Zulkifli Shamim-Afiqah[1,2], Abdul Rashid Munirah[2], Kamarudin Haireen[2], Embong Zunaina[1]

[1]Department of Ophthalmology & Visual Science, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.

[2]Department of Ophthalmology, Hospital Selayang, 68100 Batu Caves, Selangor, Malaysia.

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* Corresponding Author
Embong Zunaina
zunaina@usm.my
Zulkifli Shamim-Afiqah
shamim_211@live.com

# Orbital Apex Syndrome as Initial Presentation of Rhino-Orbital-Cerebral Mucormycosis in an Immunocompromised Patient

**Abstract -** We report a case of a 47-year-old man with underlying poorly controlled diabetes mellitus who presented with acute onset of right orbital apex syndrome a few hours after a dental extraction procedure. His symptoms initially began with tooth pain and right facial swelling for 5 days, which did not subside with antibiotics. A dental consultation revealed dental caries of the right upper molar, and the affected tooth was extracted. A few hours after the procedure, the patient developed right orbital apex syndrome, presenting with blurred vision, eye pain, ptosis, and associated headache and nausea. Nasoendoscopy found eschars, and a biopsy sample cultured *Rhizopus arrhizus*. Computed tomography of the brain, orbit, and paranasal sinuses showed acute intraparenchymal and subdural hemorrhage of the right frontal lobe with bilateral maxillary sinusitis and bony erosion. The patient was diagnosed with rhino-orbito-cerebral mucormycosis. He was immediately started on intravenous antibiotics and antifungal therapy; however, he refused further surgical intervention. Unfortunately, he passed away 3 weeks later. Mucormycosis infection is fatal, and early detection and management are crucial to improving prognosis.

***Keywords - Orbital apex syndrome, mucormycosis, proptosis, ptosis***

## 1 INTRODUCTION

Mucormycosis is an invasive and life-threatening fungal infection commonly affecting patients who are immunologically or metabolically compromised including diabetes mellitus, hematologic malignancy, organ transplantation or burns. Rhino-orbito-cerebral is one of the common presentations (40%), occurring most in patients with diabetics, and can be rapidly fatal if not diagnosed and treated early [1]. The infection may originate from the nasal cavity and paranasal sinuses, extending to palate and orbits followed by rapid spread to brain and meninges [2].

Orbital apex syndrome can occur as a complication of mucormycosis due to the angio-invasive nature of the fungus, which leads to vascular thrombosis and tissue necrosis [3]. If the infection extends beyond the sinuses into the orbital apex, it may affect the cranial nerves passing through the superior orbital fissure, resulting in proptosis, ophthalmoplegia, visual loss, and neuralgia in the distribution of the ophthalmic branch of the trigeminal nerve.

We report a case of middle-aged man with poorly controlled diabetes mellitus presented with orbital apex syndrome as initial presentation of rhino-orbito-cerebral mucormycosis.

## 2 CASE REPORT

A 47-year-old man with uncontrolled diabetes mellitus presented with sudden onset of blurred vision and pain over the right eye a few hours after a tooth extraction procedure. The patient was on oral hypoglycemic agents and subcutaneous insulin for his diabetes mellitus but was not compliant with his medications.

His symptoms initially started with a toothache in the upper right region for 5 days prior to presentation. The toothache was associated with right facial swelling. He did not seek any treatment until the right facial swelling increased in severity 3 days later. He went to a private dental clinic, where he was prescribed oral ciprofloxacin and metronidazole. The patient was compliant with the antibiotics, but the worsening of the right facial swelling and toothache prompted him to visit the emergency department.

At presentation in the emergency department, he was alert and fully conscious, afebrile, with a blood pressure of 149/91 mmHg and a high blood sugar level of 20 mmol/L, but blood ketones were negative. Full blood count revealed a raised white cell count of 12,500 cells/µL, with a normal hemoglobin level of 15

g/dL. He was started on an intravenous insulin sliding scale infusion. A dental consultation revealed dental caries of the right upper molar at position 16, and the affected tooth was extracted. A few hours after the tooth extraction procedure, the patient complained of blurred vision and pain in the right eye. It was associated with drooping of the right upper eyelid. He also experienced headache and nausea.

On examination of the right eye revealed positive relative afferent pupillary defect with visual acuity of light perception. Left visual acuity was 6/6. His right eye showed a feature of orbital apex syndrome with proptosis, almost complete ptosis (Figure 1) and limited extraocular movement on all gaze (Figure 2). He also had hypoesthesia over forehead region. Right conjunctiva was white with no chemosis, clear cornea without anterior chamber inflammation. Fundus examination was unremarkable, with normal intraocular pressure. Left eye examination was normal.

**Figure 1:** Right eye shows almost complete ptosis with proptosis in primary gaze.

Flexible nasoendoscopy showed eschar with suspected fungal involvement at right ostiomeatal complex. Urgent computed tomography (CT) of the brain and paranasal sinuses revealed acute intraparenchymal and subdural hemorrhage of the right frontal lobe, mucosal thickening at right sphenoid sinus, bilateral maxillary sinusitis with erosion of medial wall of right maxillary sinus (Figure 3) and obliteration of right ostiomeatal complex. Right medial rectus muscle was slightly bulky with no definite rim enhancing collection.

Patient was diagnosed with rhino-orbito-cerebral mucormycosis. Periodic acid–Schiff (PAS) and Giemsa stains for samples taken during nasoendoscopy revealed fungal hyphae. Fungal culture traced later revealed *Rhizopus arrizus*.

**Figure 2:** Extraocular examination shows limited gaze in all directions of the right eye.

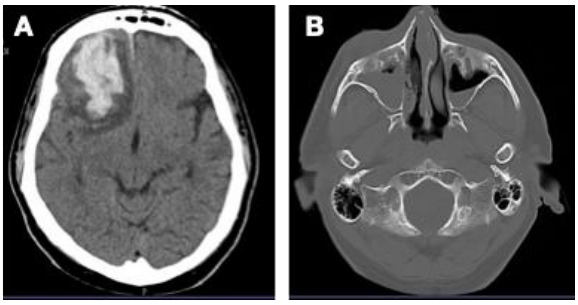


**Figure 3:** Axial computed tomography scan showing right frontal lobe intraparenchymal hemorrhage with edema (A) and bilateral maxillary sinusitis with erosion of medial wall of right maxillary sinus (B).

The patient was co-managed by the ophthalmology, otorhinolaryngology, neurosurgery, and infectious disease teams. He was treated with intravenous ceftriaxone, metronidazole, and amphotericin B. The patient was advised to undergo surgical debridement. However, due to personal reasons, the patient refused further surgical interventions and insisted on being discharged from the hospital on day 2 of admission. He was discharged with oral augmentin and metronidazole, along with instructions for daily nasal douching at home. Oral antifungal options of posaconazole or isavuconazole were unfortunately not available at the hospital at the time. He was given an appointment in a week's time but defaulted. Unfortunately, he passed away 3 weeks later.

## 3 DISCUSSION

Rhino-orbital mucormycosis is caused by fungi of the order *Mucorales*, which are life-threatening and commonly affect immunocompromised hosts. Among the Mucorales, *Rhizopus arrhizus* belonging to the family Mucoracea is one of the most common causes of infection as presented in this case [3]. The clinical presentation may vary

and depends on the patient's underlying illness, with rhino-orbito-cerebral and pulmonary presentations being the most common in diabetic patients. Other presentations of mucormycosis include cutaneous, gastrointestinal and disseminated [1].

Orbital apex syndrome is described as a syndrome involving optic nerve dysfunction with damage to oculomotor, trochlear, abducens and the ophthalmic branch of trigeminal nerve [4]. It can be caused by infection, inflammation, malignancy, trauma or vascular origins. Orbital apex syndrome is one of the common presentations of rhino-orbito-cerebral mucormycosis. Nan Jiang et al retrospectively evaluated 11 cases of rhino-orbito-cerebral mucormycosis at their centre, and found all patients had orbital apex syndrome [5].

In rhino-orbito-cerebral mucormycosis, the infection typically evolves through three stages: initial nasal and sinus involvement, often unnoticed or minimally symptomatic; orbital involvement, prompting the patient to seek medical attention; and ultimately, cerebral involvement. It starts with fungal invasion to blood vessels causing mechanical and toxic damage to the intima forming thrombosis and further invading lymphatics and veins. As a result, tissue necrosis occurs as the thrombosis creates emboli and obstructing vessels. The infection spreads progressively from the nasal mucosa to the paranasal sinuses, palate, orbits, and brain [5].

In our case, the rapid development of orbital apex syndrome only few hours after tooth extraction raises the possibility that the infection had already extended prior to the procedure, and the extraction likely unmasked existing invasive disease rather than being the primary cause. The extensive bony erosion of the medial wall of the right maxillary observed on CT imaging may also suggest that the infection had already progressed prior to the procedure.

The angio-invasive properties of mucormycosis result in the formation of extensive thrombosis, tissue infarction and necrosis, which can result in hemorrhagic complications, as observed with the intracerebral hemorrhage in our case. Although the patient's blood pressure was also elevated, it was not consistent with the severe hypertension usually associated with hemorrhagic stroke. Moreover, hypertensive bleeds are more frequently non-lobar rather than lobar hemorrhages [6]. Thus, it is likely that this bleed represented a hemorrhagic infarct from fungal arteritis rather than a primary hypertensive event.

A high index of clinical suspicion is needed for early diagnosis so that commencement of therapy can be started as soon as possible. Imaging with CT of the brain, orbit and paranasal sinuses may help but frequently the initial imaging can be negative or only with subtle findings [3]. Mucosal thickening and absence of air-fluid level in the infected sinus may be detected in early stages and eventually eroding the medial orbital wall, as demonstrated in this case. Subsequently, invasion of rectus muscles, orbital apex and ipsilateral cavernous sinus may be seen. Magnetic resonance imaging (MRI) may be more sensitive due to increased soft tissue resolution and may show hyperintense sinus wall, hyperintense lesion extending from paranasal sinus along orbital apex into intracranial structures on T2 weighted images and ipsilateral internal carotid artery narrowing [7]. The internal carotid artery narrowing signifies fungal invasion of the arterial wall or perivascular tissues, which can lead to occlusion of the lumen, leading to fatal cerebrovascular complications [8]. Interestingly, our patient did not demonstrate cavernous sinus thrombosis on imaging. This may suggest either an earlier stage of cerebral involvement, as it usually occurs in long standing cases, or a different pattern of spread [9].

Principle of management include early diagnosis, treating underlying risk factors, prompt antifungal therapy and timely surgical debridement [10]. A multidisciplinary approach consisting of ophthalmologists, otorhinolaryngologists, and neurologist is critical for management. Optimisation of underlying risk factors like ketoacidosis or hyperglycemia need to be controlled.

Amphotericin B is the main choice therapy against mucormycosis and requires monitoring of renal profile due to its side effects of nephrotoxicity. It has been shown that liposomal amphotericin B significantly decreases toxicity, and increased efficacy compared to conventional amphotericin B [11]. Posaconazole has also been used and can be used in patients who are refractory to amphotericin B. Surgical debridement should be as wide and aggressive to remove all the necrotic tissue but may demand cosmetic and functional sacrifices. It has been reported that patients who had surgical treatment together with amphotericin B had better outcome than treatment with amphotericin B alone [12].

In this case, systemic amphotericin B and

antibiotics were initiated early, and surgical debridement was planned. However, treatment could not be fully optimized as our patient refused further inpatient medical treatment, surgical intervention, and defaulted on further follow-up appointments. This significantly compromised his prognosis, highlighting the importance of patient compliance with complete treatment regimens, the necessity of combined medical and surgical interventions, and the fatal nature of this infection when inadequately treated.

## 4 CONCLUSION

Rhino-orbital-cerebral mucormycosis is a severe, emergent infection and can be fatal. Early diagnosis with multi-disciplinary management is crucial for best possible outcome.

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