PROCEEDINGS OF SINGAPORE HEALTHCARE

Short Communication

Proceedings of Singapore Healthcare
2018, Vol. 27(4) 287–289

DOI: 10.1177/2010105818758089
journals.sagepub.com/home/psh
SAGE

Orbital apex syndrome: An unusual complication of invasive mucormycosis

W J Quah and M Gunavathy

Abstract

Orbital apex syndrome is a rare manifestation of invasive mucormycosis. We report a case of orbital apex syndrome in a diabetic patient which not only posed a diagnostic challenge but also required a multidisciplinary approach in treatment and management. Prompt imaging followed by early initiation of antimicrobial therapy along with timely surgical intervention were integral in preventing further complications and reducing mortality. However, despite these measures, the patient sustained partial vision loss due to endophthalmitis as a complication.

Keywords

Orbital apex syndrome, superior orbital fissure syndrome, invasive mucormycosis, complex ophthalmoplegia, amphotericin

Introduction

Complex ophthalmoplegia can be something of a diagnostic conundrum. In particular, orbital apex syndrome, or superior orbital fissure syndrome, involves a multitude of cranial neuropathies which are cranial nerves II, III, IV, VI and V_1 and, occasionally, V_2. Causes include infections (bacterial, viral and fungal), inflammatory and vasculitic disorders, neoplasm and trauma (fracture of the superior orbital fissure).[1]

Mucormycosis is a fungal infection caused by fungi in the order Mucorales and can be potentially life threatening. According to a population-based study, the estimated incidence of mucormycosis is 1.7 cases per million people per year. However, the figure is as high as 2–3% in susceptible groups.[2] Classification of fungal rhinosinusitis can be broadly categorized into invasive or non-invasive. Invasive as in the illustrated case is defined by the presence of fungal hyphae within the mucosa, submucosa, bone, or blood vessels of the paranasal sinuses.[3]

Groups susceptible to the invasive form are those with depressed immunity such as patients with diabetes mellitus, AIDS, on chronic corticosteroid treatment, with leukaemia, lymphoma, undergoing anti-cancer chemotherapy or transplantation.[3] Complications of mucormycosis can be divided into local, orbital and intracranial, which is life-threatening. Cranial nerve findings represent extensive infection and signal a grave prognosis.[2]

We report here an intricate case of a diabetic patient presenting with visual loss and ophthalmoplegia.

Case report

A 60-year-old gentleman with underlying poorly controlled diabetes mellitus for the past two years (HbA1c of 14.3%) was allegedly assaulted and suffered superficial wounds without loss of consciousness. Three days later, the patient started gradual onset of visual loss and ptosis over the left eye. The patient had no fever. Computed tomography angiogram of the brain was initially done to rule out a bleed in view of the recent trauma. Inadvertently, it showed the possibility of a cavernous sinus thrombosis. Subsequent neurological examination revealed left cranial nerve II, III, IV, V_1, V_2 and VI palsies which correlated with the radiological findings. Treatment dose of subcutaneous enoxaparin was thus initiated as bridging to warfarin. However, further examination revealed left facial swelling/tenderness and the patient was referred to the otorhinolaryngologists.

Rigid nasal endoscopy followed by functional endoscopic sinus surgery showed left middle turbinate necrosis with mucopurulent discharge from the left maxillary antrum and anterior ethmoidal air cell as well as fungal debris (Figure 1).

Department of Internal Medicine, Shah Alam Hospital, Malaysia

Corresponding author:
Quah Wy Jin, Department of Internal Medicine, Shah Alam Hospital, Persiaran Kayangan, Seksyen 7, 40000 Shah Alam, Selangor, Malaysia.
Email: kalel_88@hotmail.com

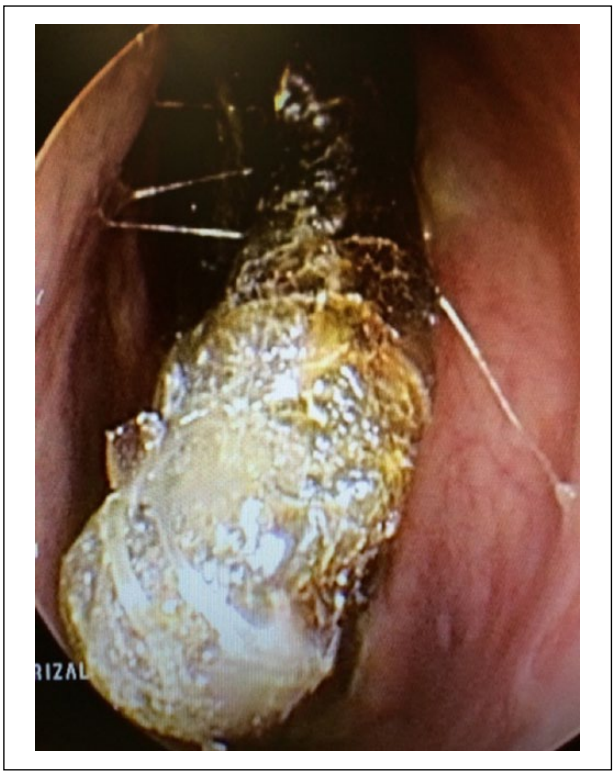

Figure 1. Rigid scope findings: left middle turbinate necrosis with slough and mucopurulent discharge from sinuses.

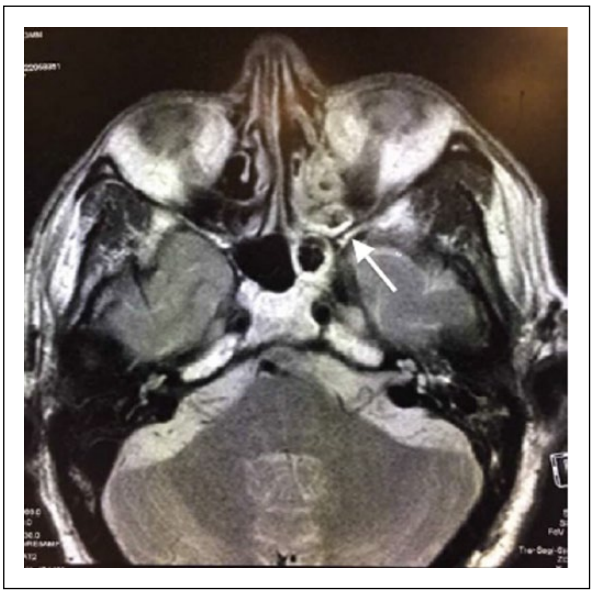

Figure 2. Magnetic resonance imaging T2-weighted axial view showing increased signal intensities at the left ethmoid sinus suggestive of mucosal thickening with possible extension into the left orbit.

Subsequently, brain magnetic resonance imaging (Figure 2) was performed, which surprisingly revealed no evidence of cavernous sinus thrombosis. The diagnosis was then revised. By that time, INR was prolonged at 5.6. Anticoagulation was immediately stopped with close monitoring of the patient for any bleeding tendencies. Methylprednisolone, which was given for one day for possible optic nerve compression, was also

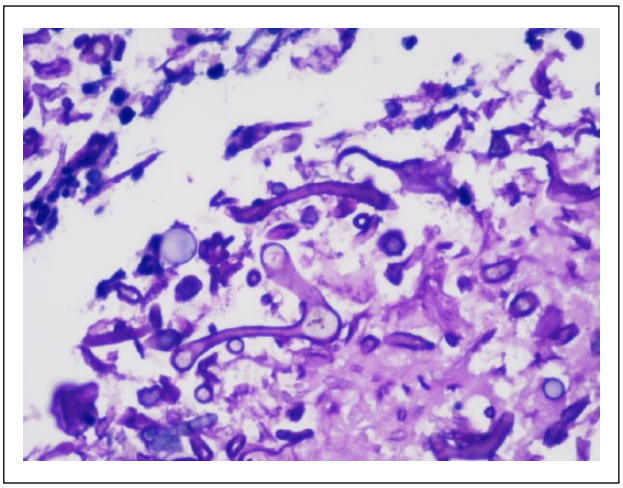

Figure 3. Biopsies performed during endoscopic ethmoidectomy. Periodic Acid-Schiff stain (40× magnification) showing scattered broad aseptate fungal hyphae within necrotic areas.

stopped. The case was consulted with the infectious disease team and IV amphotericin B was started. The histopathology report later confirmed invasive mucormycosis infection, as in Figure 3. There were also similar fungal bodies seen within the ghost outline of blood vessel lumen. The final diagnosis was left orbital apex syndrome secondary to invasive mucormycosis. Later on, fungal blood culture traced and showed *Rhizopus* sp., hence Mucormycosis fungaemia was present.

However, the patient developed left endophthalmitis and was offered conservative management in view of the guarded prognosis of the left eye. During the second week of treatment, the patient developed acute kidney injury secondary to the nephrotoxic effects of amphotericin B. Hydration was given and the dose was adjusted repeatedly with close monitoring according to protocol. Amphotericin B lipid complex, a less nephrotoxic form, was given as replacement but only for a course of one week due to financial restraints. Fortunately, the patient maintained good urine output and did not require any dialysis. The renal profile improved subsequently. Aside from that, it was challenging to manage the patient's blood glucose levels as the patient had inconsistent meals, poor appetite, due to the amphotericin B in dextrose solution and the patient's condition, which waxed and waned during his stay in the ward.

It was also an arduous task securing lines for the antifungal administration due to its propensity for thrombophlebitis. In view of the long hospital stay, the patient succumbed to hospital acquired infection with a transient episode of supraventricular tachycardia that resolved with a two week course of combination piperacillin-tazobactam streamlined to ceftazidime as the blood culture grew *Pseudomonas*. Subsequent scopes with debridement showed improvement and the patient managed to complete the six-week course of amphotericin B. The patient was then discharged well with follow-up.

Discussion

Patients that present with a constellation of cranial neuropathies need to be investigated thoroughly as the cause can be

elusive at times, as illustrated here: a case initially thought to be traumatic in origin, which subsequent imaging showed as thrombosis of the cavernous sinus but which was refuted eventually by MRI, which is the gold standard in diagnosis. This avoided the need for the patient to be subjected to long term anticoagulation, which could have led to bleeding complications.

With the aid of various diagnostic tools, the patient was started empirically on antifungal treatment early. The treatment for invasive fungal sinusitis is first identifying whether the patient is immunocompromised, whereby in this case the patient had poorly controlled diabetes and required close monitoring with adjustment of insulin dosages to achieve good glycaemic control in the presence of sepsis. Optimal glycaemic control would ensure that the patient responds well to the antifungal therapy as well as prevent worsening of the infection. Next would be appropriate systemic antifungal therapy and surgical debridement through endoscopic sinus surgery entailing procedures like curettage, sinus drainage and irrigation.[4] We were able to uphold these principles in the management of our patient.

However, it is known that with invasive mucormycosis, prognosis is poor due to its sequelae and in this case the patient lost the vision in his left eye but fortunately did not have intracranial extension of his infection. Possible causes of a poor prognosis include a delayed presentation, pre-existing lateral sphenoid bony dehiscence, advanced tissue invasion, misdiagnosis and the inappropriate use of systemic corticosteroids.[3,5]

Conclusion

This was truly a challenging case requiring an interdisciplinary collaboration in diagnosis and management of the patient during his stay in the ward. It emphasizes the need to rule out infection as the cause of orbital apex syndrome so that early antimicrobial therapy can be initiated and, as necessary, radical debridement. It also highlights the importance of good glycaemic control in patients with diabetes mellitus. In view of the rare occurrence of such a situation, there is no consensus in regard to treatment, therefore further studies are required to determine the optimal duration of antifungal therapy.

Acknowledgements

We acknowledge the following colleagues: Dr Ireen Razini Binti Ab.Rahman (histopathologist) from Hospital Tengku Ampuan Rahimah at Klang, Selangor, Malaysia; Dr Norazah A Razak (radiologist) from Hospital Shah Alam, Selangor, Malaysia; Dr Mohammad Isfa Rizal (otorhinolaryngology team) from Hospital Shah Alam, Selangor, Malaysia, for providing the HPE slides, MRI images and scope images respectively.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ORCID iD

Wy Jin Quah https://orcid.org/0000-0003-1381-2019

References

1. Yeh S and Foroozan R. Orbital apex syndrome. *Curr Opin Ophthalmol* 2004; 15: 490–498.
2. Spellberg B, Edwards J Jr and Ibrahim A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. *Clin Microbiol Rev* 2005; 18: 556–569.
3. Rao SP, Kumar KR, Rokade VR, et al. Orbital apex syndrome due to mucormycosis caused by *Rhizopus microsporum*. *Indian J Otolaryngol Head Neck Surg* 2006; 58: 84–87.
4. Ferguson BJ. Fungus balls of the paranasal sinuses. *Otolaryngol Clin North Am* 2000; 33: 389–398.
5. Cho SH, Jin BJ, Lee YS, et al. Orbital apex syndrome in a patient with sphenoid fungal balls. *Clin Exp Otorhinolaryngol* 2009; 2: 52–54.