Rhinocerebral Mucormycosis: A Retrospective Study

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Abstract Mucormycosis is an acute often fatal infection caused by fungi of family mucoracea (Kauffman and Malani Curr Infect Dis Rep 9(6):435–440). The principal pathogens in this family are rhizopus, mucor and absidia species. Mucoracea are found in soil, decaying vegetation and other organic matter. Mucormycosis is a polymorphic disease with diverse clinical manifestation. It is divided into rhinocerebral, pulmonary, cutaneous, cardiac, gastrointestinal and disseminated. Rhinocerebral mucormycosis the most commonest manifestation of mucormycosis is usually a fatal fulminant infection. Rhinocerebral mucormycosis can be further divided into rhino-maxillary and rhino-orbito-cerebral. The disease commonly occur in diabetics who have ketoacidosis but is also seen in severely debilitated or immunosuppressed patients. It has also been reported from otherwise normal individuals. Early diagnosis and treatment is mandatory for a successful management of this infection.

Keywords Rhinocerebral Mucormycosis · Amphotericin B · Pathology · Treatment

Introduction

Mucormycosis is manifested by variety of syndromes, particularly in immunocompromised patients and those with

diabetes mellitus. Rhino-orbital-cerebral and pulmonary infections are the major syndromes caused by these fungi [1].

Materials and Methods

This was a retrospective study of patients who presented with signs and symptoms of rhinocerebral mucormycosis from February 2003 to January 2006 at two institutions i.e. King Edward Memorial Hospital and PD Hinduja Hospital.

20 diagnosed cases of rhinocerebral mucormycosis was included in the study.

The study evaluated the etiology, pathology, clinical features, diagnosis, management and complications of rhinocerebral mucormycosis.

Results

A total of 20 patients (10 women and 10 men) had rhinocerebral mucormycosis. The median age was 60 years (range 24–80 years). A total of 18 patients (80 %) had underlying disease uncontrolled diabetes mellitus, one patient was immunocompetent (10 %) and one patient was a diagnosed case of carcinoma of stomach (10 %).

The patients presented with following signs and symptoms: fever (50 %), thick nasal discharge—dark and blood stained (60 %), black necrotic turbinates (50 %), periorbital or facial swelling (40 %), decreased vision (40 %), ophthalmoplegia (30 %), palatal ulceration or perforation (10 %), septal perforation (10 %), headache (30 %), oedema of lids (40 %), chemosis (40 %), sinusitis (30 %), facial paralysis (10 %), restricted movements of eyeball (40 %) and confusion (20 %).

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Direct microscopy, histopathology and culture were done to establish diagnosis.

CT scanning (20 cases) and MR scanning (15 cases) were done to support the diagnosis and to assess the extent of disease and to detect postoperative recurrent or residual disease.

Treatment consisted of control of underlying disease, systemic antifungal therapy and repeated surgical debridement of necrotic tissues.

Control of underlying cause involved correction of metabolic acidosis, control of diabetes mellitus and nutritional support.

Systemic Antifungal Therapy-Amphotericin B was given in the dose of 5 mg/kg for a period of 6–12 weeks depending upon extent and aggressiveness of disease. Renal functions tests were checked on alternate days. Serum creatinine was maintained below 2.5 mg/ml. 80 % of patients had serum creatinine below 2.5 mg/ml. In four patients amphotericin B had to be given on alternate day because of increased serum creatinine levels. In one patient amphotericin B had to be stopped because of his associated medical condition. Diagnostic nasal endoscopy, CT scanning/MRI were done to confirm the status of disease before discontinuing amphotericin B therapy.

Surgical Treatment Involved

Repeated surgical debridement of paranasal sinuses and orbital exenteration.

Approaches used for debridement of paranasal sinuses were endoscopy (75 %), lateral rhinotomy (10 %), Caldwell Luc (20 %) and combined approach (20 %).

Diagnostic nasal endoscopy were done twice weekly to diagnose recurrence of disease, if recurrence was found debridement of necrotic tissue was carried out.

The overall survival rates was 55 % in this study. Nine patients (45 %) succumbed to the disease.

Patients were followed on regular basis for a period of 1 year and diagnostic nasal endoscopy was done during follow up. A recurrence rate of 20 % was seen in this study.

Discussion

Rhino cerebral mucormycosis is an acute often fatal infection caused by fungi of the family mucoraceae [2]. The principal pathogens in this family are rhizopus, mucor and absidia species [3].

The causative organism is ubiquitous within the environment. They are found in soil, decaying vegetation and other organic matter.

Infection most often develops in individuals with immunologically compromising conditions which are

frequently the result of diabetes mellitus, cancer, chemotherapy or administration of immunosuppressive medications following organ transplantation [4–7]. Other predisposing factors include renal failure, severe burns, malnutrition, neutropenia and treatment with desferoxamine. Patients without an underlying abnormality or apparent predisposition have also been affected [4, 8]. The incidence of disease has not been demonstrated to vary based on age or gender. The predisposition of patients with diabetes to acquire the disease may be particularly related to hyperglycemia and the presence of ketoacidosis is presumed to induce a neutrophil defect, resulting in reduced phagocytosis and chemotaxis [9].

Nasal infection follows the inhalation of aerosolized fungal spores that may deposit in the nasal turbinates and extend into adjacent paranasal sinuses and orbit [10]. The pathogens are prone to invade and spread along blood vessels particularly arteries. The fungus proliferates within the internal elastic lamina, dissecting it from media. As the hyphae penetrate the endothelium, thrombotic arteritis, infarction, hemorrhage and extensive tissue necrosis follows [5]. Involvement of the internal carotid artery, cavernous sinus and ophthalmic artery is common. Involvement of venous and lymphatic structures occur later in course of illness.

Patients with rhinocerebral mucormycosis usually presents as acute sinusitis with fever, nasal congestion, purulent nasal discharge, headache and facial pain. All sinuses can become involved and spread to adjacent structures such as palate, orbit and brain usually progresses rapidly. The hallmarks of spread of disease beyond the sinuses are tissue necrosis of the palate resulting in palatal eschars, destruction of turbinates, perinasal swelling and cyanosis of the facial skin overlying the involved sinuses.

Black necrotic intranasal or palatal eschar is highly suggestive of the disease but it occurs in only 40–50 % of those affected [11]. Periorbital cellulitis, extra ocular muscle paresis, proptosis and chemosis frequently develop as a result of disease extension into orbit or cavernous sinus. Spread from the sphenoid sinuses to the adjacent cavernous sinus can result in cranial nerve palsies, thrombosis of the sinus and involvement of the carotid artery [12]. Cranial nerves are progressively involved as the infection spread visual loss may develop from central retinal occlusion or direct orbital extension. Intracranial infection may result from spread through the vasculature or contiguous progression through cribriform plate or orbital apex. Hematogenous spread to other organs is rare unless the patient has an underlying malignancy with neutropenia.

Radiographic imaging is helpful in establishing the extent of sinus, orbital or intracranial progression of mucormycosis and determining the efficacy of treatment. Precise anatomical localization of infection is important for guiding the choice of treatment modalities and for overall prognosis.

The diagnosis of mucormycosis is suggested by aggressive clinical features of the disease in the compromised host but needs to be confirmed by histopathological examination of transnasal or cerebral biopsy [13]. The diagnosis is established with the demonstration of vessel wall invasion by irregular, broad nonseptate hyphae that branch at right angles.

Successful therapy for infection involves combination of medical and surgical therapy [14].

Rapid control of underlying disease process, systemic antifungal and aggressive surgical debridement of necrotic tissue have seen associated with improved outcomes [14].

Systemic antifungal therapy amphotericin B, has significantly improved survival rates of patients with mucormycosis [15]. The usual starting dose is 5 mg/kg of liposomal amphotericin and clinicians can increase the dose as high as 10 mg/kg daily in an attempt to control spread of infection [14]. For patients who have responded to a lipid formulation of amphotericin B, posaconazole can be used for oral step down therapy. Intravenous posaconazole can be used as salvage therapy for patients who do not respond to or tolerate amphotericin B [16].

In addition to playing a role in diagnosis early and if required repeated surgery has been necessary to treat extensive disease. Because the fungus thrives in devitalized and necrotic tissue and because ischaemic tissue is difficult for chemotherapeutic agents to penetrate, debridement has been recommended. Drainage and debridement of paranasal sinuses, exenteration of necrotic orbital contents, palatectomy and craniotomy have all been associated with cure [14].

The overall mortality form rhino-orbital-cerebral mucormycosis ranges form 25–60 % with the best prognosis in patients with infection confined to sinuses. The prognosis is poor for patients with brain, cavernous sinus or carotid involvement, although some patients with these complications have been cured of infection [15, 17, 18].

Conclusions

The present study reveals that rhinocerebral mucormycosis is an acute often fatal infection caused by fungi of family mucoracea. It is most commonly associated with diabetes mellitus. Histopathology is the mainstay of diagnosis of disease. CT scans and MRI are done to diagnose the disease, to assess the extent of disease and to detect postoperative recurrent or residual disease. Treatment consists of control of underlying disease, systemic antifungal therapy and repeated surgical debridement of necrotic tissue. Rhinocerebral mucormycosis is an emerging fungal infection that continues to carry significant morbidity and mortality.

Conflict of interest No conflicts of interest.

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