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CASE REPORT

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ABSTRACT

Mucormycosis, a clinical condition caused by fungi belonging to Zygomycetes are usually life threatening because of their unique ability to invade the veins and arteries. It is classically defined as an opportunistic infection, preferentially affecting patients with diabetes mellitus, neutropenia, and acquired immunodeficiency syndrome. Lipid formulations of amphotericin B are the mainstay of treatment, along with aggressive surgical therapy. We present a case of rapidly progressing rhinocerebral mucormycosis in a 45 year old lady with type 2 diabetes mellitus. She had unilateral ophthalmoplegia, loss of vision and headache. She was on treatment for diabetes but her sugar levels were not under control. The biopsy from the retro-orbital tissue yielded *Rhizopus* species on culture. She was started on Amphotericin B but the infection had progressed and patient succumbed to the disease. Appropriate control of sugar levels, early detection of such invasive fungal infections will help in reducing the mortality of patients.

INTRODUCTION

Mucormycosis is a fungal infection caused by organisms belonging to the family Zygomycetes. It includes the genera *Rhizopus*, *Rhizomucor*, *Mucor*, and *Absidia*. Five classic forms of mucormycosis are recognized viz. cutaneous, pulmonary, gastrointestinal, disseminated, and rhinocerebral (Fu *et al*. 2015). Although it is classically defined as an opportunistic infection, preferentially affecting patients with diabetes mellitus (DM), neutropenia, malignancy, chronic renal failure, and acquired immunodeficiency syndrome and those who have received organ or hematopoietic stem cell transplants, it can affect immunocompetent hosts as well (such as trauma patients) (Carlos *et al*. 2014).

Rhinocerebral mucormycosis is characterized by paranasal sinusitis, facial pain with swelling, headache, fever, rhinitis, granular or purulent nasal discharge, nasal ulceration, epistaxis, hemiplegia or stroke, and decreased mental function. Fungal invasion, often originating from the paranasal sinuses, leads to intracranial growth usually along the base of the skull. The rhinocerebral form is the most severe and may involve a rapidly progressive, invasive infection with a high mortality rate (Gen R *et al*. 2013). The reason for its poor prognosis is that the fungus has affinity to blood vessels and invasion occurs quite early in the disease. Invasion of blood vessels leads to thrombosis and necrosis of the surrounding tissue due to loss of blood supply.

Standard treatment includes surgical debridement and liposomal Amphotericin B infusion. Posaconazole has been shown to be effective against mucormycosis, perhaps more so than amphotericin B, but has not yet replaced it as the standard of care. Despite aggressive surgical debridement and polyene antifungal therapy, overall mortality for Mucormycosis remains high, ranging from 20 to 50% (Zilberg *et al*. 2014). Depending on patient characteristics (such as critically ill or immunocompromised patients) and site of infection, mortality rises markedly, nearing 70–90% for cases of disseminated mucormycosis. We report a case of rapidly progressing rhinocerebral mucormycosis in a middle aged female patient.

Case Report

45 year old lady presented to the Neurology department with history of left sided headache & loss of vision in the left eye since 1 day. She had fever since 3 days. Patient was apparently well 3 days back when she developed fever which was of mild grade not associated with chills and rigors. She developed swelling and redness of the left eye, initially medial half was affected which progressed to involve the entire left eye. It was

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associated with headache, severe in intensity involving the left side only. She gives a history of loss of vision in the left eye since 1 day. No history of seizures, weakness of limbs, nausea, vomiting. No history of trauma to the eye or other invasive procedures. She is suffering from type 2 diabetes mellitus since 5 years and was on oral hypoglycemic drugs. No history of hypertension or pulmonary tuberculosis. Personal history was not contributory since she had normal appetite with regular bowel habits. She was not a habitual consumer of alcohol or smoking.

On examination, she was conscious, obeyed commands, not oriented to place. Her vital signs were within normal limits. General physical examination revealed average built, well nourished middle aged woman with pale skin, no cyanosis / clubbing. There was no generalized lymphadenopathy or pedal oedema. All the peripheral pulse were felt with adequate volume and rhythm. Left eye was swollen & tender. Proptosis was present, no pulsations and it was immobile. Other cranial nerves were tested and were found to be within normal limits. Oral cavity and nasal cavity were examined which did not reveal any necrotic tissue or exudate.

Laboratory investigations revealed anaemia, high blood sugar levels, ketone bodies present in urine. High white blood cell counts with neutrophilic leucocytosis. X-ray imaging of the orbit showed a radio opaque mass in the orbital cavity extending into the frontal sinuses. CT radiograph showed the presence of radio opaque mass in the retro-orbital region extending into the cranial cavity with cavernous sinus thrombosis. Retro-orbital biopsy was performed and the sample sent to laboratory for analysis. The patient was started on Amphotericin B emperically on the day of admission along with broad spectrum antibiotics but she succumbed to disease within 72 hours of admission.

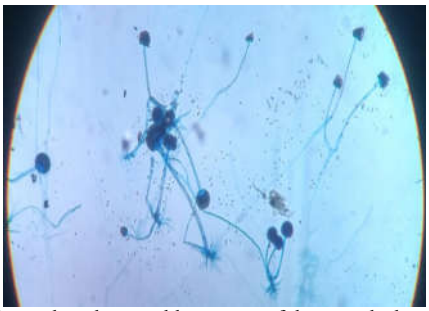

Figure 1 Lactophenol cotton blue mount of the growth showing broad aseptate hyphae with sporangiophores and nodal rhizoids.

KOH preparation on the retro-orbital biopsy tissue showed fungal elements with broad pauci-septate hyphae of varying thickness. Histopathology section also showed fungal elements and inflammatory infiltrate. The culture yielded woolly growth on Saboraud's dextrose agar which was tube filling within 4 days of inoculation. Tease mount of the growth stained with Lacto-phenol cotton blue stain (Figure 1) showed broad aseptate hyphae with sporangiophore and nodal rhizoids. The isolate was identified as Rhizopus species.

DISCUSSION

Type 2 diabetes mellitus is the most common risk factor for mucormycosis. This infection caused by organisms belonging to the family Zygomycetes, includes the genera *Rhizopus*, *Mucor, Absidia*. *Rhizopus* infects more commonly than other groups of fungi (Bhadada S, *et al* 2005). Susceptibility to infection is perhaps linked to its association with altered immune function, such as diminished T-cell responses, problems with humoral immunity, decreased neutrophil phagocytic ability because of impaired glutathione pathway (Carlos *et al*. 2014). In addition, there is reduced adherence to endothelial walls, and impaired function of monocytes and macrophages (Peleg AY *et al* 2007). Acidosis and subsequent reduced serum inhibitory activity against *Rhizopus* in lower pH values in addition to hyperglycemia and greater availability of glucose to the pathogen contribute to a favourable environment for fungal growth, enabling angio-invasion with thrombosis and tissue necrosis (Spellberg B *et al* 2005).

Mucormycosis has been implicated in various types of central nervous system involvement, such as hemorrhage, infarction, and ophthalmoplegia. In our case the patient had ophthalmoplegia in addition to other signs. The eye was fixed with no movements due to involvement of Occulomotor and Abducent nerves. The pathologic basis of the occurrence of ischemia and infarction in the setting of mucormycosis involves a combination of growth of the hyphae into the arterial lumen and direct endothelial injury resulting in mycotic thrombus (Thajeb P *et al* 2005). This mucormycosis-associated vasculopathy in combination with preexisting diabetic vasculopathy increases the risk of intracerebral infarction and acute ischemic stroke through thrombotic occlusion of major vessels of the brain, such as the carotid and basilar arteries. Cavernous sinus thrombosis is the result of carotid involvement as seen in our case.

Administration of Amphotericin B has been the recommended treatment option and antifungal treatment of choice for mucormycosis (O'Neil *et al* 2005). Liposomal formulation of the drug was started in this patient at admission. Aggressive surgical debridement in the case of a rapid-growing, aggressive, and invasive infection is often also an essential component of treatment, but was not an option with this patient given the severity of the fungal invasion.

CONCLUSION

Mucormycosis is a medical emergency that most commonly affects immune compromised individuals. Despite aggressive multimodal treatment the disease carries a significant risk of mortality and merits rapid diagnosis and treatment whenever possible.

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