Invasive rhinocerebral mucormycosis with orbital extension in poorly-controlled diabetes mellitus

Hadzri M H, Azarisman S M, Fauzi A R M, Kahairi A

ABSTRACT

Rhinocerebral mucormycosis is an invasive fungal sinusitis with a high mortality rate, especially in immunocompromised patients. A 70-year-old woman, with uncontrolled type 2 diabetes mellitus, presented with a one-month history of non-specific headaches associated with progressive swelling of her left eye. Computed tomography of the brain and orbits showed the extensive involvement of bilateral intranasal sinuses, orbits, extraocular muscle and soft tissues. The diagnosis of invasive mucormycosis was confirmed from a tissue biopsy taken from the internasal septum. Despite the extensive mucormycosis invasion, she was successfully treated with intranasal and systemic amphotericin B and minimal adjunctive intranasal sphenoidotomy.

Keywords: amphotericin B, diabetes mellitus, fungal sinusitis, proptosis, rhinocerebral mucormycosis

Singapore Med J 2009;50(3):e107-e109

INTRODUCTION

Mucormycosis is a rare rhinocerebral fungal infection of the order Mucorales in the class of Zygomycetes.[1] It is capable of becoming fatal in immunosuppressed patients. Clinically, it manifests as pulmonary, cutaneous, soft tissue, disseminated and gastrointestinal infections, but rhinocerebral mucormycosis is the most common presentation.[2,3] In the past, rhinocerebral mucormycosis has always been primarily treated with aggressive surgical management, which may include orbital exenteration. However, with the advent of newer formulations of proven drug regimes that promise to reduce toxicity and improve tolerance, surgical debridement has been relegated to an adjunctive role in the management of these patients. This report aims to highlight a case of rhinocerebral mucormycosis with orbital extension which has been successfully treated with parenteral amphotericin B colloidal dispersion and minimal intranasal sphenoidotomy despite the extensive involvement of both intranasal sinuses, orbits, the extraocular muscle and soft tissues.

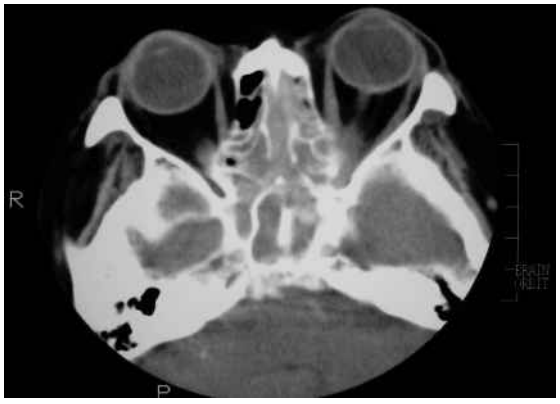

Fig. 1 Axial CT image of the orbits shows increased soft tissue density in the sinuses, and dilatation of the extraocular muscles.

CASE REPORT

A 70-year-old woman with poorly-controlled type 2 diabetes mellitus, presented with non-specific headaches and progressively painful left orbital swelling over a one-month period. Clinically, she was pyrexic with left orbital proptosis, partial ptosis and complete opthalmoplegia. Her left pupil was dilated with markedly reduced visual acuity. Clinical investigation revealed leucocytosis with predominant neutrophilia and normocytic anaemia. Skull radiograph showed normal sinuses, but computed tomography (CT) of the brain and orbits showed increased soft tissue density in her sinuses, dilatation of her left medial and inferior recti, and erosion of the left lateral wall of the body of the sphenoid and cribriform plate (Fig. 1). There was no evidence of cavernous sinous thrombosis or intracerebral pathology.

Nasoendoscopy revealed a sphenoid-ethmoidal recess oedema with mucopurulent discharges. Aspiration showed dark-coloured spores following emergency intranasal sphenoidotomy. The diseased mucosa was removed, amphotericin B flushes given and an amphotericin B-soaked nasal gauze was then applied. Histopathology of the intersinus septum showed necrotising granulomas consisting of lymphocytes, plasma cells and multinucleated giant cells (Fig. 2a). Grocott stain highlighted several fungal hyphae with

Department of Medicine, International Islamic University Malaysia, Jalan Istana, Bandar Indera Mahkota, Kuantan 25200, Malaysia

Hadzri MH, MBBCh, MMed
Assistant Professor

Azarisman SM, MBBS, MMed
Assistant Professor

Fauzi ARM, FRCP
Professor

Department of Otorhinolaryngology

Kahairi A, MD, MS
Assistant Professor

Correspondence to:
Dr Mohd Hadzri Hasmoni
Tel: (60) 9 513 2797 ext 3326
Fax: (60) 9 513 3615
Email: hadzri@iiu.edu.my

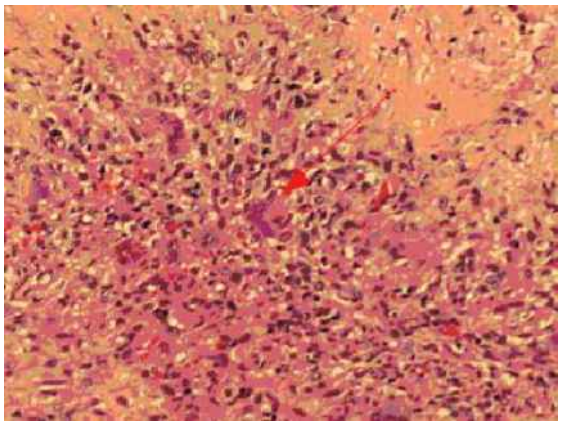

Fig. 2a Photomicrograph shows necrotising granulomas consisting of lymphocytes, plasma cells and multinucleated giant cells (Haematoxylin & eosin, × 40).

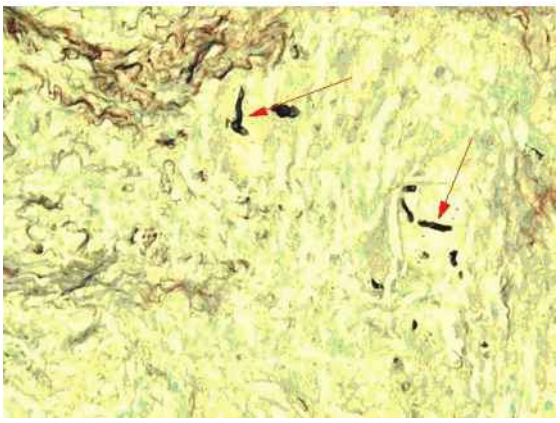

Fig. 2b Photomicrograph shows several fungal hyphae with occasional right-angled branching (arrows) (Grocott stain, × 40).

occasional right-angled branching (Fig. 2b). This fungal morphology was suggestive of *Mucor* spp. A diagnosis of acute invasive mucormycosis with orbital extension was made and she was started on intravenous amphotericin B colloidal dispersion, a lipid formulation of amphotericin B (Amphocil-Sequus Pharmaceuticals, Brentford, UK).

A total of 2 g of Amphocil was administered in divided doses over a period of two months. She was given 25–50 mg daily initially, depending on her tolerance to the medication as well as her renal profile and platelet count. The dose was gradually increased with a prolonged infusion rate of up to six hours. Her renal profile remained stable but she developed thrombocytopenia (95×10^9/L), which ameliorated following intermittent Amphocil stoppage. She showed gradual improvement of her headaches, left eye pain, left eye proptosis and left extraocular muscle weakness, although her vision remained poor.

DISCUSSION

Rhinocerebral mucormycosis is a rare but potentially aggressive and fatal fungal infection. It is characteriaed by sinusitis and a painless, necrotic black palatal or nasal septum eschar.[1] It should be considered in all patients with chronic sinusitis, especially in immunocompromised patients. Other factors predisposing to invasive mucormycosis include poorly-controlled diabetes mellitus, prolonged corticosteroid treatment, haematological malignancies, severe burns/trauma, chronic kidney disease, acquired immunodeficiency syndrome, immunosuppressant use following solid organ transplant, and intravenous drug abuse.[1] Clinically, they frequently present as fever, sinusitis, headache, periorbital or facial swelling, ptosis, visual loss and ophthalmoplegia. Cranial nerve palsies, proptosis and epistaxis have also been reported.[4] A more chronic and indolent course has also been identified.[4] These patients usually have a higher overall survival rate than those with the acute form.

The diagnosis is confirmed histologically by demonstrating tissue invasion and subsequent tissue reaction to the fungi, rather than just the presence of the organism.[5] Blood and tissue cultures, on the other hand, are used to identify the specific species. The microscopical examination of the tissue biopsy shows an acute and/or chronic inflammatory process, necrosis and hyphal elements. The hyphae are characteristically broad and ribbon-like, with irregular branching at right angles, as demonstrated in this case report.[6] The mainstay of treatment in the past has always been aggressive surgical debridement. Orbital exenteration was often indicated due to the rapid invasion and local extension to the orbits. With the advent of new therapeutic regimes, however, the treatment strategy now involves rapid diagnosis, reversal and stabilisation of underlying medical conditions, systemic antifungals and appropriate surgical debridement only as needed.[7]

Amphotericin B is the only antifungal that has been proven to be efficacious. It is administered parenterally at 1.0–1.5 mg/kg of the body weight/day to a total dose of 2.5–4.0 g in the immunocompromised.[8] Conventional amphotericin B treatment is limited by its renal and systemic toxic effects. Lipid formulation of amphotericin B, such as amphotericin B lipid complex, which incorporates amphotericin B into liposomes, enables a higher cumulative dose to be administered without an increase in adverse effects. In conclusion, rhinocerebral mucormycosis is rare but aggressive and potentially fatal in immunosuppressed patients. In the past, it has usually been fatal without aggressive surgical debridement. However, with the advent of newer formulations of proven drug regimes, such as the amphotericin B colloidal dispersion, a greater success rate can be achieved while obviating the need for extensive and potentially disfiguring surgical debridement.

REFERENCES

1. deShazo RD, Chapin K, Swain RE. Fungal sinusitis. N Engl J Med 1997; 337:254-9.
2. Sugar AM. Mucormycosis. Clin Infect Dis 1992; 14 Suppl 1:126-9.
3. Abedi E, Sismanis A, Choi K, Pastore P. Twenty-five years' experience treating cerebro-rhino-orbital mucormycosis. Laryngoscope 1984; 94:1060-2.
4. Harril WC, Stewart MG, Lee AG, Cernoch P. Chronic rhinocerebral mucormycosis. Laryngoscope 1996; 106:1292-7.
5. Parfrey NA. Improved diagnosis and prognosis of mucormycosis. A clinicopathologic study of 33 cases. Medicine (Baltimore) 1986; 65:113-23.
6. Frater JL, Hall GS, Procop GW. Histologic features of zygomycosis: emphasis on perineural invasion and fungal morphology. Arch Pathol Lab Med 2001; 125:375-8.
7. Peterson KL, Wang M, Canalis RF, Abemayor E. Rhinocerebral mucormycosis: evolution of the disease and treatment options. Laryngoscope 1997; 107:855-62.
8. Strasser MD, Kennedy RJ, Adam RD. Rhinocerebral mucormycosis. Therapy with amphotericin B lipid complex. Arch Intern Med 1996; 156:337-9.