Central retinal vein occlusion as primary ocular manifestation of rhino-orbital-cerebral mucormycosis: A case report

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Mucormycosis is a serious, rapidly progressing, life-threatening, and sight threatening fungal infection frequently seen in diabetics and immunocompromised patients. We report a rare occurrence of rhino-orbital mucormycosis presenting as unilateral central retinal vein occlusion (CRVO) and no other ocular signs of infection in a 65-year-old diabetic male. The definitive diagnosis was made by nasal biopsy which confirmed broad branching aseptate fungal hyphae. The patient was treated with amphotericin B for mucormycosis and intravitreal anti-vascular growth factor (anti-VEGF) drug for macular edema. To conclude, although ophthalmoplegia is the most common ocular presentation and retinal artery occlusion is the most common cause of visual loss in mucormycosis, it may have many varied presentations including CRVO. A high index of suspicion must be kept in diabetics and immunocompromised patients.

Key words: Central retinal vein occlusion, diabetes mellitus, macular edema, amphotericin B, rhino-orbital-cerebral mucormycosis, *Rhizopus*

Mucormycosis is a life-threatening fungal infection affecting immunocompromised hosts, including diabetics, and was recently seen in epidemics during and after the COVID-19 pandemic. It is caused by fungi of the order Mucorales and among them, *Rhizopus oryzae* (*Rhizopus arrhizus*) is the most common cause of infection.[1] Rhino-orbital infection begins with fungal spores invading the nasal and paranasal sinus mucosa. Orbital involvement occurs when the infection invades the orbital wall via the ethmoid and maxillary sinuses or via the nasolacrimal duct. Most common ocular presentation is ophthalmoplegia followed by proptosis and loss of vision.[2] Vision loss may be due to central retinal artery occlusion or orbital apex involvement affecting the optic nerve function.[3] We present a case of central retinal vein occlusion (CRVO) as a primary presentation of mucormycosis, in the absence of ophthalmoplegia or proptosis.

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Case Report

A 65-year-old one-eyed diabetic male presented with complaint of sudden onset diminution of vision in right eye for 2–3 days. He had undergone uneventful cataract surgery 5 years back in the right eye with good postoperative visual gain. His left eye was phthisical due to a childhood injury. There was no other ocular complaint.

The patient also had foul-smelling nasal discharge and facial pain on the right side. He was a recently diagnosed uncontrolled diabetic and had been on medications for the same.

Best-corrected visual acuity (BCVA) in the right eye was 1/60 and left phthisical eye had no perception of light. Anterior segment had quiet pseudophakia; rest, including intraocular pressure (IOP) was normal. Fundus examination of the right eye revealed clear media with nasal disc edema and hyperemia, dilation, and tortuosity of all branches of central retinal vein, flame-shaped retinal hemorrhages, and typical splashed tomato appearance of CRVO [Fig. 1a]. Macular edema was also present. Optical coherence tomography (OCT) of the macula confirmed cystoid spaces in inner retinal layers and subretinal fluid with central subfield thickness (CSFT) of 551 microns [Fig. 2a].

Nasal biopsy was done which reported scattered, broad, aseptate, branching fungal hyphae suggestive of mucormycosis. COVID-19 reverse transcription polymerase chain reaction (RT-PCR) was negative and COVID-19 IgM and IgG antibody titre came out negative. Contrast-enhanced magnetic resonance imaging (MRI) of the paranasal sinuses and orbit revealed pansinusitis of the left paranasal sinuses; significant erosion of sinus walls and lamina papyracea with enhancing inflammatory soft tissue extending into the left medial extraconal space of orbit corroborating with the diagnosis of orbital mucormycosis. Bilateral cavernous sinuses were symmetrical and showed normal enhancement [Fig. 1b].

Treatment in the form of liposomal amphotericin B 5 mg/kg was started and intravitreal anti-VEGF injection was given. The patient had active mucormycosis; hence rigid precautions were taken for strict asepsis during intravitreal anti-VEGF injection by using pre- and post-operative topical antibiotics and intraoperative use of povidone-iodine solution under the systemic cover of antifungal amphotericin B. The patient responded marginally well to anti-VEGF therapy, BCVA in

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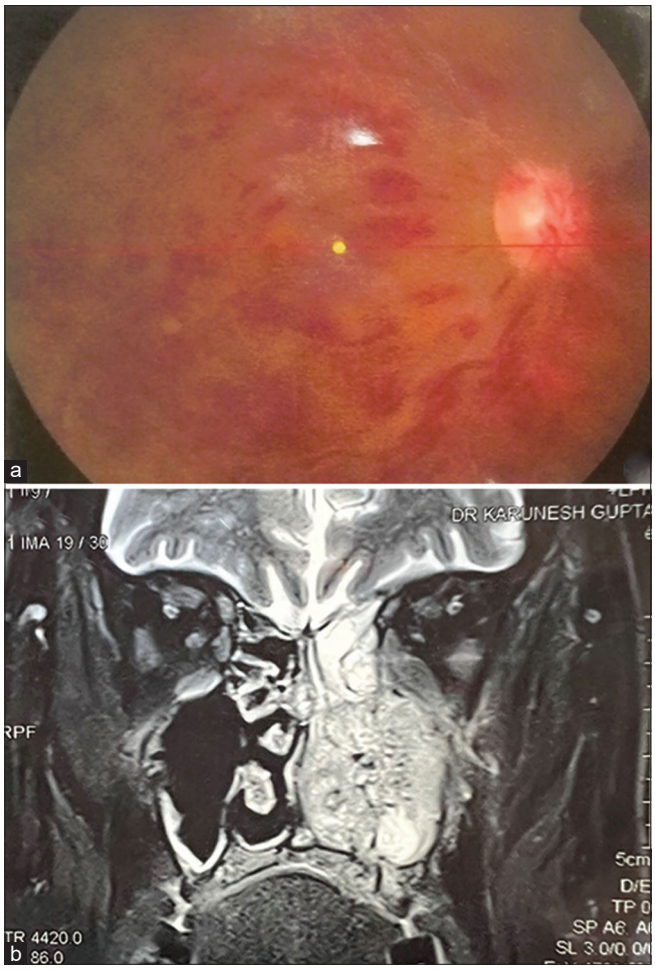

Figure 1: (a) Fundus picture showing central retinal vein occlusion in the right eye; (b) Contrast-enhanced magnetic resonance imaging (coronal section) revealed left pansinusitis; erosion of sinus walls with enhancing inflammatory soft tissue in the left medial extraconal space

OD improved to 6/60, and CSFT decreased to 415 microns after 2 weeks of injection [Fig. 2b].

Discussion

Rhino-orbital-cerebral mucormycosis (ROCM) is the most common form of mucormycosis in diabetic patients, and it may be the presenting manifestation in up to one-fourth of diabetic patients.[2,4]

Goel *et al*.[3] reported a mucormycosis patient following COVID-19 infection with combined central retinal artery and venous occlusion. However, CRVO has never been reported as the primary presentation of mucormycosis.

The pathogenesis of CRVO is believed to follow the principles of Virchow's triad for thrombosis, involving vessel damage, stasis, and hypercoagulability. Mucormycosis is an angiotropic fungus having a high tendency for damaging the internal elastic lamina of blood vessels, thus causing angioinvasion, thrombosis of the vessel lumen, and hemorrhagic necrosis specially of the arteries followed by lymphatics and veins by mechanical and toxic means.[5] This is the most likely mechanism of venous occlusion in our case.

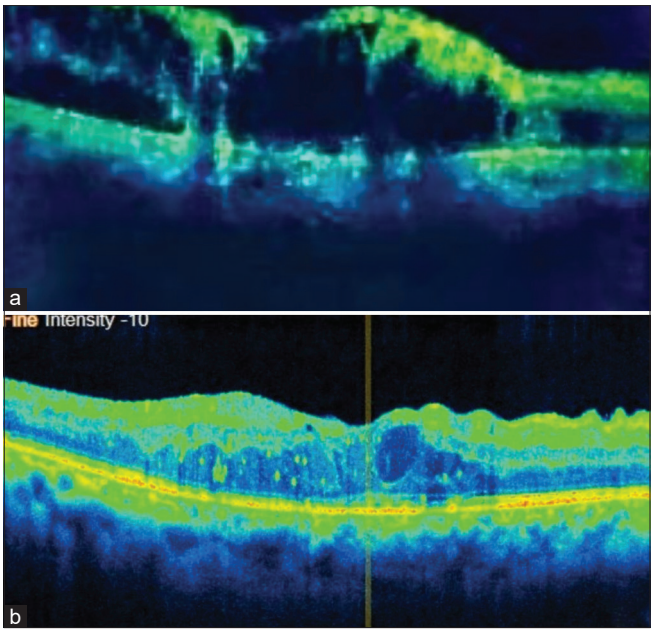

Figure 2: (a) Optical coherence tomography macula shows cystoid retinal edema and subretinal fluid with CSFT of 551 microns (b) Decreased CSFT of 415 microns with resolution of subretinal fluid after 2 weeks

Likewise, mechanical pressure by inflammatory tissue on the central retinal vein near the orbital apex is another proposed mechanism for venous occlusion. The veno-occlusive property of the disease manifested in the central retinal vein, thus causing CRVO.

Our patient did not have cavernous sinus thrombosis as the radiological evidence advocated. Cavernous sinus thrombosis in mucormycosis often occurs due to spread from the pterygopalatine fossa that is believed to be the largest fungal reservoir.[5] Further emphasizing the angiotropic nature of the virus, Yang *et al*.[6] reported hepatic mucormycosis mimicking hepatic veno-occlusive disease in pre-B cell acute lymphocytic leukemia.

CRVO is known to occur with a frequency of 10%–34% in diabetics.[7,8] Thus, CRVO in our case may be a chance occurrence unrelated to mucormycosis; however, its temporal association with nasal symptoms, evidence of inflammatory soft tissue extension into orbit on MRI, and angiotropic nature of the fungus causing veno-occlusive disease elsewhere in the body (cavernous sinus thrombosis and hepatic veno-occlusive disease) definitely point toward causal association of mucormycosis with CRVO. Definitive evidence can only be obtained by phlebotomy and subsequent histopathology showing fungal hyphae. CRVO may also have occurred secondary to inflammation or mechanical pressure on the vein in the area surrounding the central retinal vein, in which instance fungal hyphae maybe absent.

CRVO has been reported in cases of COVID-19.[9] So, COVID-19 infection can be thought of as a confounder for mucormycosis infection and CRVO, but our patient was negative for active as well as old COVID infection.

Definitive treatment for invasive fungal disease is intravenous amphotericin B and aggressive surgical debridement because

systemic medications often cannot reach the infected tissue due to vaso-occlusion and necrosis.[10] However, we administered intravitreal anti-VEGF injection in our case, which is the gold-standard treatment for CME in CRVO but has never been reported in mucormycosis.

Hence, the novelty of our case report is mucormycosis presenting as CRVO and the CME being treated with intravitreal anti-VEGF injection. A drawback of the case is our inability to present microbiological/pathological evidence of mucormycosis as the causative agent of CRVO.

Conclusion

Mucormycosis is a treatable multisystem disease in diabetic and immunocompromised individuals with varied presentations; thus, we should keep a high index of suspicion.

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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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. Clin Microbiol Rev 2000;13:236–301.
2. Bhansali A, Bhadada S, Sharma A, Suresh V, Gupta A, Singh P, *et al*. Presentation and outcome of rhino-orbital-cerebral mucormycosis in patients with diabetes. Postgrad Med J 2004;80:670–4.
3. Goel R, Arora R, Shah S, Chhabra M, Kumar J, Khurana N, *et al*. Clinico-radiological-pathological correlation of visual loss in COVID-associated rhino-orbito-cerebral mucormycosis. Ophthalmic Plast Reconstr Surg 2022;38:242–9.
4. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, *et al*. Epidemiology and outcome of zygomycosis: A review of 929 reported cases. Clin Infect Dis 2005;41:634–53.
5. Ak AK, Gupta V. Rhino-orbital cerebral mucormycosis. StatPearls. StatPearls Publishing; 2021 Available from: https://www.ncbi.nlm.nih.gov/books/NBK557429/. [Last accessed on 2022 May06].
6. Yang C, Friess SH, Dehner LP. Hepatic mucormycosis mimicking veno-occlusive disease: Report of a case and review of the literature. Pediatr Dev Pathol 2016;19:150–3.
7. Mansour AM, Walsh JB, Goldberger S, Henkind P. Role of diabetes mellitus on the natural history of central retinal vein occlusion. Ophthalmologica 1992;204:57–62.
8. Fong AC, Schatz H. Central retinal vein occlusion in young adults. Surv Ophthalmol 1993;37:393–417.
9. Sen M, Honavar SG, Sharma N, Sachdev MS. COVID-19 and eye: A review of ophthalmic manifestations of COVID-19. Indian J Ophthalmol 2021;69:488–509.
10. Nagappan V, Deresinski S. Reviews of anti-infective agents: Posaconazole: A broad-spectrum triazole antifungal agent. Clin Infect Dis 2007;45:1610–7.