CASE REPORT

Rhino-Orbito-Cerebral Mucormycosis: A Treatment Dilemma

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Summary

A case of rhino-orbito-cerebral mucormycosis is presented showing its aggressive nature and progression of disease. The typical clinical features, neuroimaging and histological findings are highlighted in this report. Amphotericin B and surgical debridement remain the mainstay of treatment. However, associated co-morbidities need to be addressed.

Key Words: Rhino - orbito - cerebral mucormycosis, Radiological imaging, Antifungal therapy, Surgical debridement

Introduction

Rhino-orbito-cerebral mucormycosis is a potentially aggressive and lethal invasive fungal infection. It is commonly seen in association with diabetic ketoacidosis but is not uncommon in other immunocompromised states and on rare occasion is seen to afflict an immunocompetent host. The classic presentation is involvement of the nasal mucosa with invasion into the paranasal sinuses, orbit and the central nervous system. Management includes aggressive surgical debridement, systemic antifungal therapy and treating the underlying co – morbidities.

Case Report

A 50 year old male presented to the Ophthalmology department with frontal headache, right orbital pain, progressive right eye swelling and acute deterioration of vision over 5 days. He also had vomiting, abdominal pain with significant weight loss recently. Comorbids included hypertension, type II diabetes mellitus and hypercholesterolemia to which he was non-compliant to treatment. He had a penchant to consume traditional medicine which was later confirmed to have contained steroids.

Examination showed a pale, dehydrated patient with acidotic breathing having thin and transparent skin with easy bruising. Ophthalmologic examination revealed total ptosis, proptosis, chemosis, raised intraocular pressure, complete ophthalmoplegia, afferent pupillary defect, facial hypoesthesia and absence of vision in the right eye. Right ethmoid sinusitis was noted on the orbit scans warranting an urgent Otolaryngology consult. Nasal endoscopy revealed crusting and pus within the middle turbinate with complete anesthesia of the nasal mucosa. An anterior ethmoidectomy with removal of the lamina papyracea was performed in order to relieve the intra – orbital pressure. In the presence of diabetic ketoacidosis cultures from blood and the nasal cavity grew mixed organisms including Pseudomonas species, Staphylococcus and Streptococcus. Histopathological examination confirmed an invasive form of fungal sinusitis confirmed by cultures which grew Rhizopus. (Figure 1).

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Broad – spectrum antibiotics was commenced along with systemic steroids to overcome the effect of hypoadrenalism secondary to exogenous steroid consumption. Electrolyte abnormalities and fluctuating sugar levels with persisting ketoacidosis contributed to a delay in initiating Amphotericin B as well as to proceed with surgical debridement under general anesthesia. This delay led to progression of the disease to involve the cavernous sinus (Figure 2). After stabilizing his condition, intravenous Amphotericin B was started and initial response to treatment was quite dramatic and preparation was made for the patient to undergo aggressive surgical debridement including evisceration of the right eye. Prior to surgery the patient developed hemiperesis with altered conscious level. Surgery was deferred due to the deteriorating neurological condition secondary to a cerebral infarct and from then on the prognosis worsened. The patient finally succumbed to the disease after three weeks of treatment.

Discussion

Rhino-orbito-cerebral mucormycosis is an aggressive and commonly fatal fungal infection arising in an immunocompromised host with a predilection for diabetic ketoacidosis[4,5]. Other predisposing conditions include hematological malignancies, transplant associated immunosuppression, acquired immunodeficiency conditions (AIDS), thermal injuries and congenital heart disease[4]. The clinical features are subtle and only become obvious with orbital or intracranial involvement. The earliest sign is facial edema followed by proptosis, chemosis and extraocular muscle paresis. Other manifestations include perinasal cellulitis, paraesthesia, periorbital edema, mucopurulent rhinorrhoea and nasal crusting. Anesthesia of the nasal mucosa is typical of mucormycosis but why this happens is unclear. This particular infection thrives in an acidic pH and a glucose rich medium which seems to enhance fungal growth, impairs neutrophil chemotaxis and decreases phagocytosis[3,4]. Infection spreads rapidly following a specific pathway from the sinuses to the orbit and the central nervous system. This transgression occurs by angioinvasion resulting in purulent arteritis and propagating thrombosis with associated tissue infarction and necrosis. Histologic features are typical with the presence of aseptate hyphae with right or obtuse angle branching[3]. Diagnosis depends on the presence of angioinvasion along the elastic lamina of blood vessels with surrounding inflammatory reaction with areas of vasculitis, thrombosis, hemorrhage, tissue infarction and necrosis[3,4]. Commonly isolated organisms include *Rhizopus, Rhizomucor, Absidia, Mucor,*

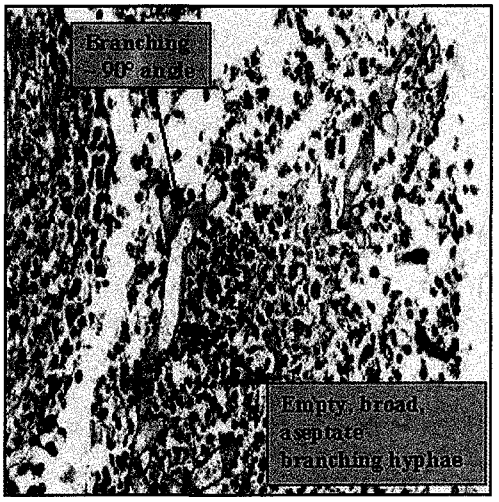

Fig 1: Histological staining with Hemotoxylin and Eosin demonstrating fungal hyphae with typical branching patterns.

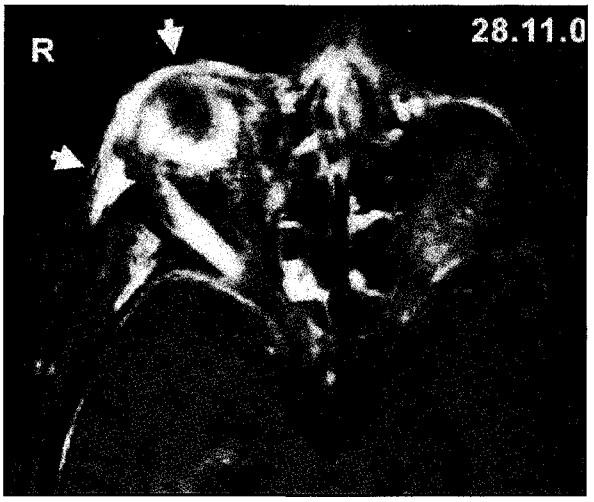

Fig 2: MR image showing diffuse orbital and peri-orbital inflammation with thickened and enhanced episcleral tissue. Spread of infection towards the orbital apex is well demonstrated

Cunninghamella, Mortirella, Saksengea and *Apophysomyces*[3,4].

Neuroimaging plays an important role in establishing the diagnosis and delineating the extent of the disease. In a retrospective review of 23 patients by DelGaudio, thickening of nasal mucosa, turbinates, septum and nasal floor was seen in 21 cases. Other findings included bony erosion, orbital invasion and facial swelling[2]. DelGaudio concluded that in cases where mucosal edema is more then expected and when the disease is unilateral, radiological diagnosis of invasive fungal sinusitis should be considered[2]. Osseous erosion and extra – sinus extension are late radiological signs. A contrast enhanced CT scan can demonstrate features of orbital inflammation and at times may show the disease progressing on to the orbital apex or cavernous sinus. With intracranial extension, the ideal imaging modality would be gadolinium - enhanced magnetic resonance imaging (MRI) which clearly defines areas of inflammatory process. Imaging, either computed tomogram or magnetic resonance imaging has it's own merits depending on the extent of disease and should be selected appropriately.

Treatment includes extensive surgical debridement, high doses of systemic Amphotericin B, control of underlying disease and other supportive measures[1]. Mortality can vary from localized disease in the paranasal sinuses at 11% to more then 80% with intracranial involvement[5]. Though most literature emphasize on radical surgical debridement and intravenous Amphotericin B as the mainstay of treatment, we tend to overlook the underlying causative factors as well as it's associated implications in the management. In a retrospective analysis of 179 patients, the underlying disease was the most important determinant of survival[1].

The diagnosis of mucormycosis begins with a high index of suspicion in an immunocompromised host. Medical therapy should be instituted as early as possible followed by aggressive surgical debridement depending on the extent and aggressiveness of disease[1,4]. Surgical debridement including orbital exanteration may carry a psychological morbidity of disfigurement and this has to be weighed against the life - threatening nature of the disease[4]. Blitzer et al in their review suggested that with early orbital involvement, even with cranial nerve involvement, decision for exenteration is dependant upon the aggressiveness of presentation, the type of underlying disease process and the response to initial therapy[1]. Amphotericin B remains the mainstay of treatment after half a century. The use of newer liposomal preparations of Amphotericin B is said to be more efficacious due to its better tissue availability with lower toxicity. Adjunctive therapeutic modalities like local irrigation with Amphotericin B, varied routes of administration and hyperbaric oxygen have been proposed with varying degrees of success. Hyperbaric oxygen has shown significant improvement in survival rates however more studies are needed to define its role as an accepted modality of treatment[3,5]. Poor prognostic factors include diabetic ketoacidosis, orbital involvement, immunosuppressive therapy with organ transplantation, significant medical conditions and medical management alone[1,4]. Yohai *et al* found that delayed diagnosis and treatment, presence of hemiplegia / hemiperesis, bilateral sinus involvement, leukemia, renal disease and desferroxamine therapy tend to lower the survival rates[5]. Rhino-orbito-cerebral mucormycosis remains an aggressive disease carrying a significant mortality rate even with the best of medical facilities.

References

1. Blitzer A, Lawson W, Meyers BR, Biller HF. Patient survival factors in paranasal sinus mucormycosis. Laryngoscope 1980; 90: 635-48.
2. DelGaudio J, Swain R, Kingdom T, Muller S, Hudgins P. Computed Tomographic findings in patients with invasive fungal sinusitis. Archives of Otolaryngology – Head & Neck Surgery 2003; 129(2): 236-40.
3. Ferguson BJ; Fungal Rhinosinusitis: A Spectrum of Disease. Otolaryngologic Clinics of North America 2000; 33(2): 349-65.
4. Peterson KL, Wang M, Canalis RF. Rhinocerebral mucormycosis: evolution of the disease and treatment options. Laryngoscope 1997; 107 (7): 855-62.
5. Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino – orbital - cerebral mucormycosis. Surv Ophthalmol 1994; 39: 3-22.