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Case Report

Sino-orbito-cerebral aspergillosis in an immunocompetent patient: a rare case report

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ABSTRACT

Invasive sino-orbito-cerebral aspergillosis is rarely seen in immunocompetent individuals; diagnosis and management of which is still a challenge. We report a case of invasive sino-orbito-cerebral aspergillosis in a 38 year immunocompetent male presenting with mild protrusion of right eye which was associated with no other complaint. His visual acuity was 6/6 in both eyes. There was mild proptosis of right eye of 2 mm on Hertel exophthalmometer with no restriction of the ocular movements. MRI brain, orbit and paranasal sinuses revealed soft tissue swelling in right ethmoid, frontal and sphenoidal air cells and orbit with bony destruction of lamina papyracea with intracranial extension of the mass with destruction of lamina cribrosa. The tissue biopsy was taken from the uncinate process and middle turbinate and sent for histopathological examination which revealed a fibrocollagenous soft tissue which was densely infiltrated by inflammatory cells with presence of large number of foreign body granulomas and filamentous aspergillus fungal hyphae. By radiological and histopathological findings, patient was diagnosed as a case of rhino-orbito-cerebral aspergillosis and given Tb Voriconazole 200 mg BD for 6 months after neurosurgery consultation. His proptosis was revealed at 3 months and repeat MRI showed slightly thickened mucosa of sinuses with no mass lesion seen in the orbit and brain with no evidence of any residual fungal granuloma. Orbital aspergillosis is quite challenging in terms of both diagnosis and treatment. Prolonged antifungal therapy is very effective in controlling infection, if patient is compliant.

Keywords: Aspergillosis, Fungal infections, Proptosis, Voriconazole.

INTRODUCTION

Fungi are an important opportunistic pathogen in immunocompromised individuals, which is very well documented in literature.[1-3] But, invasive sino-orbital fungal infections are uncommon in immunocompetent patients, whose diagnosis and treatment still remains a challenge. Sino-orbito-cerebral aspergillosis in healthy immunocompetent individuals is a relatively under-diagnosed and under-recognised clinical entity. Most common source of infection for aspergillosis is paranasal sinuses, most common being the maxillary sinus, followed by ethmoid, sphenoid and frontal sinus. Most common site of involvement is lung but invasive forms can also present as rhinosinusitis.[4] Infection can spread from the adjacent paranasal sinuses to orbit by breaching the lamina papyracea and can spread to the brain via optic nerve, making the prognosis even worse.[5,6] Here, we present a case of invasive sino-orbito-cerebral aspergillosis in an immunocompetent patient, which is rare clinical entity and often not suspected because there are numerous orbital pathologies which can present in a similar fashion. Till date, there are no standard guidelines for its treatment and outcome is poor if not diagnosed and treated timely as it can spread to middle cranial fossa via

superior orbital fissure and optic canal; with a high mortality of up to 80%.[7]

CASE REPORT

We report a case of 38 years old healthy immunocompetent male who presented to us with complaint of protrusion of his right eye for one month which was not associated with any pain, redness, and photophobia or discharge (Figure 1). There was no remarkable history of any past ocular or systemic illness or of any treatment. His best corrected visual acuity (BCVA) was 6/6 in both eyes with no relative afferent pupillary defect (RAPD). On inspection, mild proptosis of right eye was noted with no restriction of ocular movements. On palpation, orbital margins were well felt, non-tender and continuous with no orbital mass palpable. Ocular adnexa was essentially normal. On Hertel exophthalmometer, there was 2 mm proptosis in his right eye. Anterior and posterior segment examination was found to be essentially normal in both eyes. There was no lymphadenopathy with no tenderness in the area of paranasal sinuses.

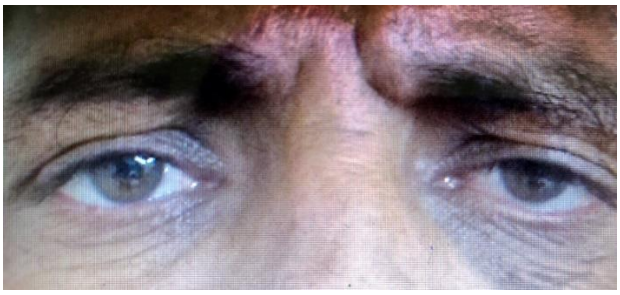

Figure 1: Mild proptosis in right eye.

Patient was thoroughly investigated for the cause of proptosis. MRI brain, orbit and paranasal sinuses revealed a soft tissue swelling in right ethmoid, frontal and sphenoidal air cells which was extending into the left ethmoidal sinus and orbit with bony destruction of lamina papyracea. There was an intracranial extension of the mass with destruction of lamina cribrosa involving the cavernous sinus. Lesion was isointense on T1W images and hypointense on T2W images (Figure 2).

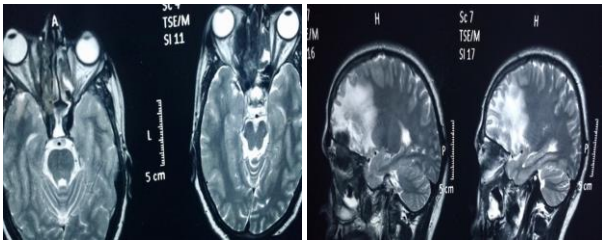

Figure 2: Axial and sagittal T2 weighted images showing mucosal thickening in paranasal sinuses, marked proptosis of right eye and altered signal intensity T2 hyperintense area in right frontal lobe suggestive of cerebritis/granuloma formation.

The tissue biopsy was taken from the uncinate process and middle turbinate and sent for histopathological examination. It showed fibrocollageneous soft tissue which was densely infiltrated by inflammatory cells with presence of large number of foreign body granulomas and filamentous aspergillus fungal hyphae with no evidence of malignancy. Based on radiological and histopathological findings, patient was diagnosed as a case of rhino-orbito-cerebral aspergillosis. The patient was immunocompetent with systemic examination within normal limits and no associated risk factors were found. After taking neurosurgery opinion, patient was started on oral anti-fungal therapy in the form of tablet voriconazole 200 mg twice daily for three months. Patient was regularly followed up with resolution of proptosis seen at 3 months. Repeat MRI revealed a significant reduction in lesion in sinuses, orbit and brain (Figure 3). The treatment was further continued for a period of 3 months and MRI was again repeated which showed slightly thickened mucosa of sinuses with no mass lesion seen in the orbit and brain. There was no evidence of any residual fungal granuloma.

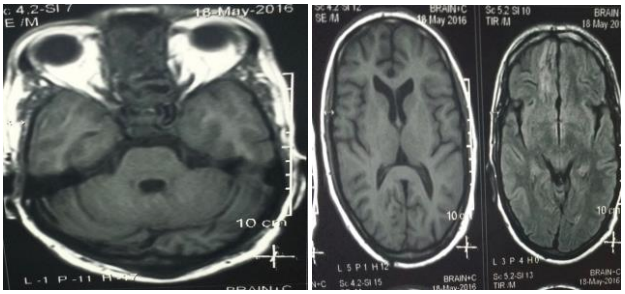

Figure 3: Axial T1 and flair images showing resolution of proptosis and brain changes following antifungal treatment.

DISCUSSION

Aspergillus infections are known to cause a spectrum of invasive and non-invasive disease in humans, but invasive aspergillosis of orbit in healthy patients is a rare clinical entity, which is quite under-recognised and under-diagnosed. There are few cases reported from tropical countries like India and Sudan as climate is very favourable for fungal spores and abundant number of fungal spores in environment increases the risk of invasive fungal infections, even in healthy immunocompetent individual.[8-10] Invasive aspergillosis is very uncommon in healthy individuals, but it still carries a high morbidity and mortality if not diagnosed and managed appropriately in time.[1] The fatality rate of 58-67% is reported in literature for invasive aspergillosis.[7] Aspergillus is next to Candida in terms of causing fungal infections with most common site of involvement being nasal cavity and paranasal sinuses. Most common source of infection for aspergillosis is paranasal sinuses, most common being the maxillary sinus, followed by ethmoid, sphenoid and frontal sinus.[4-6] The anatomical protection of the frontal sinus ostium in the anterosuperior part of

the nasal cavity makes it unusual for isolated aspergillosis of the frontal sinus to occur and frontal sinus involvement occurs secondary to spread from adjacent sinuses by focal bony erosion.[6]

Paranasal sinus aspergillosis can be classified into invasive form (acute fulminant, chronic invasive, granulomatous invasive) and non-invasive form (fungus ball and allergic fungal rhinosinusitis).[11] Early recognition of paranasal aspergillosis is utmost important to prevent its progression from non-invasive to invasive form which carry poor prognosis.[11,12] Risk factors include immunodeficient state due to various predisposing factors like HIV infection, diabetes mellitus, use of prosthetic devices or trauma, excessive environmental exposure and possibly advanced age.[13,14] Infection from paranasal sinuses can spread to orbit and brain, the mode of extension is either direct or through osseous structures like the lamina papyracea or through hematogenous spread by valve less venous plexus to the orbit, brain or skin.[15]

Proptosis is most common clinical manifestation of invasive aspergillosis which may be associated with diminution of vision, pain, restriction of ocular movements and periocular discharging sinus.[16] Orbital aspergillosis is usually misdiagnosed as malignancy, temporal arteritis, optic neuritis, orbital apex syndrome, idiopathic orbital inflammatory disorder and orbital cellulitis.[17,18] Low index of suspicion with absent sinus related symptoms leads to diagnostic dilemma in these cases.

On radiological investigations, sino-orbital aspergillosis has non-specific findings and may be confused with various orbital pathologies of similar presentation. It is most commonly confused with idiopathic orbital inflammatory disorder. On CT scan, heterogenous enhancing mass with similar density to extraocular muscles is usually seen. Concomitant paranasal sinus involvement on CT scan can give a clinch to its diagnosis and it is reported in 60-90% of cases.[19] Bone erosion is not must for its extension and seen in only 50% of cases.[20] MRI is better investigation than CT for evaluation of orbit, optic canal and cavernous sinus. Enhancement of sinus lining with focal hypointense areas are subtle signs of sinusitis which can be picked up on MRI. However, affordability and availability of MRI in developing countries like India, is a big challenge.[21]

For histopathological examination, incisional biopsy, FNAB (fine needle aspiration biopsy) or FNAC (fine needle aspiration cytology) can be planned. There is only 33% sensitivity for incisional biopsy procedures from the paranasal sinuses.[22] FNAB can be done in sino-orbital masses involving posterior orbit when there is high suspicion of aspergillosis and incisional biopsy from paranasal sinuses comes negative. FNAC is very effective in early definitive diagnosis of sino-orbital aspergillosis.[10] It is important to differentiate invasive sino-orbital aspergillosis from allergic aspergillosis on histopathology, which is characterised by mucin rich in eosinophils and Charcot-Leyden crystals which harbours *Aspergillus hyphae* with no tissue invasion.

Management of invasive sino-orbital aspergillosis is very challenging as there are no standard treatment protocols. It can be managed medically, surgically or combination of both. In orbit, surgical debridement is difficult due to presence of vital structures, bone and vessels involvement and posterior extension of disease. In retrobulbar or orbital apex involvement, exenteration is recommended but it is very disfiguring and moreover does not guarantee the eradication of aspergillosis.[22] Medical management of invasive aspergillosis includes long term administration of antifungal drugs. Amphotericin B is considered the gold standard but there are newer drugs available in market with fewer side effects i.e. itraconazole and voriconazole, but their high cost is a limiting factor. Few studies support globe conserving debulking surgery combined with antifungal drugs.[23] Pushkar et al reported resolution of retrobulbar and apical orbital disease with long term antifungal therapy only which raise a question on performing disfiguring debulking surgery.[10] Keeping this in mind, we put our patient on tablet voriconazole 200 mg BD for 6 months and it showed dramatic response.

CONCLUSION

Invasive aspergillosis has a vague presentation and commonly presents with ophthalmic or neurological symptoms after intraorbital or intracranial extension. Sino-orbital fungal disease can mimic many neoplastic and non-neoplastic orbital pathologies, therefore it should be highly suspected even in immunocompetent individuals. We came across a healthy immunocompetent patient who presented with mild proptosis associated with no other ophthalmic symptoms like ophthalmoplegia or visual loss or neurological symptoms, which are commonly seen in invasive sino-orbito-cerebral aspergillosis. So the clinical diagnosis of an aspergilloma was very unlikely as there were no associated risk factors too. But the histopathological and radiological investigations revealed it to be an invasive granulomatous sino-orbito-cerebral aspergillosis involving all the sinuses except maxillary sinus which is usually the most common involved sinus, which was a surprise to us. There is no adequate data available in literature which can establish a standard treatment protocol for invasive aspergillosis. Our case signifies a rare presentation of invasive aspergillosis, therefore high degree of suspicion is required for its diagnosis. Management should be aggressive with rapid and prompt diagnosis and treatment as delay can be fatal.

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REFERENCES

1. Fuqua TH, Sittitavornwong S, Knoll M, Said-Al-Naif N. Primary invasive oral aspergillosis: An update literature review. J Oral Maxillofac Surg. 2010;68:2557-63.
2. Sivak-Callcott JA, Livesley N, Nugent RA, Rasmussen SL, Saeed P, Rootman J. Localised invasive sino-orbital aspergillosis: characteristic features. Br J Ophthalmol. 2004;88(5):681-7.
3. Kontoyiannis DP, Bodey GP. Invasive aspergillosis in 2002: An update. Eur J Clin Microbiol Infect Dis. 2002;21:161-72.
4. Neeli AS, Kotrashetti SM, Vallavan P. Sino-orbital aspergillosis: a case report and brief review of literature. World J Dent. 2012;3(4):363-6.
5. Myoken Y, Sugata T, Kyo T, Fujihara M, Kohara T, Katsu M, Tamura M, Mikami Y. Invasive Aspergillus stomatitis in patients with acute leukemia: report of 12 cases. Clin Infect Dis. 2001; 33(12):1975-80.
6. Chambers MS, Lyzak WA, Martin JW, Lyzak JS, Toth BB. Oral complications associated with aspergillosis in patients with a hematologic malignancy. Presentation and treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1995;79 (5):559-63.
7. Shamim MS, Siddiqui AA, Enam SA, Shah AA, Jooma R, Anwar S. Cranio-cerebral aspergillosis in immunocompetent hosts: Surgical prospectives. Neurol India. 2007;55:275-81.
8. Kameswaram M, Al-Wadei A, Khurana P, Okafor BC. Rhino-cerebral aspergillosis. J Laryngol Otol. 1992;106:981-5.
9. Green WR, Font RL, Zimmerman LE. Aspergillosis of orbit: Report of 10 cases and review of literature. Arch Ophthalmol. 1969;82:302-13.
10. Pushkar N, Meel R, Kashyap S, Bajaj M, Sen S. Invasive aspergillosis of orbit in immunocompetent patients: treatment and outcome. Ophthalmology. 2011;118:1886-91.
11. Fuqua TH Jr, Sittitavornwong S, Knoll M, Said-Al-Naief N. Primary invasive oral aspergillosis: An updated literature review. J Oral Maxillofac Surg. 2010;68:2557-63.
12. Lin SJ, Schranz J, Teutsch SM. Aspergillosis case-fatality rate: systematic review of the literature. Clin Infect Dis. 2001;32:358-66.
13. Udaipurwala IH. Allergic fungal sinusitis: A perplexing clinical entity. Pak J Otolaryngol. 2008; 24:25-7.
14. Levin LA, Avery R, Shore JW, Woog JJ, Baker AS. The spectrum of orbital aspergillosis: a clinicopathological review. Surv Ophthalmol. 1996; 41(2):142-54.
15. Khanna M, Mannan R, Kaur J. A unique cytological approach in diagnosing a case of invasive aspergillosis masquerading as retro-orbital neoplasm. J Clin Diagnos Res. 2010;(4):2311-15.
16. Shamim MS, Siddiqui AS, Enam SA, Shah AA, Jooma R. Craniocerebral aspergillosis in immunocompetent hosts: Surgical perspectives. Neurol India. 2007;55:274-81.
17. Austin P, Dekker A, Kennerdell JS. Orbital aspergillosis: Report of a case diagnosed by fine needle aspiration biopsy. Acta Cytol. 1983;27:166-9.
18. Spoor TC, Hartel WC, Harding S, Kocher G. Aspergillosis presenting as a corticosteroid responsive optic neuropathy. J Clin Neuroophthalmol. 1982;2:103-7.
19. Massry GG, Hornblass A, Harrison W. Itraconazole in the treatment of orbital aspergillosis. Ophthalmology. 1996;103:1467-70.
20. Adulkar N, Radhakrishan S, Kim U. Invasive sino-orbital aspergillosis in immunocompetent patients: A clinico-pathological study. Eye. 2019;33:988-94.
21. Sivak-Calcott JA, Livesley N, Nugent RA, Rootman J. Localised invasive sino-orbital aspergillosis: characteristic features. Br J Ophthalmol. 2004;88: 681-7.
22. Dhiwakar M, Thakar A, Bahadur S. Invasive sino-orbital aspergillosis: Surgical decision and dilemmas. J Laryngol Otol. 2003;117:280-5.
23. Slavin ML. Primary aspergillosis of the orbital apex. Arch Ophthalmol. 1991;109:1502-3.

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