International Journal of
Pediatric
Otorhinolaryngology
Extra

CASE REPORT

Rhino-orbital mucormycosis—A case report

S.P.S. Yadav [a], Anuj Kumar Goel [b],*

[a] Department of ENT, Pt. B.D. Sharma P.G.I.M.S., Rohtak, India
[b] Saraswathi Institute of Medical Sciences, Hapur 245101, India

Summary   Mucormycosis is a rare and life threatening fungal infection in children that occurs in association with immunocompromised states. Very few case reports of rhino-orbital mucormycosis have been documented in pediatric age group and most of these have been fatal. We report a case of mucormycosis in a child with renal disease who was managed with lipid complex amphotericin B coupled with surgical debridement.

1. Introduction

One form of acute invasive sinusitis caused by fungi of the order Mucorales is known as mucormycosis [1]. Mucormycosis is a rapidly progressive infection that usually develops in patients who are metabolically or immunologically compromised. Left untreated, it is rapidly fatal. Mucormycosis classically involves the nasal mucosa with invasion of the sinuses, orbit, and brain [2]. The causative organisms are members of the family Mucoraceae, which belongs to the order Mucorales of the class Zygomycetes. They are saprophytes commonly found in soil, decomposed vegetation, and in the healthy human respiratory and digestive tracts, and their distribution is worldwide [3].

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 [4,5]. 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 [3—7] Most of the reported cases are in adults. Authors report a case in a 10 years old male child (Fig. 1).

2. Case report

A 10 years old boy, presented in pediatrics OPD of PGIMS Rohtak (INDIA) with renal failure and fever for which he was admitted to pediatric ward where necessary intravenous broad-spectrum antibiotic therapy as well as empirical antifungal treatment with fluconazole was given. After a few days of this

* Corresponding author. Tel.: +91 9992014141.
  E-mail address: dranujgoel@rediffmail.com (A.K. Goel).

Fig. 1 HRCT (PNS) coronal view showing right-sided oroantral fistula and bilateral maxillary and ethmoid sinus involvement.

treatment in the pediatric ward, the patient began to exhibit recurrent mild left-sided nasal bleeding, left facial edema, excessive lacrimation from the left eye, and periorbital swelling. An ophthalmologist who was consulted noticed mild proptosis with edematous, congested conjunctiva and ophthalmoplegia; however, the eye fundus and vision were normal. A preliminary diagnosis of orbital cellulitis was made, and urgent CT (PNS) with head was requested. CT showed partial opacification of the left maxillary, ethmoid, and frontal sinuses with nasal mucosal swelling and an obvious extension of the inflammatory process to the inferomedial orbital wall, But no clear collection or bony erosion was noticed, and the brain was intact. Otolaryngology examination revealed the presence of black necrotic tissue in the left nasal cavity and a patchy black discoloration of the hard palate 5 mm in diameter, opposite the molars (Fig. 2) with ulceration.
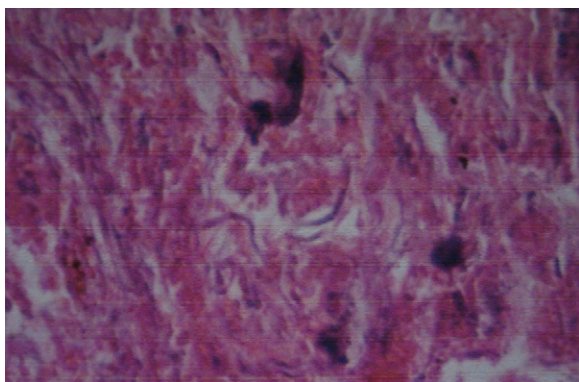

Fig. 2 Histopathology of lesion showing aseptate hyphae with right-angled branching suggestive of mucormycosis.

There was no headache, vomiting or focal neurological deficit. Immunocompromised status was ruled out by doing HIV—ELISA, which was negative. Routine blood investigations including blood sugar, blood urea, serum creatinine was done and all were within the normal limits. Urgent endoscopic debridement and orbital decompression was planned under general anaesthesia. During debridement nasal cavity was found full of black colored soft tissue along with free pieces of bone, perforated nasal septum was seen. Meticulous endoscopic debridement was done and material was sent for histopathological examination which revealed the presence of aseptate hyphae with right-angled branching, which are typical of mucormycosis. Renal profile was done prior to start amphoterecin-B and was found within normal limits. Patient was started on Lipid Complex Amphotericin-B, 5 mg/kg/day for 6 weeks. Child was under regular renal profile check up during medical treatment. Child did well with no residual visual impairment and is presently well controlled. His survival is attributed to early recognition of mucormycosis with diagnostic support of imaging studies, surgical debridement and antifungal therapy. Child was disease free up to 1 year of follow up.

3. Discussion

Mucormycosis can involve the lungs, central nervous system, gastrointestinal tract, and skin, but it is probably best known for its rhinocerebral presentation, which usually originates in the nose and sinuses and eventually extends to the orbit and brain [10].

Regardless of the causative agent, the clinical presentation and management are the same. Although the responsible fungus can be isolated in the nose of healthy subjects, it can turn pathogenic in patients with immunologic or metabolic compromise. Among the recognizable risk factors for the development of RCM are poorly controlled diabetes, hematologic malignancies, acquired immunodeficieney syndrome, severe burns, renal diseases, malnutrition, iatrogenic immunosuppression after organ transplantation, and deferoxamine therapy [4—9,13]. Few cases have been reported in patients who did not have a predisposing factor [5,14].

RCM begins with colonization of the nasal mucosa by airborne spores. In normal hosts, a phagocytic response to colonization prevents infection. In immunocompromised hosts, on the other hand, the response is suboptimal and germination ensues [15]. Mucorales hyphae have a predilection for growth into arteries and the lymphatic system. These fungi also invade the nerves, 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]. The infection spreads rapidly to adjacent sinuses and the orbit and continues into the cranium via the ethmoid bone or orbital vessels [11]. In our patient, the orbital manifestation occurred at almost the same time as did the nasal symptoms, yet the patient did not experience intracranial spread.

Fever is the most common early symptom [44% of cases], followed by nasal ulceration or necrosis, periorbital or facial swelling, and decreased vision, each of which occurs in approximately 33% of cases [14]. Ultimately, 80% of patients develop a necrotic lesion on either the nasal or oral mucosa [15]. In addition to proptosis, our patient developed all of these signs and symptoms at about the same time. Other less frequent features include facial pain or numbness, nasal congestion or discharge, headache, ophthalmoplegia, anesthesia over the cheek, and cranial polyneuropathy, which may be consistent with orbital apex syndrome [7,8,15].

When the clinical picture includes the presence of sinusitis with black discoloration in the nose and palate in addition to a predisposing factor, a diagnosis of RCM should be highly suspected. Even so, a tissue biopsy is necessary to confirm the diagnosis [2,5,7]. Invasive hyphae can be seen as ribbon-like, 10- to 20-μm-wide, haphazardly branched organisms with little or no septation.

Blood vessel invasion with thrombosis is a peculiar feature of RCM, and it contributes to its necrotic, ischemic appearance. Inflammatory response is variable and depends on the host's immune status. In fact, during the early stages of RCM, imaging features may even be normal. It is only late in the progression of the disease that bony erosion will appear.

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 [17]. Several surgical procedures have been described in the literature. They range from the simple to the complex—debridement of the necrotic mucosa; Caldwell-Luc surgery; medial maxillectomy, ethmoidectomy, and sphenoidotomy; and radical maxillectomy with orbital exenteration. Both endoscopic and open approaches have been described, in both single and multiple stages [4].

The standard medical therapy for RCM is amphotericin B in a dose of 1.0—1.5 mg/kg/day for a period of several weeks to several months, depending on the clinical response and the degree of the drug's side effects, especially nephrotoxicity [3—5,7,8]. Less toxic forms of amphotericin B — such as liposomal amphotericin B, colloidal dispersion amphotericin B, and amphotericin B lipid complex — may be more safe [18]. In our patient, early debridement of the eschar followed by intravenous amphotericin B within 24 h appeared to be very effective in controlling RCM.

Other promising therapeutic modalities worth mention include hyperbaric oxygen therapy [7] and nasally nebulized amphotericin B [8,16].

The prognosis of RCM appears to depend primarily on two factors: early diagnosis and resolution of the predisposing condition. Survival has been positively correlated with the time of diagnosis and initiation of treatment [3].

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