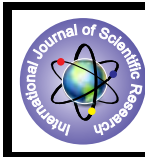


A Rare Case of Mucormycosis Keratitis in an incidentally diagnosed Diabetes mellitus patient. Opportunistic infections – is it red alert for your immune status!!



Medical Science

KEYWORDS : immunocompromised, keratitis ,mucormycosis.

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ABSTRACT

Corneal mucormycosis represents a rare form of mucormycosis in an otherwise healthy individual. Mucormycosis is an uncommon and aggressive, angioinvasive fungal infection that occurs in immunocompromised states like diabetes mellitus, chronic renal failure, hematological malignancies and deferoxamine therapy.[1] We report a rare case of mycotic keratitis caused by mucor in 48 year old patient who was incidentally detected to have diabetes.

Introduction

Mucormycosis an aggressive, angioinvasive fungal infection seen in immunocompromised hosts such as poorly controlled diabetes mellitus, neutropenia, hematological malignancies, long-term deferoxamine therapy, intravenous drug abuse and cytotoxic therapy.[1,2] Patients with diabetes constitute the single largest category of patients with mucormycosis (60-81%). [1,3] Rhino-orbital- mucormycosis (ROM) is seen as a presenting feature of diabetes in one fourth of patients.[1,4] We report a 48 year old male patient who presented with mucormycosis keratitis and incidentally known to have diabetes mellitus when tested for the same.

Case report

A 48-year-old male complained of pain, redness and watering of right eye of 3 weeks duration. There was also drop in vision. On clinical examination a 4 mm ulcer was seen on the cornea and extending over the sclera (figure 1). Biopsy from the corneal ulcer was taken. Macroscopically the specimen consisted of single tiny flattened grey white to grey yellow soft tissue bit measuring 0.3 cm across. Microscopy showed ulcerated corneal epithelium below which broad, non septate hyphae with right angle branching were seen (figure 2). A diagnosis of corneal mucormycosis was made. The patient was treated with amphotericin B and therapeutic keratoplasty was done.



Figure 1. Photograph showing corneal ulcer extending into the sclera.

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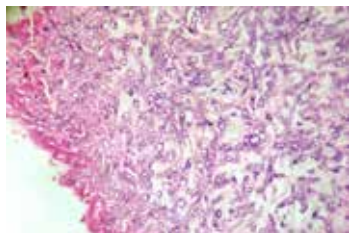


Figure 2. Microphotograph showing ulcerated corneal epithelium.

lium beneath which is broad, non-septate mucormycosis hyphae with right angle branching (H and E X40).

Discussion

Mycotic keratitis is a rare entity and the first and only case reported is keratitis caused by an Absidia species by Marshall DH et al.[5] Mucormycosis usually seen in immunocompromised patients but our case was not a known case of diabetes. Diabetes was incidentally detected during the work up of the case. Rhino-orbital- mucormycosis (ROM) is a rare disease with overall prevalence of diabetes in 0.15%.[1] However, rhino-orbital-cerebral mucormycosis, as a presenting manifestation, is rare. [6,7] Despite the advances in the diagnosis and treatment, a high mortality rate of 30-70% still exists for this disease. Death may occur within two weeks in untreated or unsuccessfully treated patients.[6] Mucormycosis can manifest as one of six different clinical syndromes; it appears in rhinocerebral, pulmonary, gastrointestinal, central nervous system, subcutaneous, and disseminated forms. Rhinocerebral mucormycosis (RCM) is the most common of these forms, and it is subdivided into three subtypes: rhinomaxillary, rhinoorbital, and rhinoorbitocerebral. [1,8,9] The classification of RCM has no effect on patient care, however, because the mainstays of therapy are similar regardless of the site of extension. The keys to management are reversal of the underlying cause of immunocompromise, be it diabetic ketoacidosis or neutropenia, and appropriate antifungal therapy and surgical debridement of the involved tissues.[1,4,8,9,10]

The organisms causing mucormycosis are Rhizopus, Mucor, Absidia, which are present in decaying vegetation and dung. Infection occurs when inhaled hyphae are deposited in upper or lower respiratory tract. The fungi penetrate arterial walls producing ischemia, thrombosis and infarction.[6] These fungi also invade the nerves, spores. In normal hosts, a phagocytic response to colonization fatty tissues, and bones; muscles are usually spared. Angioinvasion by the hyphae produces a fibrin reaction and the development of "mucor thrombi," which occlude the arteries and lead to ischemia, infarction, and consequent formation of the black necrotic eschar of the skin and mucosa that is characteristic of RCM. Vascular occlusion prevents systemic antifungal agents from reaching their targets, and ischemia favors the development of acidotic tissue, which is ideal for fungal growth.[11,12,13] The infection spreads rapidly to adjacent sinuses and the orbit and continues into the cranium via the ethmoid bone or orbital vessels.[11,12] It causes cerebro-rhino-orbital mucormycosis. Death may occur due to the cerebral abscesses. Patients usually present with low-grade fever, dull sinus pain, nasal congestion, bloody nasal discharge and diplopia.[6]

Among the recognizable risk factors for the development of RCM are poorly controlled diabetes, hematologic malignancies, acquired immunodeficiency syndrome, severe burns, renal diseases, malnutrition, iatrogenic immunosuppression after organ transplantation, and deferoxamine therapy.[11,13-19] Few cases have been reported in patients who did not have a predisposing factor.[11,14,20]. The reduced ability of serum to bind iron at a low pH may be the basic defect in the body's defense systems. The high iron, glucose-rich acid milieu facilitates fungal growth. The human resistance to fungal infections rests on the body's ability to restrict the availability of iron to the invading fungus, by binding it to proteins such as apotransferrin. The fungal hyphae produce a substance called rhizoferrin, which binds iron avidly. This iron-rhizoferrin complex is then taken up by the fungus and it becomes available for the vital intracellular processes. Diabetic patients are predisposed to mucormycosis because of the decreased ability of their neutrophils to phagocytose and adhere to the endothelial walls. Furthermore, the acidosis and hyperglycaemia provide an excellent environment for the fungus to grow.[6,21]

Mucormycosis, also known as Zygomycosis or Phycomycosis, was first described by Paultauf in 1885, who coined the term 'mycosis mucorina'. The most pathogenic species of the family, Mucoraceae is Rhizopus. Rhizopusoryzae is the predominant pathogen which accounts for 60% of all the forms and 90% of the rhinocerebral cases. In this case also, we isolated the Rhizopusoryzae species. Roden et al., who reviewed 929 reports of zygomycosis in the English-language literature since 1885, found co-existing diabetes in 36% of the patients. Zygomycosis had caused death in 44% of them. However, Chakrabarti et al., who analyzed 178 cases of Zygomycosis in hospitalized patients in northern India, found co-existing, uncontrolled diabetes in

73.6% of the patients. Moreover, Schwartz et al., noticed that Cerebro-Rhino-Orbital Phycomycosis (CROP) which was mainly caused by Rhizopus spp., occurred predominantly in the individuals with diabetic ketoacidosis. CROP leads to proptosis, loss of vision, ophthalmoplegia and death which results from a cerebral involvement.[6]

The prognosis of mucormycosis has markedly improved over past 30 years with 90% survival rate. The factors related to poor survival were delay in diagnosis and treatment, facial and eyelid gangrene, hemiplegia, cerebral invasion by mucorales and treatment with amphotericin B alone.[6,21]

The treatment of RCM involves a combination of surgical and medical modalities plus correction of the underlying medical problem if possible. The timing of surgery is very crucial; surgery should be instituted without delay once the condition is diagnosed [11]. Several surgical procedures have been described in the literature.[11,13]

Conclusion

Mucormycosis remains a severe infectious disease in diabetic patients and it is characterized by a high mortality rate. The clinical diagnosis is often difficult and it gets delayed. Sometimes diabetes can be incidentally detected in patients when the present with opportunistic infections as in our case. In diabetics, physicians should always pay special attention to the infections within the facial skeleton, especially which do not respond to antibiotic therapy. Aggressive diagnostic procedures are required for histo-microbiological studies to confirm this disease. An early diagnosis, combined with medical and surgical treatments, is necessary to improve the outcome.

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