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CASE REPORT **PEER REVIEWED | OPEN ACCESS**

Optic neuritis in post-Covid rhino-orbito-cerebral mucormycosis (ROCM): A rare presentation

Parul Singh, Perwez Khan, Anshika Gupta, Namrata Patel, Tejasvini Chandra, Dinesh Kumar Yadav

ABSTRACT

Introduction: Rhino-orbito-cerebral mucormycosis is a devastating opportunistic and fulminant infection. We report an unusual and rare case of optic neuritis as the complication of post-Covid rhino-orbito-cerebral mucormycosis (ROCM).

Case Report: A 37-year-old patient presented with ocular symptoms associated with ROCM and diminution of vision in left eye 14 days post-Covid. Radiological investigation (magnetic resonance imaging, MRI) showed heterogeneous altered signal intensity in left optic nerve. Fundus examination showed characteristic findings of optic neuritis.

Conclusion: In advanced stage of sino-invasive rhino-orbito-cerebral mucormycosis perineural invasion is a proven histological feature. In our case scenario, the optic nerve of the patient got involved through perineural spread of mucormycosis, causing inflammation along the nerve resulting in optic neuritis.

Keywords: Optic neuritis, Perineural invasion, ROCM

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INTRODUCTION

Invasive mucormycosis is a life-threatening fungal infection that most frequently occurs in patients with underlying comorbidities impacting immune system function [1–4]. Rhino-orbital-cerebral involvement is most frequently seen in those with poorly controlled diabetes mellitus, whereas immunocompromised patients (including those with hematological malignancies and transplant recipients) frequently present with pulmonary involvement and disseminated infection [3–6].

The spread of fungus occurs from paranasal sinus to orbit and then involving the cavernous sinus and brain through intracranial vasculature [7].

We herein describe a case reported in this post-Covid era where the patient presented with optic nerve involvement in form of optic neuritis as a complication of ROCM.

CASE REPORT

A 37-year-old male patient, resident of Kanpur presented with periorbital swelling, proptosis and conjunctival chemosis of left eye associated with left sided nasal discharge, approximately two weeks post-Covid infection. He was in home isolation and was

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not on supplemental oxygen therapy, but intravenous dexamethasone 1 mg BD was given for eight days. There was no history of diabetes, hypertension, cardiac disease, or any other systemic illness. He further developed diminution of vision in left eye which was progressive in nature and not associated with central nervous system (CNS) complaints.

Ocular examination revealed periorbital swelling, conjunctival chemosis, and congestion with mid-dilated pupil and sluggish reaction. Left eye ocular movements restricted in all gaze. Visual acuity 6/6 in right eye and finger count at one feet in left eye (Figure 1).

Contrast-enhanced magnetic resonance imaging (CEMRI) of orbit and peripheral nervous system (PNS) revealed heterogeneous altered signal intensity lesion seen in left orbit involving superior, inferior and lateral rectus muscles as well as left optic nerve and causing proptosis of the left eye globe and involvement of frontal, maxillary, ethmoid and sphenoid sinuses. No obvious abnormalities were seen on CEMRI brain (Figure 2).

On potassium hydroxide (KOH) mount, thin aseptate hyphae was found with right angled branching, suggestive of mucormycosis. On histopathological examination several hyaline aseptate ribbon-like fungal hyphae and few fungal spores were seen. On corroborating these findings on MRI and histopathological examination, diagnosis of post-Covid rhino-orbital-cerebral mucormycosis can be made.

Fundus examination of left eye shows obliterated physiological cup with disc pallor, blurred margins, congested tortuous retinal vessels, and multiple peripapillary splinter hemorrhages. These findings were suggestive of optic neuritis (Figure 3).

The patient was given intravenous liposomal amphotericin B injections (dose- 5 mg/kg body weight) for eight days and five retrobulbar amphotericin B injections, in dilution of 3.5 mg in 1 mL. This subsequently resulted in symptomatic improvement of the patient. The patient also underwent surgical debridement of the sinuses.

Figure 1: Pre- and post-treatment image of the eye of the patient.

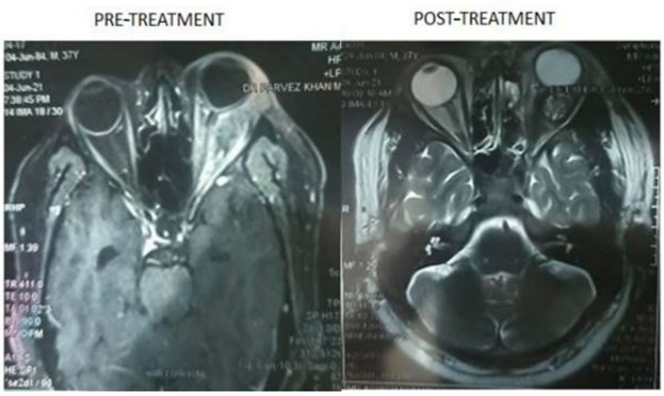

Figure 2: Pre-treatment—T1-weighted axial MRI shows left isointense signal intensity lesion, involving intraconal and extraconal spaces, extending along orbital apex. Post-treatment—T1-weighted axial CEMRI shows decrease in hyperintensity of the extraocular muscles and proptosis of left eye after treatment of mucormycosis.

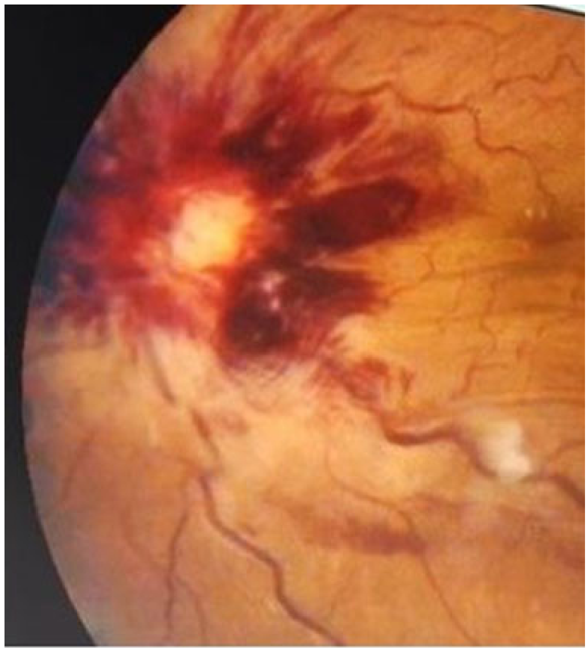

Figure 3: Fundus image depicting obliterated physiological cup with disc pallor, blurred margins, congested tortuous retinal vessels, multiple peripapillary splinter hemorrhages.

DISCUSSION

Mucormycosis is an aggressive and invasive fungal infection predisposed by uncontrolled diabetes mellitus, long-term corticosteroid use, immunosuppressive agents, primary or secondary immunodeficiency disorders, iron overload, malignancies and hematological stem cell transplantation, solid organ transplantations, etc. [8–11].

Mucormycosis invades through the thin lamina papyracea and further invades orbit and its contents extending posteriorly leading to orbital apex syndrome and since the optic nerve is involved thereby affecting vision.

Involvement of superior orbital fissure and its contents, such as cranial nerves third, fourth, and sixth and branches of fifth cranial nerve may cause diplopia, ophthalmoplegia, and sensory loss to the corresponding areas of the cornea and face. With further posterior extension, the fungus may gain access to the cavernous sinus and to the brain parenchyma.

Tissue necrosis and vessel thrombosis are important features of angioinvasion by mucormycosis which can be seen pathologically [12, 13].

The propagation and dissipation of fungus from one site to distant sites occur by this angioinvasion. Additionally this obstruction occurs of intermediate and large sized arteries and veins resulting in infarcts which can be either pale or hemorrhagic.

Also fungus can spread directly from cribriform plate to anterior cranial fossa which was considered as a perineural spread [14].

Frater et al. (2001) had also studied about the perineural invasion in patients with invasive mucormycosis and it can be an alternate route for extension of fungus into central nervous system [15].

McLean et al. (1996) reported that perineural extension of disease from cavernous sinus to pons occurs along the trigeminal nerve with no apparent meningeal or intraparenchymal brain involvement [16].

According to the case reported by Sebnem Orguc in 2005, the contrast-enhanced MRI was useful in depicting the extent of perineural spread before which the perineural invasion by fungus was considered as unusual [17–19].

Cornley et al. (2014) showed perineural invasion in 90% of biopsies that contained peripheral nerves [20].

Nerve microenvironment and neurotropic factors secreted in a gradient along nerves may play a pivotal role in the pathogenesis of perineural invasion [21]. Various hypotheses suggest that neural sheath can act as low-resistance conduit for cell growth through paracrine mechanisms, upregulation of neurotropic and axonal guidance molecules, and activation of directional cell migration toward and along nerves [21]. In conclusion, perineural invasion is one of the important histological features of invasive rhino cerebral mucormycosis and it indicates the advanced extent of invasion. In our case scenario, the optic nerve of the patient got involved through perineural spread of mucormycosis, causing inflammation along the nerve resulting in optic neuritis. The development of central retinal artery occlusion (CRAO) and optic nerve infarction occurs due to thromboembolic episodes because of angioinvasion as reported by Ghuman et al. (2015) [22], which is different from the optic neuritis in case of mucormycosis resulting from the possible perineural spread of the pathogen.

Since the involvement of trigeminal nerve and other peripheral nerves by mucor species have been noted, it cannot be a mere coincidence for the optic nerve to get involved and cause optic neuritis, though it is a rare possibility.

The patient was followed up for a period of two months. In the first follow-up visit there was improvement in the vision of the patient from finger count at one feet to 2/60, and on the subsequent follow-up visit his vision was 6/60, which supports our point of perineural spread, because had it been from optic nerve infarction or occlusion or thrombosis—there would have been no improvement in vision proving our hypothesis of perineural spread by the fungus causing optic neuritis.

Contrast-enhanced magnetic resonance imaging of brain, PNS, and orbit also showed improvement after the treatment of the patient which can be assessed by decrease in the hyperintensity of the extraocular muscles involved and resolvement of the proptosis and sinusitis (Figure 2).

CONCLUSION

This case report mainly focuses on the perineural spread of ROCM, which is already a proven histological feature. It resulted in the optic nerve involvement of the patient causing inflammation along the nerves (optic neuritis), which later got resolved with further management and intervention.

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Author Contributions

Parul Singh – Conception of the work, Design of the work, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Perwez Khan – Conception of the work, Design of the work, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Anshika Gupta – Acquisition of data, Analysis of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Namrata Patel – Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Tejasvini Chandra – Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Dinesh Kumar Yadav – Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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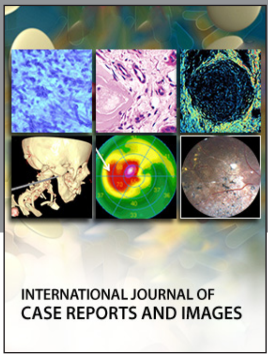

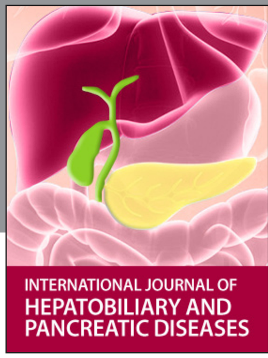

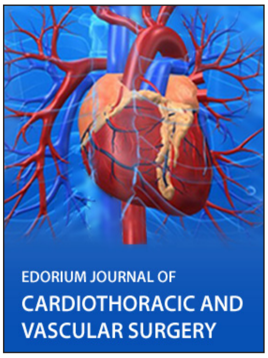

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