

Rhinocerebral Mucormycosis Presented with Cranial Nerves Deficit

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Mucormycosis is a rare opportunistic fungal infection, associated with high mortality, characterized by infarction and necrosis of host tissue. Rhinocerebral mucormycosis (RCM) is the most common clinical variant often associated with poorly controlled diabetes mellitus. The treatment is complex and involves both antifungal and surgery. There is no formal guideline regarding the duration of antifungal, timing and extent of surgical management. We present a case of RCM in a diabetic girl who presented with a 2 weeks history of left facial and

periorbital swelling associated with left facial numbness and deficit of the fifth and seventh cranial nerves. Diagnosis of RCM was confirmed by histopathological examination of tissue biopsy. She was successfully treated with liposomal amphotericin B and posaconazole, as step-down therapy, along with minimal surgical debridement. We present this case because of the rarity of RCM, calling for prompt initiation of treatment in a suspected case and to present data about therapeutic modality.

INTRODUCTION

Mucormycosis is a rare opportunistic fungal infection caused by filamentous fungi of order Mucorales. It is characterized by infection and necrosis of host tissue that is resulted from invasion of vasculature by hyphae. The genera most commonly found in human infection is *Rhizopus* and *Mucor* [1]. Based on its clinical presentation and anatomic sites invasive mucormycosis is classified into 6 clinical forms: rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated and uncommon rare form such as endocarditis, peritonitis and renal infection [2]. The most important risk factors predisposing to mucormycosis include malignant hematological diseases, prolonged and severe neutropenia, poorly controlled diabetes mellitus with or without ketoacidosis, iron overload, major trauma, prolonged use of corticosteroid and malnutrition [1,3]. In most cases the infection is rapidly progressive and results in death unless underlying risk factors are corrected and aggressive treatment, with antifungal agents and surgical excision, is initiated [3].

CASE REPORT

A 14 year-old diabetic girl presented to outpatient clinic, at Infectious Diseases Unit, with a 2 weeks history of left facial and periorbital swelling appearing 2 days after tooth extraction. Also there was history of left facial numbness but there was no fever. The patient has initially visited a dentist because of headache and left sided teeth ache. The dentist decided to extract her left upper molar tooth and prescribed for her cefuroxime but after 2 days the patient condition had worsened and the aforementioned symptoms appeared. She had medical history of diabetes which was poorly controlled. On examination she was conscious, oriented, had well body built and her vital signs were stable. There were left facial and periorbital edema with dark bluish discoloration around left eye. There was left facial hypoesthesia in the area supplied by ophthalmic, maxillary and mandibular branches of the fifth cranial nerve. Also there was left facial palsy. Laboratory results were; white blood cells $7.8 \times 10^9/L$ with 70% neutrophils; hemoglobin 13g/L; plasma glucose

11.2 mmol/L; hemoglobin A₁C 12%; ESR 90 mm/h; CRP 25; serum sodium 133mmol/L. Other biochemical results were normal. Computed tomography (CT) revealed mucosal thickening of all left paranasal sinuses (Fig. 1). Further imaging with magnetic resonance imaging (MRI) also showed involvement of all left paranasal sinuses with retro-orbital extension and there was abscess formation in the anterior maxillary area and left orbital floor (Fig. 2). There was no involvement of central nervous system. Based on the history, clinical presentation and imaging findings a provisional diagnosis of RCM was considered. Liposomal amphotericin B (5 mg/kg/day) was started immediately and blood glucose level was controlled with regular insulin. Ophthalmology and otolaryngology were consulted. She was taken for endoscopic evaluation which revealed extensive necrosis of the left maxillary sinus. Left maxillary sinus was also full of pus which was drained out and sent for fungal culture which did not reveal any growth. Biopsies sent for histopathological examination demonstrated broad non septate hyphae at right angles consistent with mucormycosis. Minimal endoscopic debridement was done because extensive surgery was refused by the patient family. Liposomal amphotericin B was continued. Over the next 2 months the patient showed continual clinical improvement and follow up MRI revealed partial resolution of the lesion. The dose of liposomal amphotericin B was increased to 7 mg/kg/day. Follow up MRI revealed regression of the lesions after 2 months. Liposomal amphotericin B was stopped, oral posaconazole started (400 mg twice daily with fatty meal) and the patient discharged. 4 months after posaconazole there was complete resolution of MRI findings.

DISCUSSION

RCM is the most common and fatal clinical form of mucormycosis which presumed to start with inhalation of spores into paranasal sinuses of susceptible host [1]. Dental care may also precede such an infection by creating a post extraction wound which may be susceptible to fungal infection as seen in our case [4]. Hyperglycemia, usually with an associated metabolic acidosis, is the most common underlying condition [1]. Rhizopus organisms have an enzyme, ketone reductase, which allow them to thrive in high glucose levels, at the same time hyperglycemia may alter the immunologic capability to resist mucormycosis through reduction of leucocytes chemotaxis [5].

RCM usually present as acute sinusitis, headache, sinus pain and purulent nasal discharge with or without fever. All of the sinuses become involved and spread to contiguous structures such as the palate, orbit and brain [6]. The hall marks of spread beyond the sinuses are tissue necrosis of the palate resulting in palatal eschar, facial swelling, erythema and cyanosis of the facial skin overlying the involved sinuses [7]. Signs of orbital involvement include periorbital edema, proptosis and blindness. Facial numbness is frequent and results from infarction of sensory branches of the fifth cranial nerve [8]. Our patient had left facial numbness.

Endoscopic evaluation of the sinuses should be performed to look for tissue necrosis and to obtain specimens to confirm the presence of infection [6]. Histopathological examination of surgical specimens confirm the clinical diagnosis with the appearance of right-branching non septate hyphae, which are considered typical for mucor species, along with the evidence of angioinvasion and tissue necrosis. Fungal culture can provide further confirmation however a large number of false negative results have been reported compared to direct histopathological examination [9].

Imaging study are of little help during the early stages of RCM. However CT and MRI scan should be frequently obtained due to the rapidity of disease progression and are indispensable for appropriate planning of surgical intervention [10].

Treatment of RCM is based on reversal of underlying predisposing factor, prompt initiation of antifungal therapy and surgical debridement of involved tissues [3]. However there was no any recommendation in the literature on the duration of antifungal, extent and timing of appropriate surgical management. Our case was successfully treated with antifungal, for 8 months, and minimal surgical debridement.

CONCLUSION

Clinician awareness, prompt initiation of antifungal and timely surgical intervention is of paramount while managing a case of RCM. Mucormycosis should be considered in a predisposed patient who presented with cranial nerves deficits or who seems to deteriorate after tooth extraction. Although extensive surgical debridement could not be performed, disease regression could be achieved with medical therapy and minimal debridement.



Figure 1

Axial CT of the para nasal sinuses showed extensive mucosal thickening of the left maxillary antrum, sphenoidal sinus and left ethmoidal air cells

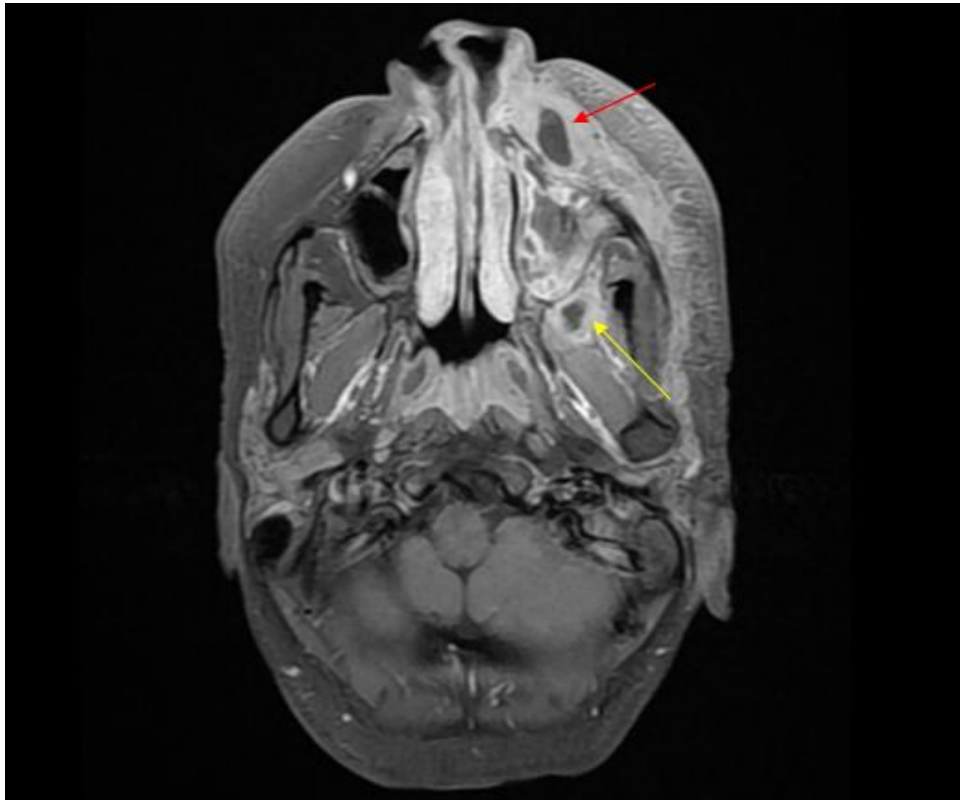


Figure 2

Axial MRI T1 fat saturation post contrast showed mucosal thickening of all left paranasal sinuses. Also it revealed thickened enhanced wall abscess in the left pre maxillary soft tissue (red arrow), retro antral region (yellow arrow) and left orbital floor.

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