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CASE REPORT

Invasive sinus-naso-orbital aspergilloma following dacryocystorhinostomy in an immunocompetent patient: A rare case report and literature review

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Background: Invasive sinus-naso-orbital aspergilloma is a rare disease with variable clinical features, but in an immunocompetent patient, it is rarely considered and often resulted in a poor prognosis due to its diagnostic and therapeutic challenges. In this article, we report a rare case of invasive sinus-naso-orbital aspergillosis with intracranial extension following dacryocystorhinostomy. To the best of our knowledge, this is the only reported case in the past 109 years.
Case description: A 61-year-old normotensive non-diabetic male was referred to us from an ophthalmologist with complaints of retro-orbital pain followed by progressive dimness of vision and later blindness on right eye after dacryocystorhinostomy.
Diagnosis and intervention: His MRI reveals an isointense lesion in the T1w and T2w images in the right maxillary, ethmoidal sinus with orbital and retro-orbital, and intracranial extension with heterogeneous contrast enhancement. A radiologist suggested a case of inflammatory pseudotumor, and initially he was treated with steroids due to a lack of clinical response; later, antifungal was given, but the patient still was non-responsive. A right pterional craniotomy was performed on the patient to access the optic nerve and perform the biopsy. Aspergillus infection was seen by histopathology. Postoperatively, he was treated with voriconazole.
Lessons: In immunocompetent individuals, invasive sino-orbital aspergillosis is uncommon. For effective care, early diagnosis is essential. Our advice is that a patient with vague symptoms or retro-orbital discomfort should encourage the doctor to investigate this diagnosis due to the diagnostic difficulties and greater mortality and morbidity rates.

Keywords: DCR, Dacryocystorhinostomy, invasive aspergillosis, sinus-orbital lesion, vision loss

Introduction

In patients who are immunocompetent, paranasal sinus aspergillosis is uncommon. If there is no invasion, it is often self-contained and has a good prognosis (1). Invasive illnesses, however, can extend into the cerebral space and cause considerable morbidity. It frequently presents with nebulous symptoms, and a lack of or unusual clinical findings makes identification challenging (2, 3). Usually, invasive aspergillosis of the sinus-naso-orbital region occurs mostly in immunocompromised patients suffering from diseases like uncontrolled diabetes

Abbreviations: DCR, dacryocystorhinostomy; PL, perception of light; PR, projection of rays.

mellitus, cirrhosis, HIV, leukemia, or patients on long-term 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 sinus-naso-orbital aspergillosis following endoscopic dacryocystorhinostomy (DCR). The patient's condition was effectively treated with surgical debridement and antifungal medication. We also went through previous literature about similar cases. So far, there have been only 19 previous case reports of invasive aspergillosis in immunocompetent patients in the past 109 years, but none of them following DCR, making this the only reported case.

Case report

A 61-year-old normotensive non-diabetic male was referred to us from an ophthalmologist with the complaints of retro-orbital pain for 3 months and progressive dimness of vision for 2 months, followed by complete loss of vision for the past 1 week. Previously, he was suffering from epiphora in the right eye and was diagnosed with dacryocystitis. For this, he underwent endoscopic DCR on the right side 31/4 months back. One week after the surgery, the patient complained of severe retro-orbital pain, which was managed conservatively with analgesics. Later, he noticed a gradual dimness of vision in the right eye, which was more evident to him after one and a half months.

Investigations and hospital course

The patient's MRI, as advised by the ophthalmologist, revealed an isointense lesion in T1W and T2W images occupying the right maxillary sinus, 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 compartments. 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 corticosteroids, but his condition did not improve. The patient told us his right eye was blind. But on clinical examination, there was some perception of light in that eye. There were also chemosis and extraocular muscle palsy in the right eye. Fundoscopic examination reveals papilledema Frisen grade 5. His ESR and CRP were 65 mmHg and 32.39 mg/L, respectively. His WBC count was −12,400/mm^3, with neutrophil 79% and lymphocyte 17%. His chest x-ray revealed no abnormality.

Management and present condition of the patient

Our provisional diagnosis was a fungal infection, and the differential diagnosis included an inflammatory pseudotumor. The patient was initially treated with systemic ketoconazole, but his condition did not improve. Later, the patient underwent surgery. We have done a right pterional craniotomy. A growth was found, which was resected, and a right optic nerve was decompressed. The sample was sent for histopathology, which revealed an aspergillus infection. Later, the patient was treated with systemic voriconazole. Postoperatively, his vision was improved both subjectively and objectively (PL/PR).

Literature review

We were only focusing on invasive aspergillosis in sinus-orbital region in immunocompetent patients. We conducted a systemic literature review covering 1970–2022 in different databases, 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 was possibly the first to report orbital aspergillosis in immunocompetent patient (7). To the best of our knowledge, so far only 19 cases of invasive sinus-orbital aspergilloma in immunocompetent patient have been reported (8). According to our knowledge, this is the first instance of invasive sinus-orbital aspergillosis in an immunocompetent adult who followed a DCR.

Clinical features

Sino-orbital aspergillosis is uncommon but severe, and it typically follows a paranasal sinus infection. It comes in invasive and non-invasive varieties. Non-invasive aspergillosis manifests as a mass-lesion or aspergillus ball (aspergilloma). However, invasive aspergillosis invades the tissue and blood vessels and causes bony erosion. Patients with immune competence are frequently reported to have non-invasive aspergillosis. However, immunocompromised people who are elderly have hematologic malignancies, long-term corticosteroid use, neutropenia, type 2 diabetes, high environmental aspergillus exposure, prosthetic devices, trauma, reside in an endemic area, or use long-term corticosteroids are frequently affected by invasive aspergillosis (9). Invasive aspergillosis again can be subdivided into localized and fulminant. Localized disease often spreads from sinus to adjacent

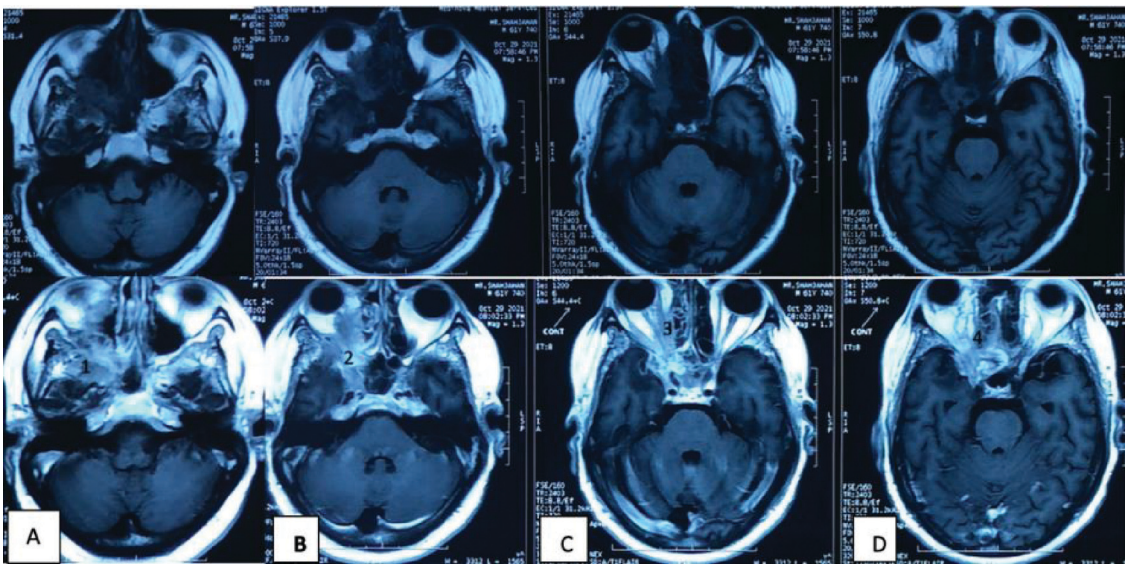

FIGURE 1 | MRI of brain T1W non-contrast (upper group) and T1W contrast (lower group), given for a side-by-side comparison. (A) Contrast enhancement is seen in the posterior wall of maxillary sinus (1) with invasion. (B) Extension of the lesion in retrobulbar (intra- and extraconal) and retro-orbital regions (2). (C) Enhancement and thickening of medial rectus (3) muscle with extension to orbital apex (D) (4) and right ethmoidal sinus are seen. There is also the presence of edema on the right temporal pole with intracranial extension.

structure. Multiorgan involvement is a characteristic of the fulminant type (2).

In immunocompetent individuals, it may be challenging to make an early diagnosis of invasive sino-orbital aspergillosis. According to Sivak-Callcot et al., there might be a diagnostic delay of up to 10 months since non-specific symptoms of retro-orbital pain often occur 1–6 months before ocular findings (10). Among the previously described patients, 15 (79%) out of 19 initially complained of a severe, persistent unilateral frontal headache or retro-orbital discomfort (11). Several of these individuals received high-dose systemic corticosteroids after first being diagnosed with orbital pseudotumor or temporal arteritis (12).

Discussion

Pathophysiology

Unlike in an immunocompromised patient, the pathophysiology of 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 hemorrhage due to ruptured mycotic aneurysm (13). A male who is physically engaged can breathe in up to 5.76107 aspergillus spores per day. It is unclear why this condition has a localized preference for the sphenoid sinus and why it is so invasive. Several mechanisms previously described include obstruction of the nose and paranasal sinuses due to hypertrophied turbinate or deviated nasal septum, allergic rhinosinusitis, nasal polyps, or infections (14). Fungus can spread intracranially via directly eroding the bones, moving down a blood artery, or spreading via a perineural extension. Our patient had hypertrophied inferior nasal turbinate bilaterally and hypertrophied middle turbinate on the right side, and the patient recently underwent DCR, which might cause obstruction of nasal flow and work as a predisposing factor for aspergillosis. Leyngold et al. suggested that a previously indolent aspergillosis could result 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 (11).

Diagnosis

A biopsy is necessary and must be performed. But diagnosis can still be difficult. Various authors have mentioned about repeated biopsies to confirm the diagnosis (2). Despite the typical microscopic appearance of the aspergillus organism, culture is still the most trustworthy way of identification. The hematoxyphilic hyphae of this fungus, which are 45° branching and 2–4 mm broad, are most visible on periodic acid Schiff and Gomori methanamine silver stains (15). All specimens should be sent for culture since other fungi may be pathologically indistinguishable and require a different therapy. Growth occurs in 2–6 days when aspergillus is incubated on a fungus medium at 30°C and 45% humidity. Colony morphology and microscopic analysis of sporulating forms provide precise diagnosis.

Treatment

It is still debatable how to handle invasive sino-orbital aspergillosis in immunocompetent individuals. From medical care alone to extensive surgery combined with adjuvant antifungal medication, recommendations have been made (10). A combination of amphotericin B and itraconazole, voriconazole, or micafungin, with or without surgical intervention, has occasionally proven successful in controlling an infection (13–15). Due to improved patient tolerance and reduced amphotericin B toxicity, voriconazole has lately replaced other medications as the treatment of choice for invasive aspergillosis. Antifungal chemotherapy has a response rate of between 40% and 60%. Due to the high rates of morbidity and death following severe debridement, Leyngold et al. suggested that in

TABLE 1 | Comparison of our treatment and outcome.

Case	Age, Sex	Treatment	Outcome	Extension	Location
Austin et al. (13)	77, M	Orbital exenteration: amphotericin B; steroids	3 months after diagnosis, death occurs	Cavernous sinus, orbital apex, middle and anterior cerebral arteries, and internal carotid	Orbit
Bradley et al.	74, F	Amphotericin B; ketoconazole; flucytosine; vibunazole; steroids	Alive at 2 years	Middle fossa, cavernous sinus, and middle and cranial anterior	Ipsilateral paranasal sinuses and orbital apex
Dalmeijer	65, F	Orbital exenteration	Death 2.5 months later	Lungs and brain	Orbit
Fuchs et al. (14)	48, F	Surgery; amphotericin B; rifampin	Alive at 1 month	Orbit, ethmoid sinus, and sella turcica	Sphenoid sinus
Heier et al. (15)	21, F	Amphotericin B	Alive at 6 months	Orbit	Paranasal sinuses
Hedges and Leung (11)	62, F	Debridement and amphotericin B: steroids	Death 5 months later	Brain	Orbit
Hutnik et al.	75, M	Amphotericin B and fluconazole: steroids	Death 2 months later	Superior orbital fissure, orbital apex, optic canal, inferior frontal lobe, cavernous sinus, and meninges	Posterior ethmoid sinus and sphenoid sinus
Leyngold et al.	61, M	Liposomal amphotericin B, debridement, I/V voriconazole and micafungin	Alive 12 months later	Left ethmoidal sinus, orbital apex, both optic nerve, and chiasm	Sphenoid sinus
Lowe and Bradley	74, F	None	Death 12 months later	Orbit and frontal lobes	Ethmoid sinus
Mauriello et al.	71, F	Amphotericin B then liposomal debridement; amphotericin B amphotericin B; local	2 months later, death	Orbit, dura	Sphenoid and ethmoid sinuses
Massry et al.	40, F	Debridement: amphotericin B: itraconazole	Alive at 2 years	Orbit	Paranasal sinuses
Our patient	61, M	Ketoconazole: before diagnosis; voriconazole: after diagnosis	Alive at 3-month follow-up	Right cavernous sinus, inferior orbital fissure, retrobulbar, and retro-orbital	Posterior ethmoidal sinus
Sivak-Callcot et al. (5)	73, F	Itraconazole; steroids amphotericin B and rifampin; amphotericin B: liposomal	18 months later, death	Extraocular muscle, inferior orbital fissure, cavernous sinus, and temporalis fossa	Sphenoid sinus and orbital apex
Spoor et al. (12)	49, F	Rifampin; steroids and amphotericin B	2 months later, death	Orbital apes, cerebellum, midbrain, internal carotid artery, and basal ganglia	Sphenoid sinus
Slavin	65, M	Amphotericin B; steroids; antibiotics, acyclovir	2 weeks later, death	Ethmoid and sphenoid sinuses	Orbital apex
Suzuki et al.	83, F	Steroids	Death 6 months later	Skull base, orbital apex, middle cerebral artery, and optic canal	Sphenoid and ethmoid sinus
Streppel et al.	50, F	Amphotericin B; postoperative itraconazole amphotericin B; debridement; liposomal	Death 16 months later	Orbit and skull base	Paranasal sinuses
Sivak-Callcott et al. (5)	77, M	Amphotericin B: oral itraconazole amphotericin B: local	Alive 13 months after that	Anterior cavernous sinks, infraorbital fissure, orbital apex, and palatine fossa	Sphenoid sinus
Townes (10)	31, M	Amphotericin B orbital exploration	Alive at 3 weeks	Orbit	Lung
Yu et al. (9)	37, M	Amphotericin B; rifampin sphenoidotomy	Alive at 1 year	Orbit and sella turcica	Sphenoid sinus and nasopharynx

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

patients who are immunocompetent, a subtotal excision followed by antifungal medication may be appropriate, even in the case of a more extensive cerebral infection (11). We initially treated our patient with ketoconazole before surgery when the diagnosis was not certain, but the treatment did not produce a response. The response was better with voriconazole after surgical debridement of the lesion. Due to the rarity of the pathology, a proper treatment protocol is difficult to establish. In **Table 1**, we have mentioned the location, extension, treatment, and outcome of previously published article and also mentioned our treatment strategies.

Conclusion

Despite its rarity, immunocompetent people can nevertheless develop invasive sino-orbital aspergillosis. We described the only case where after DCR, an otherwise healthy patient suffered from invasive sinus-orbital aspergillosis. Successful care of this illness depends on early diagnosis. Due to the disease's greater mortality and morbidity rates and difficulty in getting a diagnosis, we advise patients with nebulous symptoms or retro-orbital discomfort to push their doctor to seek an MRI/CT scan of the brain with an orbital procedure before receiving a diagnosis and beginning therapy. The surgeon should think about performing an immediate tissue biopsy with a fungus culture to rule out aspergillosis if the radiologic findings include optic nerve and/or chiasmal infiltration with accompanying adjacent paranasal sinus involvement. Injudicious use of steroids could be detrimental. If the infection is diagnosed, we advise starting antifungal medication right away and performing an emergency surgical debridement in order to preserve life and important tissues.

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