World Journal Of ENT & Head-Neck Surgery
(WJEHNS)

www.wjehns.com

ANGIOINVASIVE RHINO-CEREBRAL ASPERGILLOSIS: A CASE REPORT & REVIEW OF LITERATURE

Dr. Prithvi Das [1*], Dr. Somnath Saha[2]

[1] Senior Resident, Department of ENT, Head & Neck Surgery, Calcutta National Medical College & Hospital, Kolkata.
[2] Professor & Head, Department of ENT, Head & Neck Surgery, Calcutta National Medical College & Hospital, Kolkata.
*Correspondence:
Dr. Prithvi Das
Email: prithvidas89@gmail.com

Abstract
Background: Aspergillus spp are ubiquitous fungi. Although inhalation of its infectious conidia is common, tissue invasion is uncommon. Invasive aspergillosis is a highly lethal opportunistic infection that occurs most frequently in the setting of immunosuppression and is often rapidly progressive and fatal. Angioinvasion is a rare manifestation of disseminated aspergillosis which may result in stroke in immunocompromised individuals. Reports of such disease in patients with diabetes mellitus are rare. Rarely, aspergillosis may also occur in immunocompetent individuals.
Case Report: A 45 years old female patient, presented with proptosis, nasal obstruction and later monoparesis on right side. Nasal endoscopy showed a blackish colored mass in the right osteo-meatal complex area. Initial HPE report from that area showed granulomatous lesion suggestive of Aspergillosis. CT showed an irregular, heterogeneously enhancing mass lesion in the ethmoidal sinuses extending superiorly to the right frontal lobe destroying the floor of anterior cranial fossa. MRI showed a large area of intense, patchily enhancing, infiltrating, destructive lesion in the right basi-frontal region. Patient was started on Voriconazole. However she developed monoparesis on the right side after starting the therapy. MRI scan of brain revealed multiple, focal, altered signal intensity lesions with strong restricted diffusion in the left parafalcine region suggestive of acute cerebral infarction in the left anterior cerebral artery (ACA) territory. After initial medical management of the monoparesis, surgical debridement of the mass was done to reduce the pressure effect. Culture report was also suggestive of Aspergillosis. The patient was continued on Voriconazole therapy, but, unfortunately she succumbed to her illness despite treatment.
Conclusion: Angio-invasion in this case is most likely responsible for the monoparesis, which is uncommon in a patient with diabetes mellitus. Complete excision of the mass was not possible in this case as differentiation between brain tissue and fungal mass was not possible in this case. Voriconazole is preferred over Amphotericin-B due to its lesser toxic side-effects.
Key words: Aspergillosis, rhino-cerebral, cerebral infarctions, Aspergillus fumigatus, immunocompetent

INTRODUCTION:

Aspergillus is a ubiquitous fungus and is the most common fungal pathogen in sinus disease. Spores are also ubiquitous, usually introduced by inhalation, and are frequent inhabitants of the human upper respiratory tract[1]. Aspergillus spp. rank closely behind Candida spp. in causing invasive fungal infections in humans[2]. Aspergillus species is pathogenic in birds and mammals. 8 out of 350 aspergillus species is associated with human disease[3]. Route of infection is either gastro-intestinal or respiratory tract[4].

Invasive rhino-cerebral aspergillosis is a fatal disease, with a high mortality rate of 85%–100% despite antifungal treatment[5] . It occurs in 10%–15% of patients with disseminated aspergillosis[6,7]. Patients at risk for angioinvasion include those with prolonged neutropenia, diabetes mellitus, recipients of haematopoietic stem cell transplants or solid-organ transplants, advanced AIDS, chronic granulomatous disease and autoimmune disorders treated with intensive immunosuppressive regimens [8]

The unique ability of the fungus to digest elastin within the vessel wall makes it highly angioinvasive, leading to a wide spectrum of neurological sequelae[6,7]. Two factors play an important role in the pathogenesis of invasive aspergillosis:

i) secretion of toxic substance by fungi that penetrate tissue

ii) tissue necrosis induced by immune mechanism[9].

Amphotericin B is the one of the commonly available anti-fungal treatments for aspergillosis and has an efficacy rate of about 40% to 60% in invasive aspergillosis[10,11]. Amphotericin-B has considerable renal and hepatic toxicity[10]. Voriconazole has the advantage of better tolerance, increased efficacy, and significantly less toxicity when compared with Amphotericin B hence, is recommended as the first line treatment for invasive aspergillosis[11].

CASE REPORT:

A 45 years old female patient presented to the Otorhinolaryngology out-patient department with the complaints of a right sided proptosis, nasal obstruction and deterioration of vision on the same side for the last 10 months. The proptosis was insidious in onset and gradually progressive in nature. The visual deterioration gradually progressed to loss of vision. . There was no associated history of epistaxis. She had diabetes mellitus.

On examination there was inadequate closure of the eyelid with corneal keratinization as well as ulceration. The upper eyelid had a discharging sinus over its supero-nasal aspect. Perception of light and projection of rays was absent. Anterior rhinoscopy was suggestive of chronic rhinosinusitis. Thereafter, the patient was subjected to diagnostic nasal endoscopy which showed an irregular heterogeneous mass filling the entire ethmoidal complex area.

Fig 1: Clinical Photograph at presentation

CT scan of brain and orbit shows, irregular, heterogeneously enhancing mass lesion in ethmoidal sinuses extending superiorly to right frontal lobe destroying the floor of anterior cranial fossa with surrounding white matter edema showing mass effect. The mass extends into extraconal right orbit with the destruction of medial wall of right orbit and to the right maxillary and frontal air sinuses.

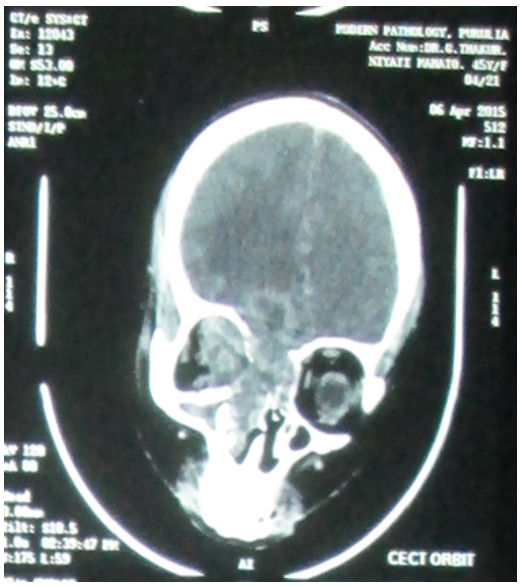

Fig 2: CT Brain and Orbit

MRI of brain in the same case showed a large area of intense, patchily enhancing, infiltrating, destructive lesion in the right basi-frontal region predominantly involving the ethmoidal sinus, nasal cavity, medial wall of the right orbit and right maxillary antrum with intraorbital and intracranial extension to the right orbito-frontal, cortical and subcortical region

Fig 3: MRI Brain and Orbit

Endoscopic biopsy provisionally diagnosed it to be a case of rhino-cerebral Aspergillosis. The hyphal morphology resembles that of Aspergillus fumigatus.

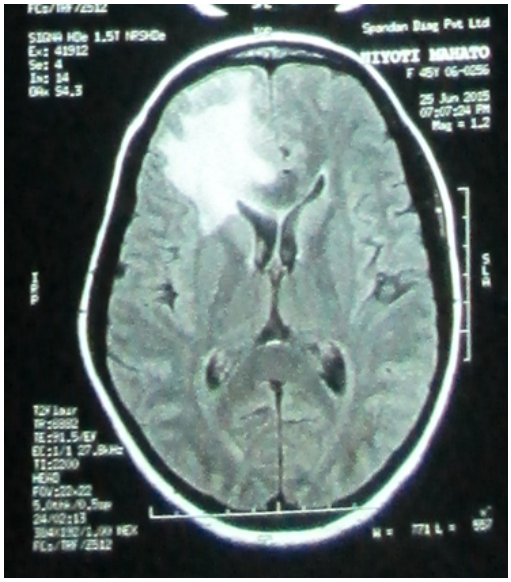

Fig 4: MRI Brain

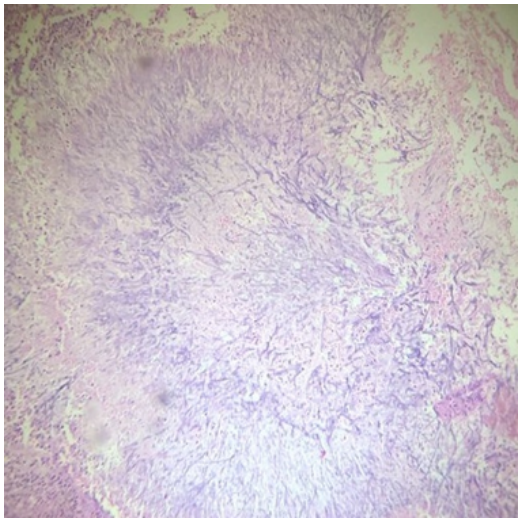

Figure 5: Slide shows hyphal elements from the material debrided from the patient (Haematoxylin-Eosin stain).

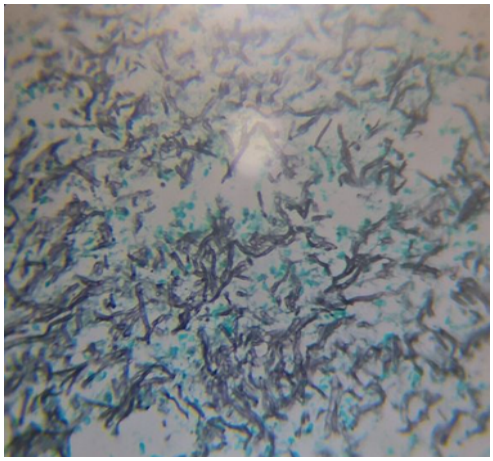

Figure 6: Slide shows hyphal elements from the material debrided from the patient (Gomori-Methanamine Silver stain).

The patient was thereafter started on Voriconazole. One week after admission and starting of medical treatment, the patient developed sudden onset right lower leg monoaresis with urinary incontinence.

There was no associated seizure, unconsciousness or vomiting.

On examination, patient was conscious, alert and co-operative. Power in the right lower leg was 1/5 while in the rest of the limbs it was 5/5. Babinski sign was positive in the right lower limb.

MRI scan of brain revealed multiple, focal, altered signal intensity lesions with strong restricted diffusion in the left parafalcine region suggestive of acute cerebral infarction in the left anterior cerebral artery territory.

Fig 7: MRI Brain after onset of CNS Features

Neurological consultation was sought and the patient was started on intravenous mannitol and phenytoin. After stabilizing her condition, debulking of the space occupying lesion with orbital exenteration was done. The fungal mass and frontal lobe tissue was indistinctable and inseparable in places; hence complete excision was not possible.

Post-operatively specimen was sent for histopathology, KOH mount and fungal culture. HPE shows chronic granulomatous reaction. KOH mount shows hyaline, septate branching hyphae. Fungal culture morphologically resembles Aspergillus fumigatus.

DISCUSSION:

Since its first description as an opportunistic infection in 1953, there has been a significant increase in the number of Aspergillosis, furthermore in the number of invasive aspergillosis[5]. They are encountered more frequently in patients, whose host defense mechanisms have been compromised due to disease or due to immune-suppression and immune-modulation used for managing malignancy, autoimmune diseases and organ transplantation[12].

Cases of CNS mycoses in apparently immunocompetent and healthy individuals have also been reported, mostly from India[13]. Rhino /sino-orbito-cerebral mycosis is a disease entity most often caused by the saprophytic molds aspergillus and mucorales[14].

Invasive aspergillosis occurs in 10%–15% of all cases with the disseminated disease[6].

Involvement of the central nervous system by Aspergillus spp. had been recognized as early as 1930s, and is usually a result of haematogeneous spread from another primary source such as the lungs or the gastrointestinal tract[5-7]. The unique ability of the fungus to digest elastin within the vessel walls makes it a highly virulent and angioinvasive organism[6,7].

There has been little data on cerebral invasive aspergillosis in patients with diabetes mellitus, thus making our patient an atypical subject. As the chest radiograph of our patient was normal, the fungal dissemination in this patient must have occurred from the paranasal sinuses. This is unusual as cerebral invasive aspergillosis is most commonly haematogeneously spread from the lungs or the gastrointestinal tract, rather than as a direct extension of sinonasal disease[5,7].

Aspergillosis causes an infective vasculopathy leading initially to acute infarction or hemorrhage and later into surrounding tissue as infectious cerebritis which may later evolve into an abscess[5-7]. It has an affinity for perforator arteries, and as they have a narrower lumen they tend to be affected much earlier thus affecting basal nuclei, thalami, corpus callosum and midbrain[5-7]. Aspergillus hyphae may grow through the vessel wall leading to the formation of mycotic aneurysms of the larger arteries which may rupture causing massive hemorrhage[5-7]. Additionally vessel lumen may be completely occluded by hyphal elements leading to ischaemic stroke.

The prognosis of cerebral angioinvasive aspergillosis is poor, with a high mortality rate of 85%–100% despite aggressive therapy[5,15]. Based on the largest randomized controlled trial, it is recommended that voriconazole be used for the primary treatment of invasive aspergillosis[16], as voriconazole has the advantage of better tolerance, increased efficacy and significantly less toxicity compared to amphotericin B. It also shows less nephrotoxicity and better compliance than with amphotericin B in clinical practice[16].

CONCLUSION:

Rhino-cerebral aspergillosis is a rare fungal infection. Angioinvasion occurs rarely in a case of rhino-cerebral aspergillosis. Orbital and cranial base aspergillosis can cause gradually progressive deterioration of vision. Angioinvasion in a case of invasive aspergillosis can lead to stroke like symptoms. The mainstay of treatment is surgical debridement with anti-fungal therapy. Although, Amphotericin-B is the traditional drug of choice but Voriconazole is better tolerated and has significantly less toxicity compared to Amphotericin-B.

REFERENCES:

1. Warder FR, Chikes PG, Hudson WR. Aspergillosis of the paranasalsinusis.Arch Otolaryngol. 1975;101:683–5.
2. Mitchell RB, Tolley N, Croft CB, Gallimore A. Aspergillosis of the larynx. J Laryngol Otol 1994; 108 :883-5.
3. Kwon J, Park KH, Park SI, Jin SY. Aspergillosis of the paranasal sinuses–diagnostic significance of the computed tomography.Yonsei Med J. 1989;30:294–7.
4. Regezi JA, Sciubba JJ, Jordan RC, editors. Oral pathology-Clinical Pathologic Correlations. 4th ed. Missouri: Saunders - An Imprint of Elsevier Science; 2003. Ulcerative conditions; pp. 23–74.
5. Denning DW. Invasive aspergillosis. State-of-the-art clinical article. Clin Infect Dis 1998; 26:781-805.
6. Miaux Y, Ribaud P, Williams M, et al. MR of cerebral aspergillosis in patients who have had bone marrow transplantation. AJNR Am J Neuroradiol 1995; 16:555-62.
7. DeLone DR, Goldstein RA, Petermann G, et al. Disseminated aspergillosis involving the brain: distribution and imaging characteristics. AJNR Am J Neuroradiol 1999; 20:1597-604.
8. Denning DW. Invasive Aspergillosis in immunocompromised patients. Curr Opin Infect Dis 1994; 7:456-62.
9. Veress B, Malik OA, el-Tayeb AA, el-Daoud S, Mahgoub ES, el-Hassan AM. Further observations on the primary paranasalaspergillus granuloma in the Sudan: A morphological study of 46 cases. Am J Trop Med Hyg. 1973;22:765–72.
10. Erbrecht R, Denning DW, Atterson TF, et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. N Eng J Med 2002;347: 408-15.
11. Thomas JW, Elias JA, David WD, et al. Treatment of aspergillosis: clinical practice guidelines of the infectious disease society of America. Clin Infect Dis 2008; 46: 327-60.
12. Dubey A, Patwardhan RV, Sampth S, Santosh V, Kolluri S, Nanda A. Intracranial fungal granuloma: Analysis of 40 patients and review of the literature. Surg Neurol 2005;63:254-60.
13. Haran RP, Chandy MJ. Intracranial aspergillus granuloma. Br J Neurosurg 1993;7:383-8.
14. Murthy JM, Sundaram C, Prasad VS, Purohit AK, Rammurti S, Laxmi V. Sinocranial Aspergillosis: A form of central nervous system aspergillosis in south India. Mycoses 2001;44:141-5.
15. Pagano L, Caira M, Falcucci P, Fianchi L. Fungal CNS infections in patients with hematologic malignancy. Expert Rev Anti Infect Ther 2005; 3:775-85.
16. Steinbach WJ, Juvvadi PR, Fortwendel JR, et al. Newer combination antifungal therapies for invasive aspergillosis. Med Mycol 2011;49(Suppl 1):S77–81.