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Case Report

Invasive Sinu-Naso-Orbital Aspergillosis Following Dacryocystorhinostomy In An Immunocompetent Patient: A Rare Case Report And Literature Review

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Abstract:

Background: *Invasive sino-naso-orbital aspergilloma is a rare disease with variable clinical features but in an immunocompetent patient it is rarely considered and often resulted in poor prognosis due to its diagnostic and therapeutic challenge. In this article we reported a rare case of invasive sinu-naso-orbital aspergillosis with intracranial extension following dacryocystorhinostomy (DCR). To our knowledge this is the only reported case in last 109 years. Case Description: A 61 years old normotensive non diabetic male referred to us from an ophthalmologist with the complaints of retro-orbital pain followed by progressive dimness of vision later blindness on right eye after dacryocystorhinostomy. Diagnosis and Intervention: His MRI reveals an isointense lesion in T1W and T2W image in right maxillary, ethmoidal sinus with orbital and retro-orbital and intracranial extension with heterogeneous contrast enhancement. Radiologist suggested a case of inflammatory pseudotumor and initially he was treated with steroid, due to lack of clinical response later antifungal was given but patient still was nonresponsive. The patient underwent right pterional craniotomy for biopsy and optic nerve decompression. Histopathology revealed aspergillus infection. Post-operatively he was treated with voriconazole. Lessons: Invasive sino-orbital aspergillosis is rare in immunocompetent patients. Early diagnosis is critical for successful management. Due to difficulty of diagnosis and higher mortality and morbidity, our recommendation is- 'a patient with nonspecific complaints or retro-orbital pain' should prompt the physician to consider this diagnosis.*

Keywords: *DCR, dacryocystorhinostomy, invasive aspergillosis, sinu-naso-orbital lesion, vision loss.*

Abbreviations: *DCR: dacryocystorhinostomy; PL: Perception of light; PR: Projection of rays*

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Introduction:

Aspergillosis of paranasal sinuses is rare in immunocompetent patient. Usually, it is self- contained and has a favorable prognosis if there is no invasion[1]. In contrast, invasive disease may result in significant morbidity from intra-orbital and intracranial extension. It often presents with vague complaints and the absence of or atypical clinical finding makes diagnosis difficult[2,3]. Usually invasive aspergillosis of sinu-naso-orbital region occur mostly in immunocompromised patients suffering from diseases like uncontrolled diabetes mellitus, cirrhosis, HIV, leukemia or patients on long time immunosuppressive drugs like chemotherapy and systemic corticosteroids.[4-6]

We present a rare case report where a 61-year-old male patient suffered from invasive sinu-naso-orbital aspergillosis following endoscopic dacryocystorhinostomy (DCR). The patient was successfully managed with surgical debridement followed by antifungal therapy. We also went through previous literature about similar cases. So far there is only 19 previous case report of invasive aspergillosis in immunocompetent patient in

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last 109 years but none of them following DCR which makes this the only reported case.

Case report:

A 61 years old normotensive non diabetic male referred to us from an ophthalmologist with the complaints of retro-orbital pain in right eye for 3 months and progressive dimness of vision 2 months, followed by complete loss of vision on the same eye for last 1 week. Previously he was suffering from epiphora on the right eye and was diagnosed with dacryocystitis. For this he underwent endoscopic DCR on right side about 3 months and fifteen days back. One week after the surgery patient complained about sever retro-orbital pain and was managed conservatively with analgesics. Later he noticed gradual dimness of vision in right eye which was more evident to him after one and half months.

Investigations and hospital course:

His MRI as advised by the ophthalmologist revealed an isointense lesion in both T1W and T2W images occupying the right maxillary sinus with extension to posterior nasal area adjacent to posterior part of the middle turbinate, superior turbinate, posterior ethmoidal sinus with orbital and retro-orbital extension and perilesional edema in the right temporal pole. The lesion was heterogeneously contrast enhancing and encased the right optic nerve with extension to conal and extraconal compartment. Optic chiasm was free from the lesion. Mild right sided proptosis was also noted. From ophthalmology he was initially diagnosed as a case of pseudotumor and was treated with systemic corticosteroid but his condition did not improve. The patient mentioned us, he was blind in right eye. But on clinical examination there was some perception of light on that eye. There were also chemosis and extraocular muscle palsy in right eye. Fundoscopic examination reveals papilledema on his right eye, Frisen grade 5. His ESR and CRP were 65mm-Hg and 32.39mg/L respectively. His WBC - 12,400/mm^3 with neutrophil 79% and lymphocyte 17%. His chest X-Ray reveals no abnormality.

Management and present condition of the patient:

Radiologically our provisional diagnosis was fungal infection and differential diagnosis include inflammatory

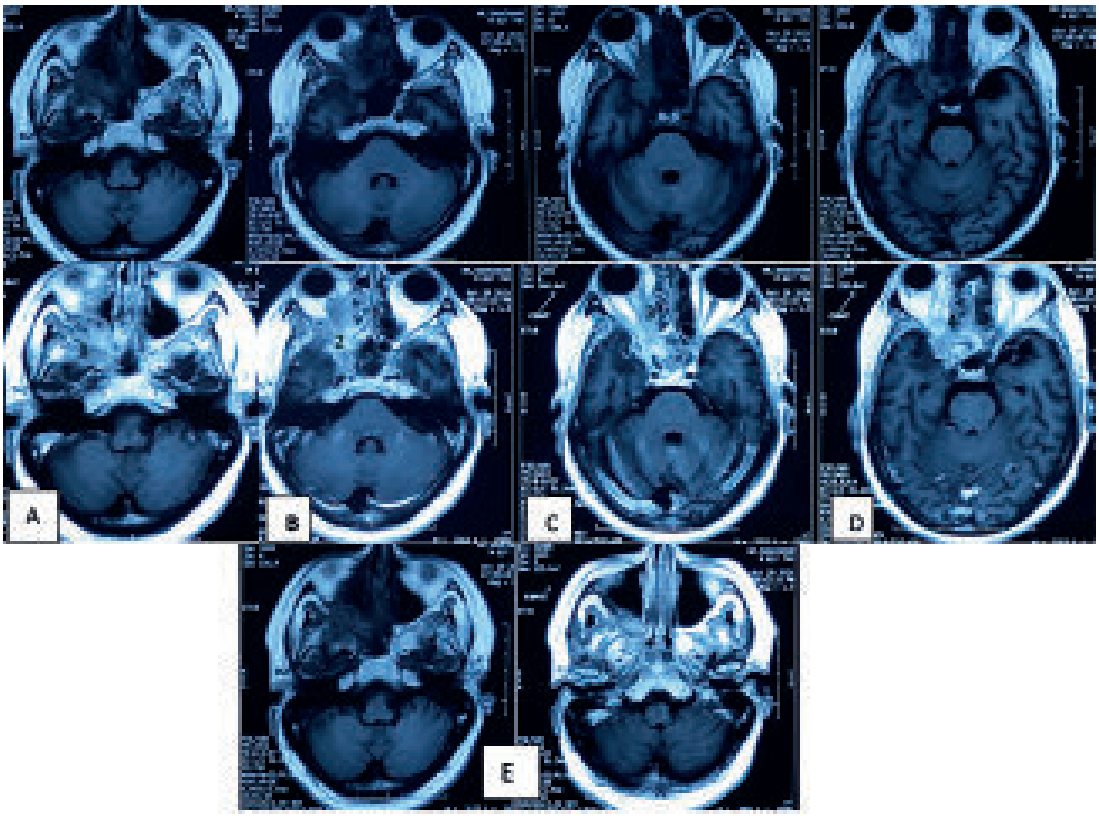

Fig.-1: *MRI of Brain T1W non contrast (Upper group) T1W contrast (Lower Group) given for a side by side comparison. In picture 'A' there is contrast enhancement seen in posterior wall of maxillary sinus (1) with invasion. In 'B' extension of lesion in retrobulbar (Intra and extra conal) and retroorbital region (2). In 'C' enhancement and thickening of medial rectus (3) muscle with extension to orbital apex picture 'D' (4) and right ethmoidal sinus is seen. In 'E' showing extension of the lesion in the nasal cavity posterior to right middle turbinate. There is also presence of edema on the right temporal pole with intracranial extension.*

pseudo tumor. Patient was initially treated empirically with systemic ketoconazole. But his condition did not improve. Later patient underwent surgery. We have done right pterional craniotomy. A growth was found which was resected and right optic nerve was decompressed. Sample was sent for histopathology which revealed aspergillus infection. Later patient was treated with systemic voriconazole. Post operatively his vision was improved both subjectively and objectively it was PL/PR. We advised the patient for a follow-up MRI but patient couldn't do due to financial reason. Follow-up over phone three months later his vision still remained same. We have requested the patient to come for a ophthalmological and neurological evaluation but he did not come.

Literature review:

We were only focusing on invasive aspergillosis in sinu-orbital region in immunocompetent patients. We conducted a systemic literature review covering 1970-2022 in different database including PubMed, Medline, Cochrane and Embase. Additionally, we searched with Google Scholar using search words "invasive lesion, nasal, paranasal sinus, aspergillosis, aspergilloma, dacryocystorhinostomy, immunocompetent" with year parameter 1900-2022. Dalmeijer possibly the first to report orbital aspergillosis in immunocompetent patient.[7] To our knowledge so far only 19 cases of invasive sinu-orbital aspergilloma in immunocompetent patient were previously reported.[8] As far as we can tell this is the first reported case where invasive sinu-naso-orbital aspergillosis occurred in an immunocompetent adult after dacryocystorhinostomy.

Clinical Features:

Sino-orbital aspergillosis is rare but aggressive, usually occurring after paranasal sinus infection. It can be divided into invasive and noninvasive types. Noninvasive aspergillosis forms a mass-lesion or a ball of aspergillus (aspergilloma). However invasive aspergillosis invades the tissue, blood vessel and causes bony erosion. Noninvasive aspergillosis is typically found in immunocompetent patients. But Invasive aspergillosis is often found in immunocompromised patients with neutropenia, long-term corticosteroid use, type 2 diabetes mellitus, hematologic malignancy, prosthetic devices, trauma, excessive environmental exposure to aspergillus, residence in an endemic area, or old age.[11] Invasive aspergillosis again can be subdivided in localized and fulminant. Localized disease often spreads from sinus to adjacent structure. The fulminant form is characterized by multi-organ involvement.[2]

Early diagnosis of invasive sino-orbital aspergillosis in immunocompetent patients can be challenging. Sivak-Callcot et al. reported a delay in diagnosis of up to 10 months as a result of nonspecific complaints of retro-orbital pain preceding the ophthalmic findings by 1-6 months.[9] 15 out of 19 (79%) previously reported patients initially presented with persistent severe unilateral frontal headache, or retro-orbital pain as their chief complaints.[10] Several of these patients were diagnosed initially with orbital pseudotumor or temporal arteritis and were treated with high-dose systemic corticosteroids.[12]

Discussion:

Pathophysiology:

Unlike immunocompromised patient pathophysiology in an immunocompetent person is not clearly understood. Regardless of immune status, sino-orbital aspergillosis may be resulted in poor prognosis if the treatment delayed, due to complication of CNS infection and subarachnoid haemorrhage due to ruptured mycotic aneurysm.[13] An active man can inhale as many as 5.76107 aspergillus spores in a day. The characteristic predilection for the sphenoid sinus in localised form and the invasive nature is poorly understood. Several mechanisms previously described which include obstruction of the nose and paranasal sinuses due to hypertrophied turbinate or deviated nasal septum, allergic rhinosinusitis, nasal polyp or infections.[14] Intracranial spread of fungus can occur by direct erosion of the bones or by migration along the blood vessel or spread along the perineural extension. Our patient had hypertrophied inferior nasal turbinate bilaterally and hypertrophied middle turbinate on right side and patient recently underwent DCR which in all together might cause obstruction of nasal flow and worked as a predisposing factor for aspergillosis. Leyngold et al, suggested that a previously indolent aspergillosis could be resulted in acute spread and progression of disease after an endonasal intervention which may also explain the short course of symptoms (1 week) of our patient after DCR.[10]

Diagnosis:

Biopsy is necessary and must be performed. But diagnosis still can be difficult. Various authors have mentioned about repeated biopsy to confirm the diagnosis.[2] The aspergillus organism has a characteristic microscopic appearance but culture is the gold standard for identification. This fungus is haemotoxophilic with 45 branching septate hyphae that are 2–4mm wide, best seen on periodic acid Schiff and Gomori methanamine silver stains.[15] Because other fungi can be pathologically indistinguishable and require different treatment, all specimens should be sent for culture. Aspergillus incubated on fungal

medium at 30 C in 45% humidity will grow in 2–6 days. Colonial morphology and microscopic examination of sporulating forms allows for precise diagnosis.[16]

Treatment:

Management of invasive sino-orbital aspergillosis in immunocompetent patients is still an area of controversy. Recommendations have ranged from medical management alone to radical surgery with adjuvant antifungal therapy.[9] Combination antifungal therapy with amphotericin B and itraconazole, voriconazole, or micafungin with or without surgical intervention has been used successfully to control the infection in some cases.[13-17] Voriconazole recently has become the drug of choice for invasive aspergillosis because better patient tolerance and lower toxicity to amphoterecin B.[17] The response rate

Table-I

Comparison of our treatment and outcome with previously published articles

Case	Age, Sex	Location	Extension	Treatment	Outcome
Dalmeijer [7]	65, F	Orbit	Lungs, brain	Orbital exenteration	Death 2.5 months later
Townes [19]	31, M	Lung	Orbit	Orbital exploration; amphotericin B	Alive at 3 weeks
Hedges and Leung [20]	62, F	Orbit	Brain	Debridement and amphotericin B: steroids	Death 5 months later
Yu et al.[21]	37, M	Sphenoid sinus, nasopharynx	Orbit, sella turcica	Sphenoidotomy; amphotericin B; rifampin	Alive at 1 year
Spoor et al.[22]	49, F	Spfienoid sinus	Orbital apes, internal carotid artery, basal ganglia, midbrain, cerebellum	Amphotericin B and rifampin; steroids	Death 2 months later
Austin et al.[23]	77, M	Orbit	Orbital apex, cavernous sinus, internal carotid, middle and anterior cerebral arteries	Orbital exentaration: amphotericin B; steroids	Death 3 months after diagnosis
Fuchs et al. [24]	48, F	Sphenoid sinus	Orbit, ethmoid sinus, sella turcica	Surgery; amphotericin B; rifampin	Alive at 1 month
Lowe and Bradley[25]	74, F	Ethmoid sinus	Orbit, frontal lobes	None	Death 12 months later
Bradley et al.[26]	74, F	Ipsilateral paranasal sinuses, orbital apex	Cavernous sinus, anterior and middle cranial middle fossa	Amphotericin B; flucytosine; ketoconazole; vibunazole; steroids	Alive at 2 years
Slavin[27]	65, M	Orbital apex	Ethmoid and sphenoid sinuses	Amphotericin B; steroids; antibiotics, acyclovir	Death 2 weeks later
Heier et al.[28]	21, F	Paranasal sinuses	Orbit	Amphotericin B	Alive at 6 months
Mauriello et al.[29]	71, F	Sphenoid and ethmoid sinuses	Orbit, Dura	Debridement; amphotericin B then liposomal amphotericin B; local amphotericin B	Death 2 months later
Suzuki et al.[30]	83, F	Sphenoid and ethmoid sinus	Orbital apex, optic canal, skull base, middle cerebral artery	Steroids	Death 6 months later
Massry et al.[31]	40, F	Paranasal sinuses	Orbit	Debridement: amphotericin B: itraconazole	Alive at 2 years
Hutnik et al.[32]	75, M	Posterior ethmoid sinus, sphenoid sinus	Orbital apex, optic canal, cavernous sinus, superior orbital fissure, inferior frontal lobe, meninges	Amphotericin B and fluconazole: steroids	Death 2 months later
Streppel et al.[33]	50, F	Paranasal sinuses	Orbit, skull base	Amphotericin B; debridement; liposomal amphotericin B; postoperative itraconazole	Death 16 months later
Sivak-Callcott et al.[9]	77, M	Spenoid sinus	Orbital apex, alatine fossa, infraorbital fissure, anterior cavernous sinks	Amphotericin B: local amphotericin B: oral itraconazole	Alive 13 months later
Sivak-Callcot et al.[9]	73, F	Sphenoid sinus, orbital apex	Cavernous sinus, inferior orbital fissure, temporalis fossa, extraocular muscle	Amphotericin B: liposomal amphotericin B and rifampin; itraconazole; steroids	Death 18 months later
Leyngold et al.[10]	61, M	Sphenoid sinus	Left ethmoidal sinus, orbital apex, both optic nerve, chiasm	liposomal amphotericin B, Debridement, I/V Voriconazole & Micafungin	Alive 12 months later
Our patient	61, M	Posterior ethmoidal sinus	Rt cavernous sinus, inferior orbital fissure, retrobalbar, retroorbital	Ketoconazole- before diagnosis Voriconazole- after diagnosis	Alive at 3-month follow-up

On the basis of *Table 1,* female to male ratio: 1.5:1, age of most of the patients were above 50- 13 patients (65%). Total mortality was 55% (11 out of 20).

to antifungal chemotherapy ranges from 40% to 60%.[18] Leyngold et al, mentioned due to high rates of morbidity and mortality after radical debridement, even in a more widespread intracranial infection, a subtotal excision followed by antifungal therapy may be reasonable in immunocompetent patients.[10] We initially treated our patient with ketoconazole before surgery when diagnosis was not certain but the treatment did not response. The response was better with voriconazole after surgical debridement of the lesion. Due to rarity of the pathology a proper treatment protocol is difficult to stablish. In table-1 we have mentioned the location, extension, treatment and outcome of previously published article and also mentioned our treatment strategies.

Conclusions:

Invasive sino-orbital aspergillosis, although rare, can still present in immunocompetent patients. We described the only case where after dacryocystorhinostomy, an other- wise-healthy patient suffered from invasive sinu-orbital aspergillosis. Early diagnosis of this infection is critical for successful management. Due to difficulty of diagnosis and higher mortality and morbidity of the disease our recommendation is a patient with nonspecific complaints or retro-orbital pain should prompt the physician to consider MRI/CT scan of brain with orbital protocol before making a diagnosis and initiating therapy. The radiologic findings of optic nerve and/or chiasmal infiltration with associated adjacent para-nasal sinus involvement should lead the surgeon to consider an urgent tissue biopsy with fungal culture to rule out aspergillosis. Injudicious use of steroid could be detrimental. If the infection is confirmed, we recommend urgent initiation of antifungal therapy with immediate surgical debridement with the goal to preservation of life and vital structures.

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