

Rhino-cerebro-orbital Mucormycosis caused by *Mucor indicus*: A case report

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ABSTRACT –

Mucormycosis is a rare opportunistic infection caused by fungi belonging to phylum Glomeromycota. Rhinocerebral mucormycosis is most common and fulminating type of mucormycosis, which may lead to fatal consequences within a week of disease onset if left untreated. It is invariably associated with diabetes mellitus, hyperglycaemia, ketoacidosis or with debilitating disease such as leukaemia and lymphoma. *Mucor indicus* was first discovered in the late 19th century and is generally considered a non-pathogenic organism. We have reported rhino-sino-orbito-cerebral mucormycosis in a 17 years old male, known case of diabetes mellitus came to OPD unconscious with diabetic ketoacidosis and was diagnosed with *M. indicus*. It can be said to be the first case report globally to the best of our knowledge.

Key words - Mucormycosis, *Mucor indicus*, Type 1 diabetes mellitus, Diabetic ketoacidosis.

INTRODUCTION –

Mucormycosis is a rare opportunistic infection caused by fungi belonging to phylum Glomeromycota. The hyaline moulds are classed in the order Mucorales in the Mucoromycotina, a subphylum of lower fungi.¹ Formerly, the disease caused by moulds referred to as zygomycosis but, in view of the revised higher-level classification of fungi, it is appropriate to refer to the disease as mucormycosis, a name well known in clinical medicine. The former phylum Zygomycota is no longer taxonomically valid.¹ It is a rapidly progressive disease, thereby may prove fatal if timely diagnosis is not made and proper treatment is delayed. The main reason of rapidity being involvement of blood vessels, i.e., angioinvasive nature leading to necrosis of infected tissue. It presents as six clinical types according to the anatomical sites infected in the patient. These are as follows – Rhino cerebral, pulmonary, cutaneous, gastrointestinal, isolated cerebral and disseminated mucormycosis².

Rhinocerebral mucormycosis is most common and fulminating type of mucormycosis, which may lead to fatal consequences within a week of disease onset if left untreated. It is invariably associated with diabetes mellitus, hyperglycaemia, ketoacidosis or with debilitating disease such as leukaemia and lymphoma. Even though it is extremely rare, it has been reported from all corners of the world.³

CASE HISTORY -

A 17 years old male, came to Emergency OPD with history of redness along with blackening on the right side of the face for 1 week. He was unconscious at the time of admission and a known case of type 1 diabetes mellitus. There was no history of hypertension, alcohol consumption. But he gave history of covid-19 and received steroids 6 months back. He was diagnosed with type 1 diabetes at the age of 5 years he was on long-acting insulin injections which he himself used to inject. At the time of admission, he had blood sugar levels 640 mg/dl and ketones were high on his blood reports. He received insulin shots immediately and was transferred to ENT department for further examination. The signs and symptoms include chemosis, periorbital cellulitis, ophthalmoplegia, abrupt visual loss, pain on right side of the face and facial hyposthesia. Physical examination revealed brownish, blood-stained nasal discharge on right side, black eschar on palate due to haemorrhage and tissue necrosis, fixed dilated pupils and global proptosis and ptosis with dysfunction of cranial nerves, especially 5th and 7th nerves. There was an extensive and rapid destruction of surrounding tissues (Fig:1). He received prompt administration of high dose of liposomal amphotericin B (5 mg/kg/day) and meropenem 1 mg IV 8 hourly along with surgical resection of infected regions was planned. He was posted for debridement surgery. However, he died 2 days after surgery.

MATERIAL AND METHOD –

Intra operative nasal swab was collected and send to Mycology section of Microbiology laboratory, Government medical college, Nagpur. It was processed for direct microscopy in KOH mount, gram staining and culture on Sabouraud's dextrose agar (SDA). On 10% KOH mount, ribbon-like, broad and non-septate branching hyphae was seen (Fig:2). Gram staining showed gram positive fungal hyphae.

The specimen grew faster after 24 h of incubation at 37°C. Hyphal growth from the sample could be noticed which after four days had developed a deep yellow thallus on SDA. Lactophenol cotton blue (LPCB) mount from the colonies grown on SDA revealed nonseptate hyphae; sporangiophores (15 mm wide) bearing sporangia (up to 50×55 mm) with a sub-spherical columella (Fig:3). Rhizoids and stolons were absent. Sporangiospores were pleomorphic, smooth walled, mostly sub-spherical to ellipsoidal (Fig:4); chlamydospores were also present and especially abundant in presence of light (Fig:5).

The patients' isolate grew well at 40°C as well as 42°C but fail to grow at 45°C and 47°C. Colonies are characteristically deep-yellow, aromatic and have a maximum growth at 42°C. We sub cultured the fungus on SDA and incubated in the dark at 30°, 37° and 40°C to obtain sporulation and to test for thermotolerance. The isolate was identified as *Mucor indicus* on the basis of macro and microscopic morphology and on thermotolerance. After 3 days of incubation at 30°C, fast growing, deep yellow colonies were seen (Fig:6 A, B).

DISCUSSION –

Mucormycosis is the third most common invasive mycosis after candidiasis and aspergillosis. Even though it is extremely rare, it has been reported from all corners of the world. As in aspergillosis, phagocytes, polymorphonuclear neutrophils and macrophages plays a critical role. Infection is caused by inhalation, percutaneous inoculation or ingestion. They evade antifungal property of macrophage and germinate into mycelial forms, polymorphonuclear neutrophils and peripheral macrophages are expected to work against fungi as they are fungicidal against mucoromycetes. Thus, leukocytopenia patients are extremely susceptible.³

Mucoromycetes show minimal intrinsic pathogenicity to normal individuals, but they can initiate aggressive and fulminant infections under certain clinical conditions, such as diabetic ketoacidosis, dialysis, treatment with deferoxamine, an iron chelator, neutropenia, high dose systemic steroids, protein energy malnutrition (PEM), solid-organ and bone marrow transplants, immunodeficiency, leukaemia and intra venous drug abusers who may inject spores of mucorales with drugs and then present with space occupying lesions of central nervous system.

Rhinocerebral mucormycosis is usually fatal as patient dies within a week's time and invariably diagnosed in autopsy, if clinician couldn't reach tentative diagnose in life. Most commonly it spread via nasal mucosa to turbinate bones, paranasal sinuses, orbit, palate with eventual extension into brain where massive invasion of blood vessels cause major infarct. Therefore, due to cerebral involvement overall mortality in patients is very high.

Mucor indicus was first discovered in the late 19th century and is generally considered a non-pathogenic organism. It has wide industrial application, for example, it is used in the production of ethanol and beer, and for taste in meat-substitute products like tempeh.^{4,5,6}

In contrast to most other *Mucor* species, *M. indicus* is thermotolerant to temperatures up to 42°C.⁷ In the above-mentioned case, patient was unconscious when he came to Emergency OPD, suggestive of diabetic ketoacidosis. In diabetic ketoacidosis, risk of mucormycosis may increase due to release of iron bound protein. In ketoacidosis, low serum pH diminishes phagocytic effect of macrophages, chemotactic and oxidative burst of neutrophils.

Global cases reported:

S J Taj-Aldeen et al⁸ published on 2017 from Qatar, showed mucormycosis caused by *Mucor indicus* in liver transplantation recipient. A 55-year-old Qatari male who underwent orthotopic liver transplantation for progressive liver dysfunction due to alcoholic liver cirrhosis in January 2007. Despite profound immunosuppression and infection with *M. indicus*, the patient made a full recovery, which may in part be the result of early diagnosis, treatment and aggressive surgical intervention. Thoracotomy and removal of the fungal ball was done 2 months after the initiation of antifungal therapy.

Deja et al.⁹ published on 2006 from Germany, showed gastrointestinal infection caused by *Mucor indicus* in a patient with severe head injuries. Monotherapy with high-dose liposomal amphotericin B successfully eradicated it. Nevertheless, subsequently a hemicolectomy

was necessary due to recurrent bleeding from a deep ulcer. *Mucor indicus* is an uncommon fungal pathogen, typically found in starters used for food fermentation. Primary gastrointestinal manifestations seem to be typical and indicate an oral route of infection.

Bloch D et al¹⁰ published on 2018 from Atlanta, Georgia showed mucormycosis in an immunocompromised 4-year-old female with necrotizing fasciitis of groin due to a rare fungal organism, *Mucor indicus*. The patient underwent multiple surgical debridements and was treated for 10 months, first on liposomal amphotericin B (2 months) then posaconazole (8 months). Though the source of infection was never discovered the patient survived.

Among all the cases of mucormycosis due to *M. indicus* reported from all over the world, none of them were causing rhino-orbito-cerebral mucormycosis. Hence, it can be said to be the first case report globally to the best of our knowledge.

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Fig 1: Showing tissue

right side of the face.

necrosis and swelling on



Fig. 2: KOH mount showing ribbon-like, broad and non-septate hyphae.

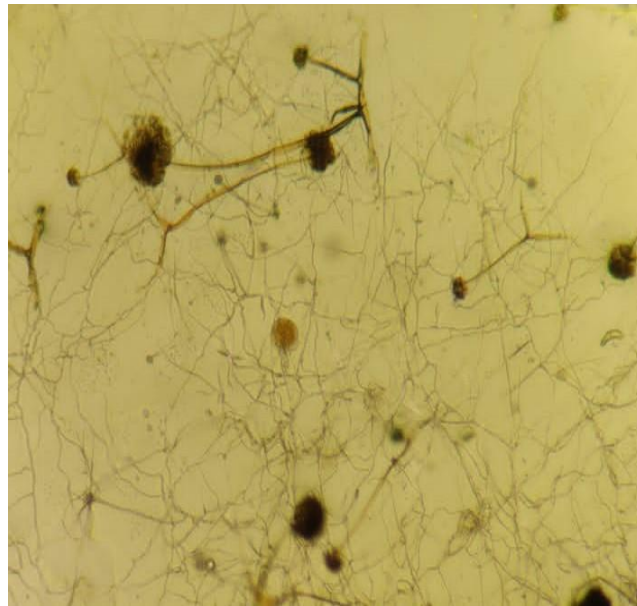


Fig.3: LPCB mount of colonies from SDA showing nonseptate hyphae; sporangiophores bearing sporangia with a sub-spherical columella and absence of rhizoids.

Fig.4: Showing sporangiospores which are pleomorphic, smooth walled, mostly sub-spherical to ellipsoidal.

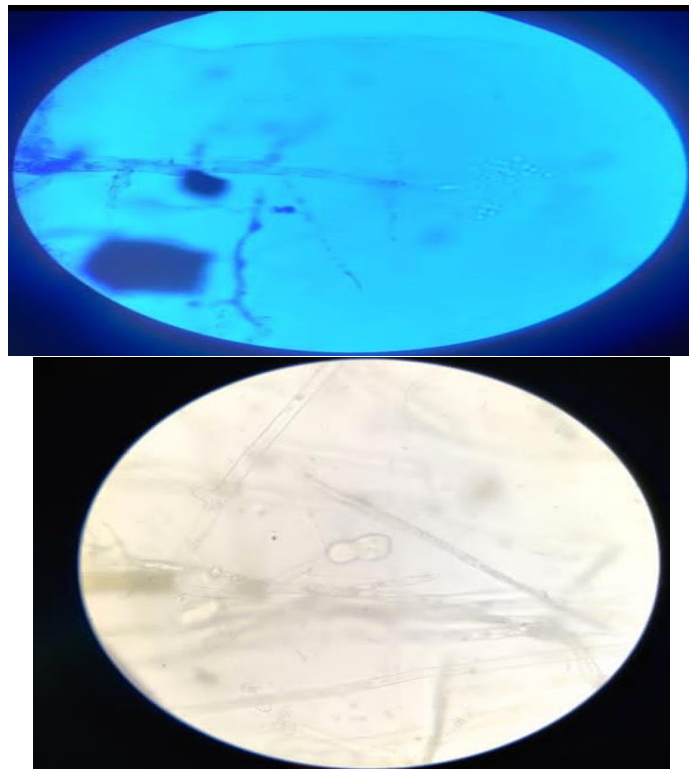


Fig.5: Slide culture on corn meal agar showing chlamydozooids.



Fig 6A: No pigmentation on SDA after growth in presence of light.



Fig 6B: Deep yellow pigmentation on SDA after the growth in dark.