· Monograph ·

Rhino-orbital mucormycosis in immunocompetent patient

Lai Yong Tai, Keat Ween Khaw, Amir bin Samsudin, Zurina ZA, Mimiwati binti Zahari, Visvaraja Subrayan

Department of Ophthalmology, University Malaya Medical Centre, Lembah Pantai, 50603 Kuala Lumpur, Malaysia
Correspondence to: Visvaraja Subrayan. Department of Ophthalmology, University of Malaya, Lembah Pantai, 50603 Kuala Lumpur, Malaysia. dvisva@ hotmail. com
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Abstract

• We present an atypical case of rhino-orbital mucormycosis in an immunocompetent patient and a literature review on this topic. A 17-year-old immunocompetent male presented with 2-month history of painful slowly progressive swelling of the left eye. The diagnosis of mucormycosis was made by histopathological examination of tissue specimens. The patient had successful eradication of the fungal infection with the use of multiple treatment modalities including aggressive endoscopic excision and debridement of ethmoid and maxillary sinuses, left orbital exenteration, intravenous amphotericin B and intraorbital amphotericin B. This case suggests that rhino-orbital mucormycosis can occur in a young healthy individual. Early diagnosis with aggressive medical and surgical management is vital to successfully treat this rare and potentially fatal disease.
• KEYWORDS: rhino-orbital mucormycosis; immunocompetent; exenteration; amphotericin B
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INTRODUCTION

Rhino-orbital mucormyocosis is an acute medical and surgical emergency. This opportunistic infection usually causes rapidly progressive devastating fungal infections in immunocompromised patients through vascular thrombosis or central nervous system involvement[1]. Early diagnosis and appropriate treatment are important for saving sight and life. The most common underlying co-morbidities include diabetes mellitus (most have diabetic ketoacidosis at presentation[2]), haematological malignancies, organ transplantation, renal disease with desferoxamine administration, severe burn and major trauma. Rhino-orbital mucormyocosis in an immunocompetent patient is uncommon and only a few have been reported in the literature[2-4], and majority have history of trauma as a predisposing factor[5,6]. In this paper, we present an unusual case of rhino-orbital mucormycosis in an immunocompetent young boy who was managed with a multidisciplinary approach including systemic amphotericin B, endoscopic excision and debridement of paranasal sinuses, left orbital exenteration and intraorbital amphotericin B.

SPECIAL CASE

A 17-year-old Cambodian boy was referred for evaluation of a 2-month history of left eye swelling. Patient was well until 2 months prior to presentation when he developed left eye lower lid swelling. There was no trauma or drug abuse. He was initially treated as having lower lid abscess which did not improve with conservative management. However, his condition worsened. He was subsequently referred to our centre for further management.

On examination, the vision of his left eye was no perception of light while the best-corrected visual acuity of his right eye was 20/20. There was marked proptosis of left eye with periorbital oedema and erythema (Figure 1). There was chemosis and hyperaemia of the left conjunctiva. The left pupil was 5mm, dilated and unreactive to direct light. He exhibited complete ophthalmoplegia. The left fundus examination showed pale disc, vessels dilatation and tortuosity, and multiple choroidal folds with retinal detachment (Figure 2). The right eye was normal. Magnetic resonance imaging (MRI) and computed tomography (CT) scan of the brain and orbit showed a heteregenously enhancing soft tissue mass with nodular mucosal thickening seen involving left maxillary, ethmoidal, and inferior frontal sinuses, and which extended to the left orbital apex. The mass involved the entire orbit and was infiltrating into left lateral and medial recti muscle as well as optic nerve. The mass was abutting the left cavernous sinus (Figure 3). There was no evidence of intracranial extension. On day two of admission, after a tentative diagnosis of rhino-orbital mucormycosis, he was started on systemic antifungal, amphotericin B 0.75mg/kg per day with tight renal function monitoring and intravenous ceftriaxone 2mg per day as well as metronidazole 500mg three times per day. The patient's condition showed no improvement. After obtaining parents consent, on day seven of admission, the patient underwent aggressive surgical debridement including endoscopic excision and debridement of ethmoid and maxillary sinuses and left orbital exenteration. Large amount of extensive necrosis fungal masses and hyphae elements were extracted from the ethmoidal and maxillary sinuses (Figure 4). Paranasal tissue biopsy, left globe and lower eyelid were sent for HPE, bacterial and fungal culture and sensitivity.

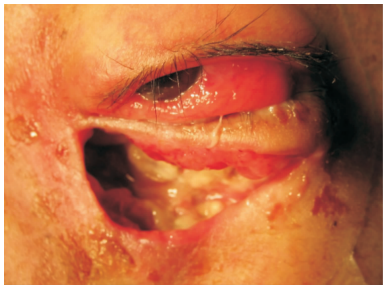

Figure 1 Left eye colour photograph of the 17-year-old Cambodlan boy showing large amount of fungal masses are seen in surgical wound.

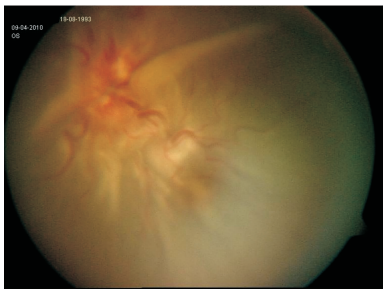

Figure 2 Preoperative left eye fundus photograph showing pale disc, vessels dilatation and tortuosity, and multiple choroidal folds with retinal detachment.

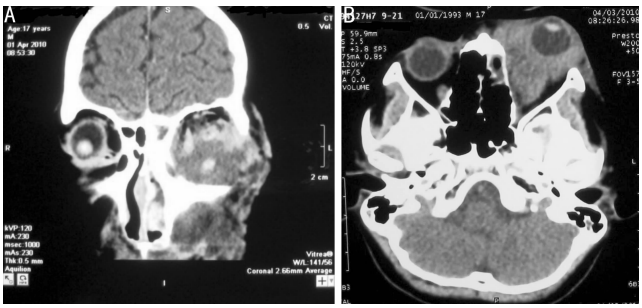

Figure 3 A: Coronal CT scan of brain showed a heteregenously enhancing soft tissue mass with nodular mucosal thickening seen involving left maxillary, ethmoidal, and inferior frontal sinuses, and which extended into the left orbital apex; B: Axial CT scan showed extension of infection into the entire orbit and was infiltrating into left lateral and medial recti muscle as well as optic nerve.

After histopathologic evaluation, the definite diagnosis of rhino-orbital mucormycosis was made. The left globe pathologic section stained with hematoxylin and eosin demonstrated microscopically granulomatous lesion on the outer surface of sclera that was characterized by central necrosis, multinucleated giant cells, macrophages and other inflammatory cells. In the inflamed and necrotic areas, fungal hyphae with mainly aseptate, haphazardly branching broad hyphae which were positive for both PAS and GMS stains, consistent with mucormycosis (Figure 5) were noted. The features were very similar to nasal sinus lesions. There was no evidence of malignancy. No organisms grew from the cultures taken at the time of surgery.

Postoperatively, the patient was given five weeks of intravenous amphotericin B and two weeks of broad-spectrum antibiotics. The patient underwent multiple surgical debridements

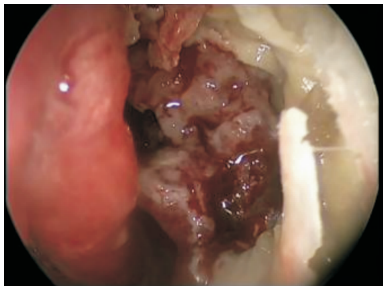

Figure 4 Endoscopic sinus surgery picture showed fungal masses with hyphae element at left nasal mucosa.

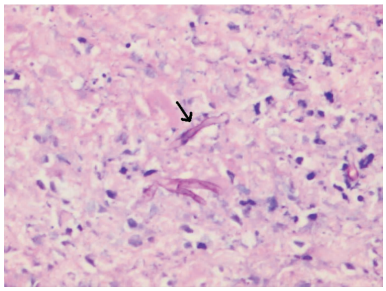

Figure 5 HPE slide photo of tissues from left eyeball demonstrating the fungal hyphae (arrowed) with are broad, aseptate, haphazardly branched.

with daily irrigation of orbital wound with 15mL of standard amphotericin B (1mg/mL). Final aggressive debridement and reconstruction with chin flap were performed on day 77. Three months after the hospitalisation, the patient remained asymptomatic and was discharged home. On his last follow-up visit, he was free of the infection.

DISCUSSION

Rhino-orbital mucormycosis is an acutely fatal opportunistic fungal infection in humans caused by organisms in the order *Mucorales* (class *zygomycetes*) and the family *Mucoraceae* includes the genera Rhizopus, Mucor, and Cunninghamella. Absidia, Rhizomucor, Saksenaea, and Apophysomyces are genera that are less commonly causing infection[2]. The zygomycetes are ubiquitous saprophytes and can be found on decaying vegetation and soil[7]. These fungi grow rapidly and undergo spore formation[8]. Inhalation of the airborne spores allows them to be cultured from the oral and nasal mucosa. Humans are frequently exposed to these fungi because they are commonly found in the environment. The spores are easily cleared by phagocytosis in the presence of effective human immune system thus mucormycosis is usually seen only in immunocompromised patients[3,7].

Diagnosis of mucormycosis relies upon the identification of organisms in tissue by histopathology with culture confirmation[7]. However, diagnosis may have to be based on histology alone as culture may be negative. This has been reported in few cases of rhinocerebral mucormycosis[3,9]. Histopathological examination typically shows sparsely septated or non-septated hyphae with right-angle branching invading viable tissue and often invading blood vessels. It is not easy to culture zygomycetes from clinical specimens due to the fragile nature of the hyphae which is the result of the lack of regular septations. Therefore, immediate treatment should be initiated based on this characteristic histopathologic appearance.

Further evaluation with either CT scan or MRI of the head, orbit and paranasal sinuses is essential to assess for intracranial involvement and involvement of the sinuses, ophthalmic and central retinal arteries, superior ophthalmic vein, and cavernous sinus.

In this case, delay in diagnosis lead to progression of infection and delay in initiation of antifungal therapy, necessitating extensive debridement and mutilating surgery as well as left eye exenteration. This indicates that physicians do not normally associate fungi with immunocompetent patient. In a review of 72 cases of mucormycosis involving any site by Elinav H *et al* [3], the proportion of apparently normal hosts among cases of rhinocerebral mucormycosis was found to be 9.06%. These findings suggest that rhinocerebral mucormycosis in healthy patients without known predisposing factors is more prevalent than previously believed. It is very important for the ophthalmologist to consider the possibility of rhino-orbital mucormycosis, irrespective of the immune status, especially in patients presented with orbital cellulitis but not responding to multiple antibiotics, mixed cranial nerve palsies and cases of retinal or orbital infarction.

Paranasal sinus mucor infection may extend into the orbit and then spread further into the cranium via orbital apex. Since the introduction of amphotericin in the 1960s, a combination of this powerful antifungal agent with extensive sinus debridement and orbital exenteration has been the mainstay of treatment of rhino-orbital mucormycosis to prevent intracranial extension of infection[8,10]. However, Fairley C *et al* [5] and Kohn R *et al* [11] have reported cases that were treated successfully without orbital exenteration. Adjunctive hyperbaric oxygen has been used in some patients with rhino-orbital mucormycosis but the efficacy of this therapy has not been established[8]. Early initiation of intravenous amphotericin B improves the outcome of the infection with mucormycosis[11]. The therapy should continue until patient shows favourable response and all signs of infection have resolved. It often extends for months. In this case, we managed this patient with aggressive combined surgical and medical therapy including 5-week intravenous amphotericin B, endoscopic parasinus debridement, orbital exenteration and daily intraorbital amphotericin B irrigation. Intraorbital irrigation and packing with amphotericin B help for better delivery to poorly perfused necrotic tissues.

Mucormycosis is difficult to treat. The keys to successful therapy include suspicion of the diagnosis with early recognition of the signs and symptoms, and aggressive medical and surgical intervention. The use of all available therapeutic modalities in the treatment of this often fatal infection, including intravenous amphotericin B, hyperbaric oxygen, surgical debridement with frozen section monitoring, direct local irrigation and packing of the involved orbit and sinuses with amphotericin B[7,8], may further reduce the role of mutilating surgery and replace the previously dismal prognosis with a more favourable outcome[12]. The prognosis of rhino-orbital mucormycosis has improved greatly. In 1961, the mortality was 88% and now varies from 15% to 34%[5]. The prognosis is especially poor for patients with intracranial, cavernous sinus or carotid involvement, although some patients with these complications have been cured from the infection.

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免疫功能正常患者鼻眶部毛霉菌病的研究

Lai Yong Tai, Keat Ween Khaw, Amir bin Samsudin, Zurina ZA, Mimiwati binti Zahari, Visvaraja Subrayan
(作者单位:马来西亚吉隆坡,马来亚大学医学中心眼科)
通讯作者:Visvaraja Subrayan. dvisva@ hotmail. com

摘要

报告1例免疫功能正常患者鼻眶部毛霉菌病非典型病例,并对该病例进行相关文献回顾。患者,男,17岁,免疫功能正常,左眼2mo缓慢进行性疼痛肿胀。行组织活检,病理学诊断为毛霉菌病。采用综合疗法,包括筛窦及上颌窦侵入性内窥镜切除和清创、左眼眶内容物刮除术、静脉注射两性霉素B和眶内两性霉素B冲洗,成功根除真菌感染。该病例说明,鼻眶部毛霉菌病可发生在年轻健康的个体身上。早期诊断,积极的药物和手术治疗对成功地治疗这种罕见的具有潜在致命性的疾病是至关重要的。

关键词:鼻眶部毛霉菌病;免疫功能正常;内容物刮除术;两性霉素B