Case Report

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# Central retinal artery occlusion as the presenting manifestation of invasive rhino-orbital-cerebral mucormycosis

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**Abstract:**

Rhino-orbital-cerebral mucormycosis (ROCM) is a rare but devastating fungal infection caused by filamentous fungi of the family Mucoraceae. We report a rare case of unilateral ROCM in a diabetic patient where central retinal artery occlusion (CRAO) was the first manifestation of the disease. Magnetic resonance imaging scan revealed orbital and intracranial spread of the disease. Definitive diagnosis was established by culture of the biopsy specimen which showed *Rhizopus oryzae* on Sabouraud's dextrose agar. The patient was successfully treated with extensive debridement of sinuses and intravenous liposomal amphotericin B; however, the left eye remained blind following the CRAO.

**Keywords:**

Central retinal artery occlusion, diabetes mellitus, ophthalmoplegia, ptosis, rhino-orbital-cerebral mucormycosis

## Introduction

Mucormycosis is an uncommon, lethal opportunistic infection caused by filamentous fungi of the family Mucoraceae. Mucormycosis almost invariably affects persons with immunocompromised states, especially those with diabetes complicated by ketoacidosis, organ-transplant recipients, patients on steroid or cytotoxic therapy, and those with leukemia and other disseminated cancers. The accepted clinical forms of mucormycosis are rhino-orbital-cerebral mucormycosis (ROCM), pulmonary, cutaneous, gastrointestinal, disseminated, and miscellaneous.[1] ROCM is an invasive and often fatal form of mucormycosis occurring in several immunocompromised states including diabetes, which is the most common (60%–81%) predisposing factor.[2] ROCM originates in the nasal or paranasal sinus mucosae after inhalation of fungal spores and thereafter shows a contiguous spread to the neighboring tissues, including the orbit, and sometimes to the brain.

Herein, we report a case of invasive ROCM in a diabetic patient where central retinal artery occlusion (CRAO) was the first manifestation of the disease.

## Case Report

A 55-year-old male patient was referred to our outpatient department for severe loss of vision in the left eye (LE) for 5 days. Subsequently, he was noted to have drooping of the left eyelid associated with significantly decreased ocular motility. It was also associated with an intermittent headache, facial pain, and left-sided nasal blockage. He was diagnosed as CRAO in the LE by a local ophthalmologist and referred to us for further management.

He was conscious, oriented, and afebrile at the time of presentation. Best-corrected

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visual acuity in the right eye (RE) was 20/20 and there was no light perception in the LE. Ophthalmologic examination revealed complete ptosis and total ophthalmoplegia in the LE with impairment of cranial nerves III, IV, V1, and VI. He had left infraorbital hypoesthesia. Anterior-segment examination showed dilated fixed pupil in the LE. Fundus examination of the LE revealed a generalized retinal edema, retinal arterial attenuation, and the presence of a cherry-red spot at the posterior pole, suggesting CRAO of the LE [Figure 1a]. Fundoscopy of the RE was unremarkable. Current medical history revealed poorly controlled type 2 diabetes. His random blood sugar level was 398 mg/dl, urine glucose was 4+, but urine ketone was negative.

A magnetic resonance imaging (MRI) scan of the brain and orbit [Figure 2a and b] showed enhancing soft tissue in the left ethmoid sinus eroding the fovea ethmoidalis and lamina papyracea with soft-tissue extension into the left orbit involving medial and inferior recti muscles and surrounding the optic nerve. Posteriorly, this soft tissue was seen to occupy the orbital apex and superior orbital fissure and infiltrating into the left cavernous sinus, causing its thrombosis. Loss of flow void was seen in the left internal carotid artery, suggesting thrombosis. Conglomerate abscesses were seen in the left frontal region. An ear, nose, and throat specialist evaluated the patient and concurred with the possible diagnosis of mucormycosis. The patient underwent emergency functional endoscopic sinus surgery with debridement of the sinuses. Fungal smear of the affected tissue showed broad, aseptate right-angled hyphae on 10% KOH mount. Culture of the biopsy specimen from the sinuses showed *Rhizopus oryzae* on Sabouraud's dextrose agar [Figure 2c]. The patient was started on subcutaneous insulin and amphotericin B (liposomal) at 0.3 mg/kg/day and this was gradually increased to 1 mg/kg/day (total cumulative dose 2 g) with the monitoring of the serum electrolytes and the renal functions. The patient showed a dramatic clinical response, with improvement in his diabetes. He had completed intravenous liposomal amphotericin B and discharged well after 10 weeks of hospitalization. Last controlled visit revealed that his LE remained blind, with complete ptosis and total ophthalmoplegia. Fundus examination of the LE revealed optic atrophy, generalized retinal arterial attenuation, and retinal atrophy at macula, which was confirmed on optical coherence tomography [Figure 1b]. There was complete resolution of fungal sinusitis and abscesses in the left frontal region.

## Discussion

Mucormycosis is an infection caused by a group of distinctive mycoses, which include the genera *Rhizopus*, *Mucor*, and *Absidia*.[3] These are ubiquitous, saprophytic fungi which can be found in fruits, soil, dust, manure, and can be cultured from the nasal mucosa of normal persons.[4] Sporulation and growth of these fungi requires the host defenses to be compromised or the existence of some debilitating illness. Diabetes mellitus is the commonest predisposing factor for mucormycosis, especially if complicated by ketoacidosis. Diabetes alters the immunologic capability to resist mucormycosis through hampering of host phagocytosis and mobilization of polymorphonuclear leukocytes.[5] Furthermore, elevated blood glucose levels, acidosis, and increased availability of free serum iron at low pH aid in the growth of fungus. These fungi have a predilection for the internal elastic lamina of blood vessels, thus causing angioinvasion, thrombosis, and hemorrhagic necrosis, which is the most likely mechanism of the sinus disease spreading into the orbit and brain.[1]

In ROCM, the disease usually begins in the nose or sinuses and then spreads in the continuum to the adjacent structures such as the orbit and brain. Patients usually report facial pain, headache, fever, and purulent or bloody

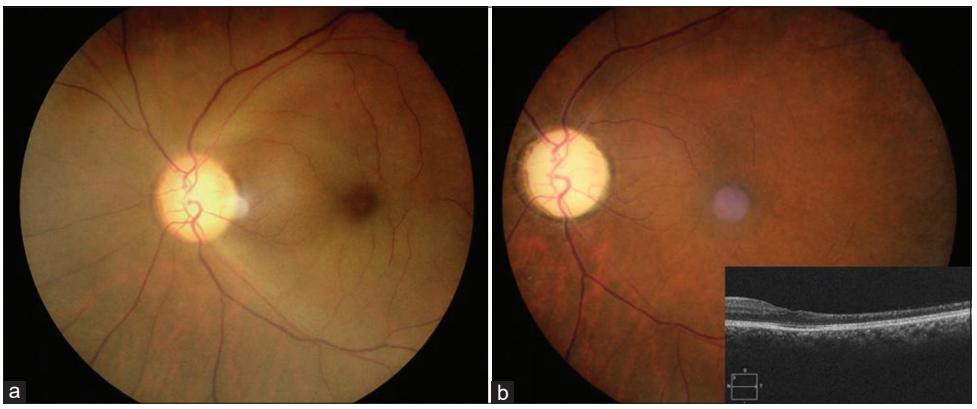


**Figure 1:** Color fundus image of the left eye showing (a) retinal edema, retinal arterial attenuation, and cherry-red spot at macula, suggesting central retinal artery occlusion at the time of presentation. (b) at the last visit, fundoscopy showing optic atrophy, generalized retinal arterial attenuation, and retinal atrophy at the macula, confirmed on optical coherence tomography

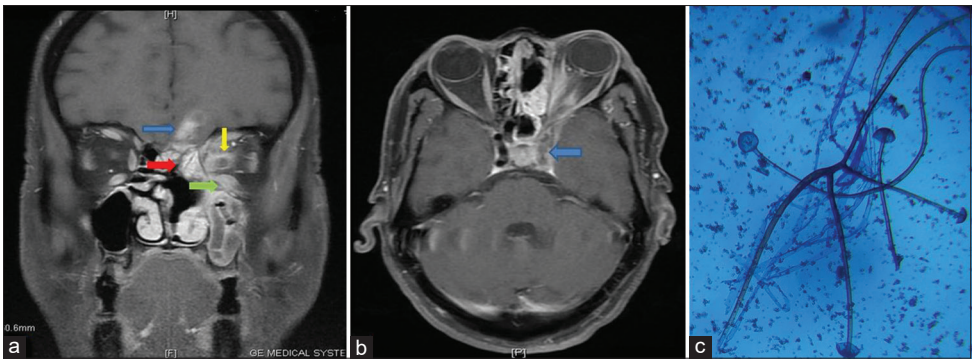

**Figure 2:** T1-weighted gadolinium contrast-enhanced magnetic resonance imaging images of the brain, orbit, and paranasal sinuses showing (a) enhancing soft tissue involving the left ethmoid sinus (red arrow) with its extension into the left orbit involving medial and inferior recti muscles (green arrow), surrounding the optic nerve (yellow arrow) and the left frontal lobe abscess (blue arrow). (b) Axial image showing enhancing soft tissue involving the orbital apex and infiltrating into the left cavernous sinus, causing its thrombosis (blue arrow). (c) Biopsy specimen showed growth of *Rhizopus* on lactophenol cotton blue mount

nasal discharge. Rhinoscopy at an early stage may reveal a black, necrotic turbinate or septum due to infarction of tissue. Orbital involvement presents as chemosis, periorbital cellulitis, infraorbital anesthesia, proptosis, and ophthalmoplegia.[2,6] Intracranial invasion occurs by way of the superior orbital fissure, cribriform plate, ophthalmic vessels, and possibly via a perineural route.[7,8] Altered sensorium, hemiparesis, brain abscesses, meningeal signs, and blindness herald central nervous system involvement.[1] Our patient presented with an intermittent headache, facial pain, left-sided nasal blockage, complete ptosis with concomitant ophthalmoplegia, CRAO, cavernous sinus thrombosis, and brain abscesses, suggesting the orbital and intracranial spread of the disease.

CRAO is a rare manifestation of ROCM with an incidence of 16%–20%. It is attributed to direct infiltration of a central retinal artery by angioinvasive fungal infection from the orbit. Ho *et al*.[9] had reported a case of ipsilateral ROCM with contralateral endogenous fungal endophthalmitis presenting with sudden loss of vision secondary to CRAO. However, CRAO in this case was associated with the intermittent fever, headache, ipsilateral complete ptosis, and ophthalmoplegia at the time of presentation. Bhansali *et al*.[10] and Yohai *et al*.[2] in their published study reported that the visual loss in ROCM usually has been attributed to CRAOs and cavernous sinus thrombosis. Our patient had both of these blinding conditions where CRAO was the first manifestation of the disease. Furthermore, CRAO has not been reported as the sole initial presenting feature of ROCM before based on our PubMed search.

Diagnosis was established by biopsy samples taken from the margins of the necrotic lesion, and extensions of the disease were reported in MRI findings. Our patient had been treated aggressively with intravenous liposomal amphotericin B and extensive surgical debridement, which remained the mainstay of treatment. Fungi thrive on dead organic tissues and continue to spread along the injured blood vessels; therefore, debridement is necessary. Liposomal form is more effective, less nephrotoxic, and has an enhanced therapeutic index to over 20 folds.[11] The infection was controlled with an appropriate therapy; however, the LE remained blind following the CRAO.

To conclude, CRAO presenting as the first manifestation of ROCM is a rare occurrence. MRI is an effective technique for diagnosing ROCM, with biopsy being the most reliable. Early diagnosis, appropriate treatment of the underlying disorder, aggressive surgical debridement, and the use of liposomal amphotericin B are keys to improve outcome in patients with ROCM.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.


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## Conflicts of interest

The authors declare that there are no conflicts of interest of this paper.

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