Fungal Cerebral Embolic Infarction by Rhino-Orbitocranial Aspergillosis

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Abstract
Aspergillosis of paranasal sinuses is a rare infection with invasion of surrounding soft tissues, orbit and anterior cranial base. Eighteen years old immunocompetent man presented with gross facial swelling, proptosis and unilateral blindness. Histopathology was reported as invasive aspergillosis. The patient was given systemic antifungal therapy in the form of liposomal amphotericin B. He died of cerebral infarction by fungal embolism. Aspergillus fumigatus was the causative organism.

Keywords: Invasive aspergillosis, intracranial aspergillosis, cavernous sinus thrombosis.

INTRODUCTION
Aspergillosis is a relatively rare infection of the paranasal sinuses usually in immunocompromised individuals. Invasive form of aspergillosis cause tissue invasion. Intraorbital spread readily occurs through the thin bony partition between ethmoid sinuses and orbit. Invasion of orbit leads to proptosis due to mass effect and progressive visual loss due to involvement of optic nerve. It usually involves the species Aspergillus fumigatus and Aspergillus flavus. The maxillary, ethmoid and sphenoid sinuses are affected in that order. Fulminant form can invade the overlying maxillofacial soft tissue. Invasive aspergillosis originating from the paranasal sinuses can spread intracranially mainly along the skull base and larger vessels. Vascular invasion and cerebral embolism which are characteristic of mucormycosis is extremely rare in invasive aspergillosis. Intracranial spread should be suspected in patients with deteriorating neurological status, meningitis and focal neurological signs.

We report a case of invasive Rhino-Orbitocranial aspergillosis in an immunocompetent young male with cerebral embolic infarction and cavernous sinus thrombosis.

CASE REPORT
Eighteen years old man presented to the emergency services of our hospital with 2 weeks history of pain and swelling on the right side of face and eye, which was painful and gradually increasing in size (Fig. 1). There was history of gradual diminution of vision in right eye for the similar duration. There was no history of any immunecompromise, diabetes, chemotherapy or steroid use.

On examination patient was conscious, oriented but irritable. There was gross swelling of right side of the face with proptosis and ophthalmoplegia of right eye. Perception of light in right eye was negative. Skin in the maxillary region was necrosed with blackish discoloration. Patient was admitted and started on antibiotics and analgesics along with intravenous fluids. Biopsy was taken for histopathology, from the ulcerated region of right maxillary area and material was also sent for fungal mount and histopathology. Routine blood investigations were normal and blood culture showed no growth, diabetes was ruled out and patient was HIV negative. CT scan showed gross thickening and invasion of facial soft tissue and right orbital invasion with involvement of optic nerve (Fig. 2). Mucosal thickening was seen in maxillary, ethmoid and sphenoid sinuses.

The wet fungal smear examination showed branching septate fungal hyphae suggestive of aspergillosis. Provisional diagnosis of invasive aspergillosis was made.
and patient empirically started on liposomal amphotericin B at the dose of 1 mg/kg/day. After 72 hours of admission patient developed severe headache, drowsiness and left hemiplegia. Neurosurgical consultation was sought. CSF examination was normal on biochemistry and microscopy. CSF culture was reported as sterile. MRI was done which showed marked periorbital soft tissue swelling with anteriorly displaced and collapsed globe (Fig. 3). There was well-defined area of restricted diffusion in right caudate lobe, thalamus, basal ganglia, internal capsule, subcortical and paraventricular white matter in right medial posterior temporal lobe and right occipitoparietal region, hyperintense on T2 and isointense on T1 and was suggestive of acute
Invasive Rhino-Orbitocranial aspergillosis is a rare fungal infection of paranasal sinuses, occurring predominantly in immunocompromised patients. Immunocompromised patients frequently show only slight symptoms of non-specific sinusitis like headache, rhinorrhea, nasal obstruction and fever. There is no specific symptom which might be typical of fungal sinus infection, and diagnosis is difficult. Infiltration of neighbouring tissues like orbit and anterior skull base is typical. Invasive aspergillosis originating from the nose and paranasal sinuses can spread to the orbit and cranial cavity mainly along the skull base and larger vessels. The patients present with symptoms like proptosis, facial swelling, ophthalmoplegia, loss of vision and hypoesthesia of the ophthalmic and maxillary nerve. Intracerebral spread with meningitis and brain abscess occur in advanced cases.

Cerebral aspergillosis is an extremely rare disease in immunocompetent patients, with very poor prognosis and high mortality rate. Aspergillus infection of brain can occur in continuity or may be caused by hematogenous spread. Hematogenous spread has three major forms, namely, meningitis, brain abscess and vasculopathy, leading initially to acute infarction and hemorrhage. Infarcts are due to invasion of cerebral vessels by fungal hyphae. Further, neurological symptoms, cavernous sinus thrombosis or pseudotumor of orbit can occur as the disease advances. Nasal endoscopy findings do not correlate with the extent of disease as disease is confined to the posterior ethmoid and sphenoid sinuses. Our case had black necrotic appearance of the middle turbinate and surrounding lateral nasal wall. Histopathology provides the definitive proof of the tissue invasion along with fungal culture which differentiate the fungal species. In case of high suspicion of invasive aspergillosis, antifungal therapy should be started before microbiological or histopathological results are available. We got wet fungal mounts of the biopsy materials, results of which were available immediately, which enabled us to start systemic antifungal therapy.

Computed tomography and MRI usually show extensive sino-orbital and skull base lesions. Radiographic diagnosis of cerebral and craniofacial aspergillosis has varied and has been relatively nonspecific. Patients with cerebral aspergillosis have multiple lesions, an irregular ring of contrast enhancement, and hypointensity of the ring on T2-weighted MR images. Patients with cortical and subcortical hypodensities on CT scanning or hyperintensities on MR imaging are consistent with cerebral cortical and subcortical infarction. Abnormal enhancement of the optic nerve and sheath with infiltrating enhancing soft tissue within the intraorbital fat is seen in introrbital lesions. Localization of disease in the corticomedullary junction and basal ganglia is pathognomonic of neuroaspergillosis.

Conventional treatment of invasive aspergillosis is surgical debridement and systemic antifungal therapy, usually amphotericin B. We used liposomal amphotericin B, as it penetrates the brain parenchyma and results in higher drug concentration. The combination of amphotericin and itraconazole should be preferred for cerebral aspergillosis. Prognosis is poor when cranial and orbital involvement has occurred. The treatment of cerebral aspergillosis with antifungal therapy alone has very disappointing results, with mortality rate more than 90% in many series. The most likely reason for poor efficacy of treatment is poor penetration of antifungal drugs into CNS, except for newer antifungal agent voriconazole.

Hyperbaric oxygen therapy has also been used as apart of combination therapy, especially in case of cerebral abscess. Hyperbaric oxygen therapy increases the free oxygen radicals which directly kills microorganisms. It stimulates the oxygen dependent peroxidase system which enables leucocytes to kill microorganisms. There is no clear evidence of its benefit in cerebral aspergillosis.

Conclusions

Intracranial spread and cerebral embolism should be suspected in cases of invasive aspergillosis with deteriorating consciousness and neurological symptoms. High index of suspicion, prompt and aggressive treatment by surgical debridement and antifungals is required for clinical cure. Despite that disease is fatal in most patients.

References


