 months, headache for 1 year and vomiting for 2/3 months. His headache was mild and had started from the right side. His tonic clonic seizure would start from the left hand then would spread to the whole body, without losing consciousness. He had no history of trauma, fever or night sweat. He was diagnosed as a patient of epilepsy and was treated with antiepileptic drugs.

His MRI revealed a contrast enhancing lesion in the right frontal lobe. It had central necrosis with marked peri-lesional edema and midline shifting. The radiological diagnosis was glioblastoma and patient was prepared for surgery. (Fig: 1).

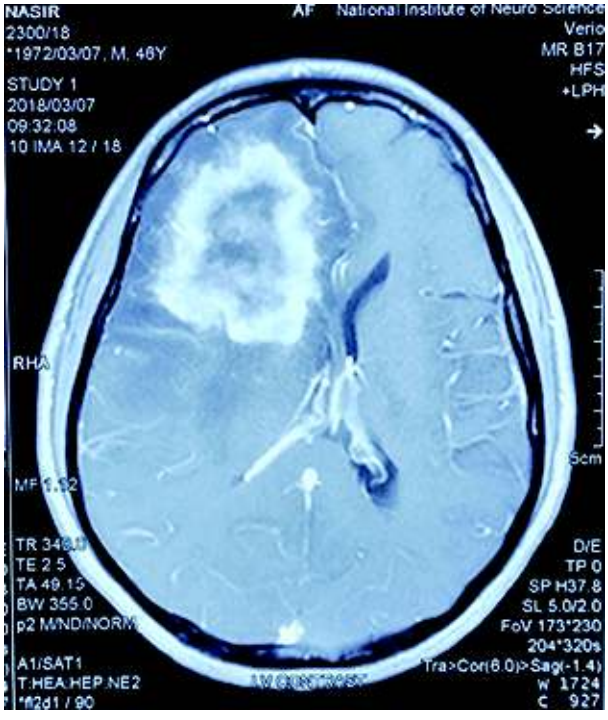

Fig.-1: *MRI of brain axial section with contrast in T1 showing inhomogeneous contrast enhancing lesion at the rt. Frontal region.*

He had undergone right frontal craniotomy and removal of tumor. The tumour was partly suckable, without any cleavage plane and grayish in colour. It had no capsule. The tumour was moderately haemorrhagic. It was removed in piecemeal.

The histopathological report was “sections of brain tissue reveal foreign body granuloma,fibrous tissue and infiltration by lymphocytic plasma cells and eosinophills. Broad fungal hyphae are present in the granulomas and within the giant cells. Angioinvasion are present, hyphae are broad, PAS negative and show obtuse angle branching. Impression: fungal granuloma compatible with mucormycosis”.

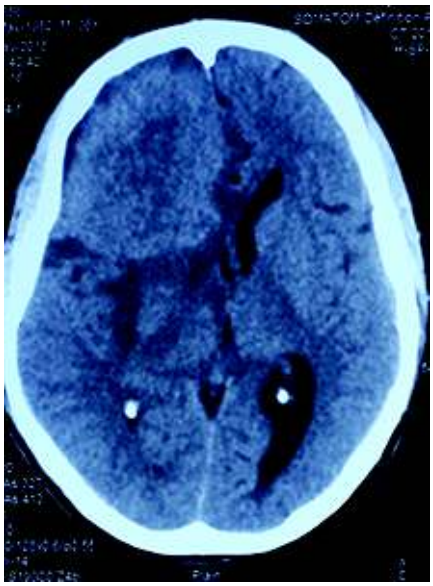

Fig.-2: *Pre operative CT scan showing the tumour on the rt. Frontal lobe*

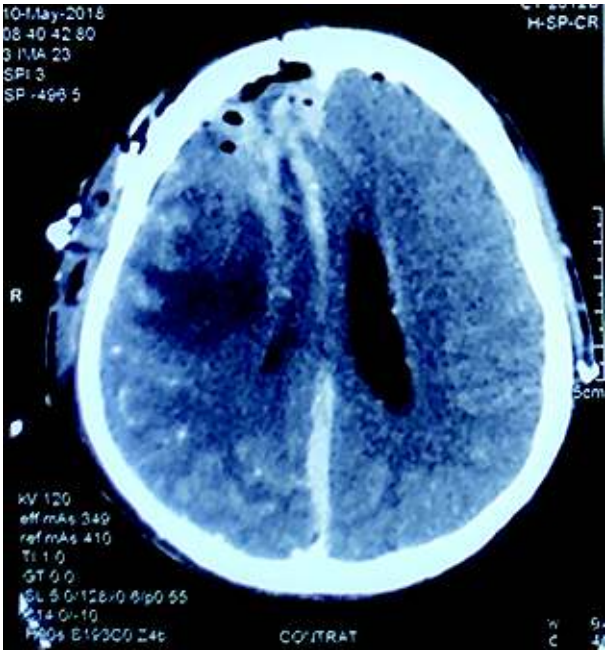

Fig.-3: *Contrast CT scan showing residual lesion .*

After surgery the patient had improved. On the 3rd post operative day he had developed CSF rhinorhoea and which was treated successfully with lumber drainage. The patient was treated with amphotericin B and fluconazole. Slowly the patient started to deteriorate and on the 25th POD he died.

Discussion:

Mucormycosis is an invasive and potentially fatal mycosis. Mucormycosis is caused by

Rhizopus and *Mucor* species in humans. The most common classic form of this mycosis is its rhinocerebral form[4]. Our patient was also diagnosed as mucormycosis by histopatholgical examination.

Combined surgical debridement and amphotericin B therapy play major role in management of the disease. Better survival rate (75.2%) was noted when the patients were managed with a combination of surgical debridement and amphotericin B therapy confirming the findings of other studies[3].

Fungal infections are frequently lethal, and their diagnosis and therapeutic management are challenging[6]. Mortality in the course of rhino-orbital-cerebral mucormycosis varies between 30–97% depending on the time of diagnosis and progression of lesions[1]. Fungal infection tends to be falal after10-15 days after surgery. A case of aspergillosis also had died , as reported by the author [7].

Joarder et al, had also reported one case of mucormycosis of the right frontal lobe with similar MRI characteristics[8]. In our patient also there was peripherally contrast enhancing lesion in the right frontal lobe.

Góralska has advised to use Amphotericin B, Posaconazole Isavuconazole against Mucor infection[1]. However Amphotericin B is very toxic. Our patient was treated with Amphotericin B (Non-lipsomal) and the patient ultimately died.

Conclusion:

Cerebral fungal infection is very uncommon. It is often diagnosed following surgical removal of tumour. However the outcome is not satisfactory even after surgery. Anti fungal drugs may be used but they are

not much effective. Eventually the patient is lost. Newer antifungals, eg, voriconazol may be more effective.

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