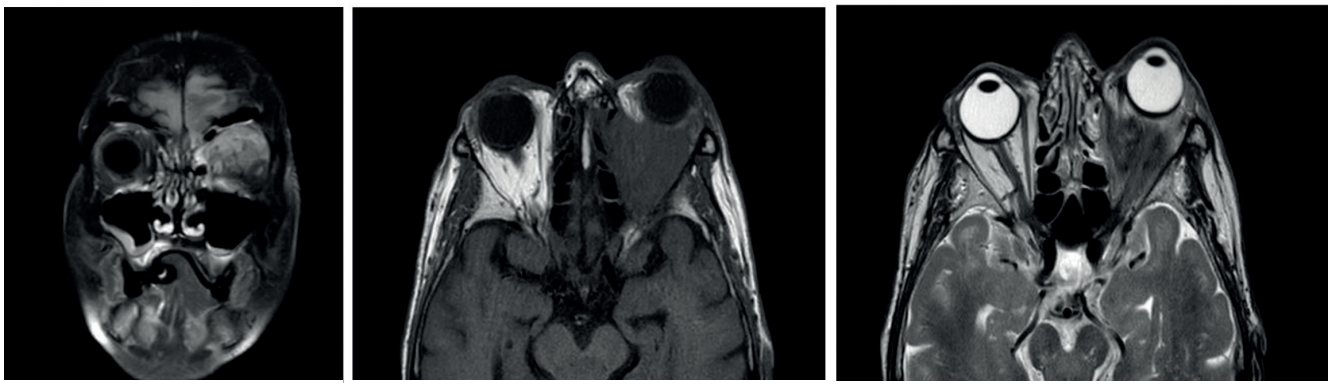
Behind the eyes: Unravelling the mystery of a painless progressive proptosis

BY NETRA KALLA AND TRISTAN MCMULLAN



T1 weighted – axial | T1 weighted – traverse | T2 weighted – traverse

Figure 1: MRI head and orbit images of patient: (a) Axial T1 weighted image; (b) Transverse T1 weighted image; (c) Transverse T2 weighted image.

Orbital fungal infections have the potential to give rise to serious complications. While these infections typically originate in the sinuses, patients may initially exhibit ocular symptoms. As a result of the diverse and often vague clinical manifestations (especially during the initial phases), misdiagnosis is a common occurrence. This case study underscores the critical need for ophthalmologists to be well-acquainted with the wide range of clinical manifestations and the variable ways in which fungal infections can present themselves. Early identification and swift initiation of appropriate treatment are essential components in managing patients effectively [1].

Presentation

An 89-year-old woman presented to her GP with pain and swelling to the left eyelid with ptosis and hyper-lacrimation. This further followed with reduced sensation and numbness in the eyebrow and left part of the lip. She was initially diagnosed with Bell's palsy. She subsequently had an MRI brain and MRI orbits which showed a low-signal soft tissue mass posteriorly and superiorly in the conus of the left orbit (Figure 1). The mass extended medially into the ethmoid sinus and nasal cavity and the superior rectus muscle was engulfed. She was referred to the ophthalmology department where she presented with a history of a painless progressive proptosis with ptosis on her left eye. Her past medical history was positive for goitre, but she didn't experience nose bleeding, not a diabetic, no history of immunosuppression or trauma.

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On examination, the left eye had a restriction in adduction and hypoglobus, however there was no diplopia in primary gaze and her pupils were equal and reactive to light. Intraocular pressure was 12 in both eyes and colour vision was intact. Slit-lamp examination of the anterior and posterior segment was unremarkable. There was marked exophthalmos of the left eye with an exophthalmometer measurement of 14mm in right eye and 22mm in left eye. Visual field testing was not possible due to the patient's posturing problems however a comparative visual field test was grossly normal. Blood tests were unremarkable and ruled out thyroid eye related disease (Figure 2).

Computed tomography orbit showed "a large mass occupying the superior half of the left orbit extending posteriorly below the frontal bone towards the orbital foramen causing some constriction upon the ophthalmic nerve but not extending into the inferior aspect of the conus."

Clinical impression was of orbital lymphoma / metastasis given the slow progressive course of the disease. She subsequently underwent two orbital biopsies. The first one, performed through an endoscopic endonasal approach, showed a fungal disease but the lab examination was inconclusive regarding the fungal genre. The second one was performed through a skin crease incision and the diagnosis of orbital aspergillosis was then made. The patient was then treated with a course of Voriconazole 200mg orally. She tolerated well to treatment and was followed up in clinic with regular bloods tests.

Discussion

This case report underscores noteworthy aspects in the diagnosis of a rare and vaguely presenting ophthalmological condition.

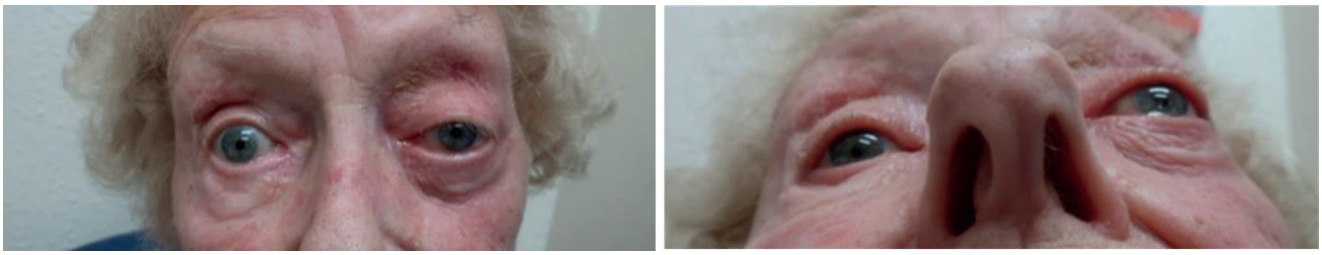

Figure 2: Shows face and inferior angle view of patient, seven months after initial onset of symptoms.

Aspergillus spp. are ubiquitous saprophytes responsible for a rising number of infections in humans, although still relatively rare. Only 17 documented instances of invasive sino-orbital aspergillosis in individuals who are not immunosuppressed have been recorded in English literature since 1966 [2]. Life-threatening invasive forms of aspergillosis are primarily observed within the expanding demographic of immunocompromised patients. Other risk factors include paranasal mycosis, diabetic ketoacidosis, neutropenia, neutrophil dysfunction, prosthetic devices, trauma, severe burns, alcoholism, intravenous drug use, HIV infection, hematologic malignancy, bone marrow transplantation, liver cirrhosis, corticosteroid use, antibiotics, chemotherapy and smoking contaminated marijuana [3]. Our patient had none of these risk factors not only highlighting the rarity of the case but also the manifestation of non-specific symptoms in orbital fungal cases like these. The unconventional presentation of the patient posed an additional obstacle in reaching a definitive diagnosis without a tissue biopsy. Diagnostic delays often occur due to the clinical resemblance of various orbital pathologies, which frequently manifest with non-specific symptoms such as exophthalmos, limited eye movements, swelling, ptosis, deterioration in vision, redness, hyper lacrimation and more [4].

Since orbital aspergillosis is often contingent with the patient's immune status, the presentation is typically chronic and indolent in immunocompetent patients and more acute and progressive in immunocompromised patients, perhaps explaining the nature of her seven-month duration of symptoms whilst still preserving vision [3].

Broadening the discussion to all types of orbital fungal brings the topic of mucormycosis, which should also be taken into consideration when investigating slowly growing orbital masses. Mucormycosis is typically a fulminant presentation. Regarding conservative management, there are studies that show that Voriconazole 200mg orally is a more effective and better tolerated antifungal treatment than Amphotericin B for aspergillosis, whereas Amphotericin B is better for mucormycosis [5]. The treatment is usually long and requires blood monitoring of voriconazole level, potassium, renal and kidney function. In addition to oral medication, surgery has a role in diagnostic and therapeutic management.

Recent advancements in detection methods e.g. polymerase chain reaction testing and new treatment strategies provide opportunities for earlier diagnosis and improved patient outcomes ultimately preserving vision. Ongoing research offers promising prospects for more conservative approaches, like utilising oral antifungal medications as an alternative to radical surgery in select cases. Polymerase chain reaction testing plays a crucial role in expediting the initiation of appropriate therapy by identifying the specific fungus, such as *Aspergillus* species and testing the potential resistance to enable more targeted treatment [1].

Conclusion

While orbital fungal infections are relatively uncommon, they can lead to significant health challenges, particularly among immunocompromised individuals. It is crucial for ophthalmologists to maintain a heightened level of suspicion regarding fungal infections, as a delay in diagnosis and improper treatment can result in increased complications and mortality rates. Advancements in detection techniques and ongoing pre-clinical research into immunomodulation therapies for fungal infections, has resulted in a positive shift in the approach to management, allowing patients to undergo more conservative treatments rather than aggressive surgical procedures, potentially resulting in better patient outcomes [1]. In the challenging realm of diagnosing and treating orbital aspergillosis, the essential strategy for optimal disease management hinges on fostering an interdisciplinary collaboration involving ophthalmologists, ENT specialists, maxillofacial surgeons, pathologists, microbiologists, and infectious disease specialists [4].

References

1. Mukherjee B, Raichura N, Alam M. Fungal infections of the orbit. *Ind J Ophthalmol* 2016;**64(5)**:337.
2. Sivak-Callcott JA, Livesley N, Nugent RA, et al. Localised invasive Sino-orbital aspergillosis: Characteristic features. *Br J Ophthalmol* 2004;**88(5)**:681–7.
3. Orbital Aspergillosis (2024). *EyeWiki.* https://eyewiki.org/Orbital_Aspergillosis [Link last accessed September 2024].
4. Lever M, Wilde B, Pförtner R, et al. Orbital Aspergillosis: A case report and review of the literature. *BMC Ophthalmol* 2021;**21(1)**:22.
5. Herbrecht R, Denning DW, Patterson TF, et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. *N Engl J Med* 2002;**347(6)**:408–15.

AUTHORS

Netra Kalla,
FY2 Doctor, Leicester Royal Infirmary, UK.

Tristan McMullan,
Consultant Ophthalmologist, Northampton General Hospital NHS Foundation Trust, UK.

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