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*Case Report*

# Extensive Rhino-Orbital-Cerebral mucormycosis in kidney transplant recipient associated with COVID-19 infection: A Case Report

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**Abstract**

Rhino-orbital-cerebral mucormycosis is an invasive disease caused by fungi. Diabetes mellitus and solid organ transplantation are known risk factors, while it is increasingly recognized in patients with COVID-19 although the exact causal relationship is unknown. Early diagnosis and treatment with liposomal amphotericin B with surgical debridement carries a better outcome in these patients.

We present a case of extensive rhino-orbital-cerebral mucormycosis involving the paranasal sinuses, left orbit, cavernous sinus, middle cranial fossa with abscess formation in the left middle cerebellar peduncle in a 46-year-old kidney transplant recipient with concomitant COVID-19 infection.

## Introduction

Mucormycosis is an invasive fungal infection caused by the genera from the order Mucorales, who live everywhere in the environment (1), that causes infections particularly in the immunocompromised host (2).

Genera including Rhizopus, mucor, Rhizomucor, Cunninghamella, Absidia, Sakenaea, and Apophysomyces are the commonly observed organisms causing human infections (1). Risk factors are diabetes mellitus, diabetic ketoacidosis, deferoxamine and iron overload, glucocorticoid treatment, hematological malignancies, solid organ and hematopoietic transplantation, trauma, broad-spectrum antifungal treatment, and malnutrition (2,5).

COVID-19 infection appears to be associated with mucormycosis (3,4). In some case reports mucormycosis developed sometime after the diagnosis of covid-19 or simultaneously (3,4). It may manifest involving many organ systems including, paranasal sinuses, orbits, brain, respiratory tract, gastrointestinal system, skin, kidneys or may cause disseminated infection with hematogenous spread. Rhino-orbital-cerebral infection is the commonest (2,5). It usually begins as acute sinusitis and then spreads to adjacent structures such as orbits, palate, the base of the skull, brain, and brainstem rapidly over several days to a couple of weeks (3).

We report a case of extensive rhino-orbital-cerebral mucormycosis in a kidney transplant recipient with concomitant COVID-19 infection.

## Case presentation

Our patient was a 46-year-old male teetotaler and a non-smoker with type 2 diabetes mellitus and hypertension for the last 13 years. He underwent live donor kidney transplantation 4 months before the presentation due to diabetic nephropathy. He was on routine immunosuppressant medications (prednisolone, mycophenolate mofetil, and tacrolimus) with successful graft functioning.

Two days after the 1st dose of the Sinopharm COVID vaccine he experienced fever, cough, runny nose, loss of appetite, and diarrhea. He started to have pain and numbness in the left side of the face 7 days later and rapidly progressive left-sided visual loss and diplopia. He got admitted to the tertiary care hospital due to worsening headache and complete blindness of left eye.

On admission, he had a blind left eye and left-sided marked proptosis, complete ophthalmoplegia, hemifacial sensory loss, jaw drop, lower motor type facial nerve palsy, and cerebellar signs without pyramidal signs. After taking blood for cultures, he was started on IV meropenem and IV vancomycin. A nasopharyngeal swab for SARS COVID -19 was positive. He did not have evidence of severe COVID infection/pneumonia. His investigation results on admission were as follows [Table 01].

Table: Investigation Results

| Investigation | Results |
|---|---|
| White Cell Count (WBC) | $12.6 \times 10^9$ /L |
| Hemoglobin | 10.5 g/dL |
| Platelet Count | $83 \times 10^9$ /L |
| Serum Creatinine | 0.7 mg/dL |
| Serum sodium | 136mmol/L |
| Serum potassium | 4.2 mmol/L |

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|---|---|
| Alanine Transaminase (ALT) | 7 U/L |
| Aspartate Transaminase (AST) | 19 U/L |
| Random blood sugar | 180 mg/dL |
| Total protein | 6.7 g/dL |
| Albumin | 2.4 g/dL |
| Globulin | 4.3 g/dL |
| Bilirubin | 0.7 mg/dL |
| Urine Full Report | Sugar +++<br>Albumin – nil<br>Pus cells – 1-2/high power field<br>Red cells – 20-25/ high power field |
| Serum Calcium | 8.4 mg/dL (8.6 – 10.2 mg/dL) |
| Serum phosphate | 1.3 mg/dL (2.3 -4.7 mg/dL) |
| Serum magnesium | 1.5 mg/dL (1.6-2.6mg/dL) |
| Blood cultures | No bacterial growth |
| C-reactive protein | 245 mg/dL |
| Venous blood gas | pH -7.42<br>PCO2 - 28 mmHg<br>PO2 – 86 mmHg<br>HCO3 – 20.9 mmol/L<br>Lactate – 0.6 mmol/L |
| Urine ketone bodies | positive |
| SARS-CoV-2 real time RT-PCR | On 1st day of admission -RNA detected ct value 15 |
| | On 12th day of admission- RNA detected ct value 26 |
| SARS-CoV-2 total Antibody level | >10.00 Index reactive |
| Melioidosis antibodies | negative |
| Cerebrospinal fluid analysis | Proteins – 104 mg/dL<br>Glucose 92 mg/dL<br>(Plasma Random blood sugar – 299 mg/dL)<br>Polymorphs – 10/mm$^3$<br>Lymphocytes – 03/mm$^3$<br>Red cells – 03/mm$^3$ |
| Chest Xray | Normal |

With high clinical suspicion of mucormycosis he was started on liposomal amphotericin B 5mg/kg daily (150 mg/day). Immunosuppression was maintained at the minimum required level by adjusting the tacrolimus dose by observing the serum levels. Urine ketone bodies were positive, but there were no overt features of diabetic ketoacidosis.

MRI scan of the paranasal sinuses, orbits and brain revealed pan sinusitis with preorbital and orbital cellulitis, with spreading infection into the orbital apex, cavernous sinus, Meckel's cave, trigeminal nerve complicated with abscess formation in the left middle cerebellar peduncle, and cerebellum [figure 01 and 02]. There was no evidence of other organ involvement such as lungs, kidneys, and gastrointestinal tract.

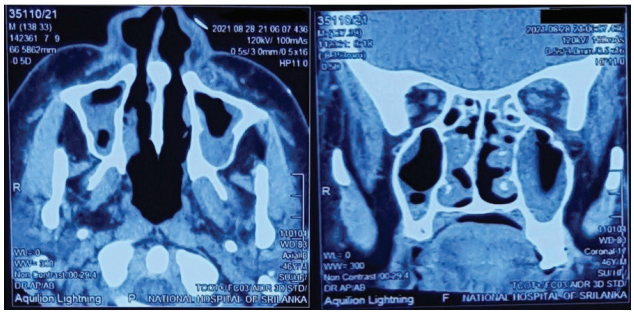

Figure 1: Transverse (left) and coronal (right) MRI images showing maxillary sinusitis and inflammation of nasal turbinates

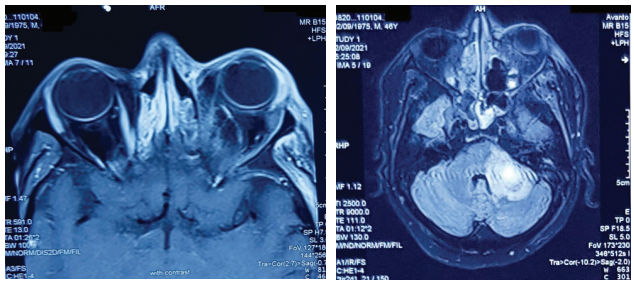

Figure 2: A transverse MRI image showing left orbital cellulitis and loss of enhancement of left nasal mucosa- "black turbinate sign" (left) and follow-up MRI image showing abscess formation in the left cerebellum (right)

He underwent left orbital decompression and repeated functional endoscopic sinus surgeries (FESS) for debridement of necrotic tissues. Rhizopus species was isolated by the culture of the necrotic tissue from the debridement surgery. Liposomal amphotericin was continued for a total of 12 weeks. Follow-up MRI scans showed regression of the lesions and swelling. The patient was ultimately neurologically stable but left with the blind left eye, left-sided total external ophthalmoplegia, trigeminal and facial palsy with cerebellar symptoms and signs.

**Discussion**

Our patient had rapidly progressive extensive rhino-orbital-cerebral mucormycosis extending into the base of the skull and cerebellum which started to manifest 7 days after the onset of COVID-19 symptoms. The infection had spread rapidly within hours to days into the surrounding structures of the brain and skull. On admission to the hospital 13 days after the onset of runny nose, fever and cough his PCR for COVID -19 was positive with a reactive antibody level of > 10.00 index to COVID-19. Therefore, he probably had COVID-19 infection and rhino-orbital-cerebral mucormycosis simultaneously. Diabetes and kidney transplantation with immunosuppression have predisposed the infection in our patient.

## Conclusion

Rhino-orbital-cerebral mucormycosis is a rare fungal infection that can cause devastating clinical manifestations involving multiple organ systems, in immunocompromised hosts.

Early diagnosis and vigorous treatment with liposomal amphotericin B and appropriate surgical debridement carry a better outcome.

It is an emerging clinical entity observed in the context of COVID-19 infection. When patients present with symptoms of sinusitis and multiple cranial nerve lesions and other focal neurological signs the clinician should suspect rhino-orbital-cerebral mucormycosis. In addition, multicentered studies should be carried out to identify the exact causal relationship between these two infections.

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