Rhino-orbital Mucormycosis Manifesting as Orbital Apex Syndrome with CRAO in An Immunocompetent Patient

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Abstract

Rhino-orbital mucormycosis (ROM) is an uncommon opportunistic infection affecting immunocompromised individuals. Poorly controlled diabetes mellitus is the commonest predisposing factor. A 42-year-old female with well controlled diabetic status, presenting with orbital apex syndrome (OAS) and Central Retinal Artery Occlusion (CRAO) is discussed in this report. There was no evidence of cellulitis, necrotic eschar or facial palsy. There were no features suggesting immunosuppression. The biochemical parameters including blood sugar and electrolytes were normal. Serology for HIV was negative. MRI showed pan sinusitis with thickening and enhancement of extraocular muscles. Urgent debridement of paranasal sinuses was done. Histopathological examination disclosed broad based, filamentous, aseptate hyphae suggestive of mucormycosis. Prompt treatment with systemic Amphotericin B and debridement of sinuses resulted in a favourable outcome. Mucormycosis presents with a constellation of clinical features including ophthalmoplegia, proptosis, ptosis, visual loss, chemosis, nasal discharge, abducens nerve palsy, palatal necrosis, cerebral involvement, hemiparesis and eye lid gangrene. The coexistence of sinus disease with OAS in a diabetic patient should trigger a vigilant search for a fungal etiology, despite the absence of immunosuppression. Microbiological culture may yield negative results and histopathological examination is mandatory. This report emphasizes the rare occurrence of ROM in an immunocompetent diabetic patient with good metabolic control. Early diagnosis and a multidisciplinary approach with intravenous antifungals, adequate sinus drainage and surgical debridement can greatly reduce the morbidity and mortality.

Keywords: Rhino-orbital mucormycosis, Orbital apex syndrome, Central retinal artery occlusion, Immunocompetent.

Introduction

Mucormycosis is an opportunistic fungal infection with acute and fulminant manifestations. This lethal disease invariably affects immunocompromised patients, especially those with diabetic ketoacidosis (60%–81%). It is seldom documented in immunocompetent individuals. Rhino-orbital mucormycosis (ROM) presents as an orbital apex syndrome (OAS) characterized by proptosis, ophthalmoplegia and visual loss. The myriad of atypical clinical manifestations and complexity in demonstration of the causative organism poses a diagnostic challenge, which heralds a poor prognosis. We report an intricate case of an immunocompetent patient with well controlled diabetic status, presenting with Rhino-orbital Mucormycosis, manifesting as an OAS with Central Retinal Artery Occlusion (CRAO).

Case report

A 42-year-old female presented with sudden loss of vision and drooping of eyelid in the left eye for one week, associated with headache, vomiting and low-grade fever. There was no epistaxis, nasal obstruction or nasal discharge. The medical history was consistent with well controlled diabetes mellitus, maintained on oral hypoglycaemic therapy. She was well nourished, conscious and afebrile with no signs of meningeal irritation. There was no history of systemic malignancy, long-term use of corticosteroids or immunosuppressive therapy.

The visual acuity was perception of light in the left eye. Examination revealed mild proptosis, complete ptosis and total ophthalmoplegia (Figure 1 and 2). The corneal sensation was diminished, and facial hypoaesthesia was noted in the ophthalmic division. Fundus revealed disc edema, severe arteriolar attenuation, cannon ball hemorrhages in the veins and cherry red spot at macula, suggesting Central Retinal Artery Occlusion (CRAO) (Figure 3). There was no evidence of cellulitis, necrotic eschar or facial palsy. Examination of nasal and oral cavities were unremarkable. Right eye examination was within normal limits.

The fasting and post prandial blood sugar levels were 130 and 155 mg% respectively. The other biochemical parameters like urea, creatinine, potassium, electrolytes and arterial blood gas (ABG) analysis were normal. Ketone bodies were absent in urine. Mantoux test was non-reactive, chest radiograph was normal and serology for retrovirus was negative. P-ANCA and C-ANCA were negative. Diagnostic nasal endoscopy showed mucosal thickening and turbinate hypertrophy with no evidence of eschar. Magnetic resonance imaging (MRI) showed abnormal T2 hyperintensities filling the left ethmoidal sinus. There was mucosal thickening and opacification of left ethmoid, frontal and sphenoidal sinuses. Abnormal thickening and enhancement of extraocular muscles and optic nerve was noted. There was no distinct mass lesion in the orbit (Figure 4). CT scan revealed no bony erosion. Based on the clinico-radiological profile, a diagnosis of left orbital apex syndrome with CRAO was entertained. Endoscopic sinus surgery with limited debridement of...
sinuses was performed. A specimen consisting of multiple grey white to grey brown soft tissue fragments was sent for laboratory confirmation. The microbiological evaluation failed to reveal the causative organism. Histopathological examination showed polypoidal nasal mucosa with a necrotic focus infiltrated by broad based, filamentous, aseptate and irregular hyphae, suggestive of mucormycosis (Figure 5).

A thorough debridement of necrotic tissue in sinuses and irrigation with amphotericin B was performed at a second sitting. Treatment with systemic Amphotericin B was promptly initiated. The blood sugar was well controlled with the same antidiabetic regimen. Clinical improvement was observed in two weeks with gradual resolution of ptosis and extraocular movements.

Discussion
Mucormycosis of orbit is a fulminant fungal infection associated with high morbidity and mortality. The most common aetiological agents include Rhizopus oryzae, Mucor, Cunninghamella, Apophysomyces and Lichtheimia species. The common forms of mucormycosis are rhino-orbito-cerebral, cutaneous, pulmonary, disseminated, gastrointestinal and isolated renal. The infection has a predilection for immunosuppressed states like diabetic ketoacidosis, immunosuppressive therapy, thermal burns,
chronic renal failure, cirrhosis, steroid or cytotoxic therapy, hematological malignancies, malnutrition, solid organ transplantation and HIV infection. It is scarcely ever reported in patients with healthy immune status.

Uncontrolled diabetes mellitus is the commonest predisposing factor for mucormycosis. 60–80% of cases occur in diabetic ketoacidosis. Hyperglycemic status and metabolic acidosis nourish fungal colonies by interference with neutrophilic phagocytosis and increase in serum unbound iron. This report emphasizes the rare occurrence of ROM in an immunocompetent diabetic patient with good metabolic control.

The inciting event in ROM is inhalation of fungal spores. The fungi colonize the sino-nasal mucosa and enters the orbit through the ethmoid and maxillary sinuses or via the nasolacrimal duct. Orbital involvement often presents as an orbital apex syndrome (OAS). The exact pathogenesis of Rhino-Orbito-Cerebral Mucormycosis (ROCM) is not known. It is speculated to be due to spread from the paranasal sinuses to pterygopalatine fossa, from where it spreads to the cranium via orbital apex, orbital vessels or cribiform plate. A conglomerate of clinical features may signalize the disease including external ophthalmoplegia, proptosis, visual loss, chemosis, nasal discharge, abducent nerve palsy, palatal necrosis, cerebral involvement, hemiparesis and eye lid gangrene. The patient discussed here presented with proptosis, ophthalmoplegia and visual loss, thus constituting an orbital apex syndrome (OAS). The absence of nasal symptoms and necrotic eschar should not prompt a dismissal of diagnosis of mucormycosis.

Sinusitis is universal in ROM with ethmoid and maxillary sinuses being most frequently involved, followed by sphenoid and frontal sinuses. The coexistence of sinus disease with OAS in a diabetic or immunocompromised patient should trigger a vigilant search for a fungal etiology. The sinus involvement was notably conspicuous in this case. The vascular invasion of hyphae results in widespread occlusive vasculitis and thrombosis. This thrombosing vasculitis causes emboli and vascular obstruction, culminating in tissue necrosis. The ominous manifestations like Central Retinal Artery Occlusion (CRAO), cavernous sinus thrombosis and endophthalmitis have been variably reported. The unfortunate eventualty of CRAO bears an incidence of 16%–20%. ROM in this case apparently exhibited itself as orbital apex syndrome coexisting with CRAO.

Intracranial extension and orbital involvement may be visible on CT scan. T2-weighted MRI and contrast-enhanced T1-weighted MRI are considered superior to CT for better delineation of the fungal mass. Mucosal thickening and opacification of sinuses are visualized as T2 hyperintensities on MRI.

The diagnosis is aided by recognition of typical clinical and radiological findings. A biopsy of the debridged necrotic tissue from the nasopharynx, sinuses or orbit substantiates the diagnosis. KOH mounts may reveal aseptate branching hyphae at right angles. Calcofluor white, Gomori’s methenamine silver (GMS), hematoxylin and eosin (H and E), and periodic acid–Schiff stains may also provide reliable information. Microbiological culture results may be variable and are often unrewarding, similar to this case. Histopathological examination (HPE) shows large non-septate mycelial filaments with angioinvasion within the necrotic material.

Orbital apex syndrome is a common sequela with a high risk of mortality. The prognosis depends on the extent of infection, immune status of the host and response to treatment. There is ample evidence of high success rates with local amphotericin B and sino-nasal debridement, when the disease is restricted to sino-nasal or rhino-orbital sites. In case of cerebral involvement, surgical debridement provides no survival benefit and imminent mortality is inevitable. The absence of intracranial spread stimulates a favourable prognosis in this patient. Early diagnosis of sino-nasal mucormycosis, management of the predisposing factor and prompt therapeutic interventions are critical for arresting intracranial spread of this fatal disease.

A multimodality approach with intravenous antifungals, adequate sinus drainage and surgical debridement is warranted.

### Conclusion

Mucormycosis must be considered in the differential diagnoses of a diabetic patient with coexisting sinus disease and Orbital apex syndrome, despite the absence of immunosuppression. An expeditious neuroimaging should be strongly considered. Microbiological culture may yield negative results and histopathological examination is confirmatory. Early diagnosis and a multidisciplinary approach can greatly reduce the morbidity and mortality.

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