

Optic neuritis in Covid-19 associated rhino-orbital-cerebral mucormycosis

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Introduction

Mucormycosis is a rare invasive fungal infection caused by the genera from the order of *Mucorales*. These organisms are ubiquitous and can be found in soil and vegetation (1). Humans get infected by coming in contact with the fungal spores present in the environment. The infection most commonly affects the paranasal sinuses and the lungs after inhaling fungal spores (2). Occasionally the infection can occur on the skin following a cut injury, burn, etc.

Mucormycosis can present as rhino-orbital-cerebral infection which is the commonest presentation. The other presentations include pulmonary, gastrointestinal, renal, cutaneous, or even disseminated disease (3).

Only susceptible individuals get infected. Commonly identified risk factors are diabetes mellitus, particularly with ketosis, and immunocompromised states. Treatment with deferoxamine can enhance the growth and pathogenicity of the organism (4).

The spread of the fungus from one site to distant sites occurs by angioinvasion which causes vessel thrombosis and tissue necrosis, the hallmark of the disease. Perineural invasion is recognised as an alternate route for propagation (5).

A surge in the incidence of mucormycosis is being observed with the Covid-19 pandemic (6-9). Current hypotheses are that Covid-19 tends to worsen diabetes and precipitate diabetes in previously normal individuals.

Furthermore, Covid-19 infection itself is associated with leukopenia and may lead to a state of immunocompromise as a result of impaired or inappropriate immune responses and immunosuppressive treatment used in Covid-19 (2).

We describe a case of an elderly man with poorly controlled diabetes mellitus who presented with optic neuritis and rhino-orbital-cerebral mucormycosis and who was simultaneously diagnosed with COVID-19 infection. Optic neuritis is an inflammatory, demyelinating condition that causes subacute, usually monocular visual loss and it is seldomly reported as a presentation of mucormycosis (10).

Case Presentation

Our patient was a 65-year-old man, with type II diabetes mellitus, hypertension, chronic kidney disease stage IV, and dyslipidaemia for 21 years.

He presented to us with fever, left-sided headache, and reduced vision in the left eye for one-week duration associated with nasal congestion and anosmia.

Examination revealed a febrile patient with sinus tenderness over the left side frontal and maxillary sinuses. Examination of the eyes revealed bilaterally low visual acuity (right eye 6/18, left eye 6/60) and relative afferent pupillary defect in the left eye. There was no periorbital oedema, proptosis, chemosis, red eye, or ophthalmoplegia at the time of presentation. The left side fundus had a hyperaemic

and swollen disc with blurred margins. Both fundi showed features of non-proliferative diabetic retinopathy. The rest of the neurological and other system examinations were normal. The patient had bilateral occasional coarse crepitation in the lower zones of the lungs.

On the third day of admission, he developed left-sided periorbital swelling, proptosis, and complete blindness along with complete ophthalmoplegia suggestive of cavernous sinus thrombosis. Investigations are summarized in Table 1.

Table 1: Summary of investigations

Investigation	Results
White Cell Count (WBC)	$20.23 \times 10^9 /L$
Haemoglobin	10.1 g/dL
Platelet count	$429 \times 10^9 /L$
Serum creatinine	3.63 mg/dL
Serum sodium	135 mmol/L
Serum potassium	4.1 mmol/L
Blood cultures	No bacterial growth
C-reactive protein	150 mg/dL
ESR	80 mm/h
Capillary blood sugar	315 mg/dL
Urine ketone bodies	Negative
Cerebrospinal fluid analysis	Proteins – 55 mg/dL Glucose – 90 mg/dL (Plasma random blood sugar – 190 mg/dL) Polymorphs – Nil/mm ³ Lymphocytes – Nil/mm ³ Red cells – 05/mm ³ Tuberculosis PCR – Negative pyogenic culture – No growth
Chest X-ray	Normal
Blood culture	No growth

Magnetic resonance imaging (MRI) of the brain, sinuses, and orbits showed left maxillary, frontal, and ethmoid sinusitis, changes with left orbital inflammatory lesions, and left-sided optic neuritis (Figure 1). A nasopharyngeal swab for SARS-CoV-2 real-time RT-PCR became positive confirming Covid-19 infection.

Rigid nasal endoscopy showed necrosis of the left middle and inferior turbinates. The right nasal cavity was normal. Biopsy from the left middle turbinate showed acute inflammation and necrosis with invasive fungal infection likely of mucormycosis. Tissue culture direct microscopy-fungal filaments were seen and the culture-isolated *Rhizopus* spp.

As the patient clinically deteriorated on day 03 of admission, a repeat MRI was performed which revealed cavernous sinus thrombosis on the left side.

The diagnosis of rhino-orbital-cerebral mucormycosis (ROCM) complicated with left-sided optic neuritis and left-side cavernous sinus thrombosis with simultaneous Covid-19 infection was made. A multidisciplinary approach was taken and the patient was started on IV. Liposomal amphotericin B 5 mg/kg/day for 60 days which was stepped down to oral posaconazole 6 mg/kg/day. Along with antifungal therapy, surgical debridement was done by a left-side full-house functional endoscopic sinus surgery with endoscopic septoplasty.

He was discharged following twelve weeks of hospital stay with oral antifungals. He had a satisfactory recovery along with improvement in visual acuity. Follow-up with regular MRI brain with sinus view and rigid nasal endoscopy with fungal culture was planned. The target was to continue antifungals till stable disease with non-progressive symptoms and imaging with the hope of achieving fungal clearance if possible.



Figure 1: MRI showing Rhino-orbito-cerebral mucormycosis and optic neuritis (yellow arrows)

Discussion

Orbital involvement of mucormycosis can present with various clinical symptoms such as eye pain, periorbital oedema, proptosis, chemosis, ophthalmoplegia, and visual impairment (11). Farooq *et al* who studied 148 patients with predominant orbital mucormycosis observed that the most common manifestation (68.25%) in their patient cohort was the orbital apex syndrome (11). Optic nerve involvement in ROCM could be due to ischaemic optic neuropathy, infiltrative or compressive disease (12 - 14). Optic neuritis as the initial manifestation of rhino-orbital cerebral mucormycosis is rarely reported in the literature (10,13–15). Our patient presented with left-sided optic neuritis that later progressed to the orbital cavity and cavernous sinus involvement on the same side.

The spread of the fungus from one site to distant sites occurs by angioinvasion, which is the hallmark of the disease (5). Apart from this, the perineural invasion is also an alternate route for propagation (16). Mclean *et al.*, in 1996 (5) and Sebenem Orguc in 2005 (15) have reported the perineural spread of mucormycosis. Cornely *et al* reported that 90% of peripheral nerve biopsies performed had demonstrated perineural invasion of the fungus (17).

Therefore, optic neuritis can be considered as a sequela of perineural invasion by the fungus.

Gupta *et al* who reported a case series of cranial nerve involvement in mucormycosis in post-COVID patients observed optic nerve is the most commonly involved cranial nerve followed by the trigeminal nerve (13)

The current recommendation for the management of mucormycosis includes amphotericin B, surgical debridement with functional endoscopic sinus surgery (FESS), or orbital exenteration in severe cases (17). Several case series reported the use of intra-orbital amphotericin for poorly responding to orbital mucormycosis (11, 18). However, despite intensive treatment outcome of ROCM is poor (11,18) A retrospective observational study conducted in India that studied 2826 patients with ROCM reported that even after extensive treatment of ROCM, 66% had achieved final visual acuity of >20/200 (18).

Conclusions

Rhino-orbital mucormycosis is a rapidly progressive invasive fungal infection caused by ubiquitous saprophytic *Mucorales* which had become relatively common with the Covid pandemic.

Early diagnosis and vigorous treatment with liposomal amphotericin B and appropriate surgical debridement carry a better outcome. Optic neuritis is an unusual and rare presentation of mucormycosis due to perineural invasion by the fungus at its advanced invasive state.

Informed written consent was obtained from the patient to publish the case report with figures.

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