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Case Report

A rare case of invasive mucormycosis with thrombosis of cerebral vasculature in diabetic ketoacidosis

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ABSTRACT

Mucormycosis is a rare fungal infection. It is an aggressive angio invasive infection hence if left untreated is always fatal. This necrotising infection commonly involves the nose, paranasal sinuses, orbits and brain. Uncontrolled diabetes, immunosuppression, transplant recipients, COVID-19 infection are the commonest risk factors. Most common form is rhino orbital cerebral involvement. Antifungal agents along with surgical debridement is the mainstay of treatment. We are reporting such a case of invasive mucormycosis in a young diabetic male to stress the importance of clinical examination and early recognition of clinical signs of this rare invasive infection and aggressive management.

Keywords: Mucormycosis, Diabetes, Fungal infection

INTRODUCTION

Mucormycosis is a rare fungal infection. It is an aggressive angio invasive infection hence if left untreated is always fatal. This necrotising infection commonly involves the nose, paranasal sinuses, orbits and brain and it can also involve the skin, lungs and the gastrointestinal system.

Mucormycosis is caused by the members of zygomycotic and Mucorales species. In the year 1885, Paltauf first described phycomycosis or zygomycosis.[1] American pathologist R.D. Baker in the year 1957 coined the term mucormycosis.

Soil or rotten materials are the source for mucormycotina which are the common saprobes.[2] Rhizopus, Mucor, Rhizomucor, Cunninghamella, and Absidia, subphylum Mucormycotina, order-Mucorales, class-Zygomycetes are the causative fungal agents of mucormycosis and the characteristic feature of this infection is tissue necrosis and infarction.[3] *Rhizopus oryzae* is the most common causative agent in 60% of human cases and 90% involves rhino-orbital-cerebral pattern (ROCM).[4]

During the COVID-19 pandemic many cases had concurrent development of mucormycosis during the course of clinical illness. The primary reason behind mucormycosis in such patients were hypoxia, hyperglycemia due to diabetes or steroid-induced, diabetic ketoacidosis (DKA), metabolic acidosis and increased ferritin levels. The main pathogenesis is decreased phagocytosis of the WBC leading to immunosuppression.[5]

CASE REPORT

A 30 years old male who is a known case of type II diabetes mellitus (DM) and a chronic alcoholic with poor compliance on medications presented with giddiness and fever for two-days duration. On examination he was found to be conscious, oriented and was febrile. His vitals were stable. His CBG was 576 mg/dl. Total leucocyte counts were 31150 ml, urine ketones +++. ABG showed metabolic acidosis.

He was started on intravenous fluids, insulin infusion, piperacillin tazobactam 4.5 gm IV tds and sodium bicarbonate. During the course in the hospital, he developed ptosis with restricted eye movements (third nerve palsy), periorbital edema and become drowsy.

Magnetic resonance imaging (MRI) brain with MR angiography (MRA) was done which showed acute lacunar infarcts in right antero superior pons and left cerebellum. MRA showed complete occlusion of left vertebral artery showing loss of flow signal. He was started on anticoagulants and antiplatelets.

Fundus examination revealed pale optic disc and an ischemic retina. Examination of the oral cavity showed a black necrotic patch over the hard palate associated with necrosis and erosion of hardpalate. KOH mount showed fungal elements suggestive of mucormycosis. Figure 1 shows black necrotic patch over the palate. Imaging of paranasal sinuses revealed acute maxillary sinusitis.

Patient was given nasal irrigation of the sinuses and started on injection liposomal amphotericin B 5 mg/kg and was subsequently planned for FESS and surgical debridement was done. Currently he is symptomatically improving with good glycaemic control.

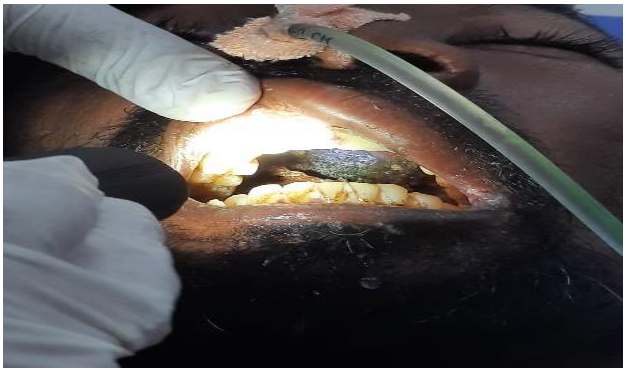

Figure 1: Black necrotic patch over the palate.

DISCUSSION

The prevalence of mucormycosis ranges from 0.005 to 1.7 per million people worldwide and with increased prevalence rate in India (0.14 per 1000).[6] Inhalation of fungal spores either by air or by direct inoculation into the mucosa is the mode of contamination.

The incidence of mucormycosis in greater in acute myelogenous leukemia (AML) ranging from 1% to 8%.[7] In solid organ transplant (SOT) recipients, it is associated with increased mortality rate, while the incidence ranges from 0.4% to 16.0% in solid organ transplant recipients. The incidence of mucormycosis in liver transplant recipients, heart transplant recipients, renal transplant recipients and lung transplant recipients were 0-1.6%, 0-0.6%, 0.2-1.2% and 0-1.5% respectively.[8]

Uncontrolled diabetes mellitus mainly ketoacidosis, neutropenia, hematological malignancy, patients on steroids, elderly age, AIDS, renal insufficiency, skin trauma, patients on broad-spectrum antibiotics, intravenous drug abuse, prophylactic voriconazole, organ or stem cell transplantation, iron overload and malnutrition are the risk factors for mucormycosis.

Decreased defence mechanisms and impaired neutrophil function in patients with diabetes mellitus is the main reason for mucormycosis leading to increased morbidity and mortality.[9] Pulmonary macrophages in diabetes seems to have reduced inhibition of the germination of Rhizopus species.[10] In the presence of Rhizopus, the glucose and acidic environment are increased due to ketone reductase. In patients with DKA, occurrence of all types of mucormycosis can be seen and it may accelerate the fungal invasion.[11] Diabetes provides suitable atmosphere for fungal duplication due to low levels of dialyzable inhibitory factors.[12]

Rhino orbital presentation is common in diabetes. It usually originates from the paranasal sinuses leading to bone destruction and later invading to the orbit, eye, and brain.[13] Facial oedema, proptosis, and in severe cases palatal or palpebral fistula may be seen along necrosis. Mucormycosis involving lungs is seen in profound neutropenia and graft-versus-host disease.[14,15]

Immunocompetent patients develop cutaneous and soft-tissue mucormycosis predominantly after traumatic skin injury.[16] Mucormycosis involving the gastrointestinal disease is very rare but it is commonly seen in neonates with higher mortality rates.[17]

Patients with suspected mucormycosis, computed tomography (CT) scan or MRI is indicated. In cases with pulmonary involvement CT pulmonary angiogram may also be done. Endoscopy, FESS are done in sinus involvement. Serial imaging of other systems is strongly recommended in worsening cases. Biopsy is strongly recommended and staining the with haematoxylin-eosin (HE), periodic acid-Schiff stain (PAS), or Grocott-Gomori's methenamine-silver stain (GMS) showing non-pigmented hyphae.[18] Histopathologically the characteristic features are haemorrhagic infarction, coagulation necrosis, angioinvasion and perineural invasion.[19]

The main stay of management is surgical excision, antifungal medications like liposomal amphotericin B along with strict glycaemic control. Few circumstances patients can have refractory mucormycosis or there can be drug intolerance. In such instances, isavuconazole or posaconazole can be used.[20,21]

CONCLUSION

Mucormycosis is a rare angio invasive fungal infection. It warrants surgical debridement and antifungal medications along with rapid reversal of underlying precipitating

factors. Clinical and neurological examination is very important in patients with uncontrolled hyperglycemia presenting with orbital swelling to look for sinus and cerebral involvement. There is a propensity of causing vascular thrombosis of vessels or cerebral extension of rhino orbital mucormycosis. Early diagnosis of this disease and prompt management of the patient is the cornerstone in reducing the mortality.

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