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Invasive rhino-orbito-cerebral mucormycosis in a diabetic patient – the need for prompt treatment

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ABSTRACT

Mucormycosis is a rare life threatening fungal infection predominately seen in immunocompromised or diabetic patients. The following case is of a known type II diabetic patient who presented with sepsis and sudden unilateral loss of vision secondary to infective rhino-orbito-cerebral mucormycosis. Treatment of the condition required extensive surgical intervention and medical management for a life saving outcome.

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1. Introduction

Mucormycosis refers to a spectrum of diseases caused by infection with fungi in the order of mucorales. Mucorales with 7 genera: *Rhizopus*, *Mucor*, *Absidia*, *Saksenaea*, *Rhizomucor*, *Apophysomyces*, and *Cunninghamella* are documented to be pathogenic organisms that produce invasive disease in humans, with the most common causative agent being of the rhizopus species. Endemic worldwide, mucorales are predominantly saprobic soil organisms found on decaying organic material. However, these organisms also act as opportunistic pathogens causing an acute angioinvasive infection seen primarily in the immunocompromised [1].

Over the last few decades there has been an increase in the number of reported cases of infections caused by mucorales [2]. This has been attributed to a rise in awareness of the disease and improvement in methods of identifications. The rise however has also coincided with an increase in risk factors such as immunosuppression, malignancy and diabetes [3].

Patients with poorly controlled diabetes and ketoacidosis are at high risk of developing rhinocerebral mucormycosis, with systemic acidosis creating an ideal environment for the growth of *Rhizopus*. However initial presentation of rhinocerebral mucormycosis infection can often appear non-specific making correct diagnosis extremely difficult until the disease has caused significant morbidity, aggressive fungal invasion of the paranasal sinuses, orbit, hard palate and brain [4,5].

The basis of mucormycosis treatment remains a combination of extensive surgical debridement and amphotericin B for a protracted period of 4–6 weeks [6]. Although not currently used as first line treatment, the concurrent use of posaconazole, a triazole antifungal drug has been shown to be effective against mucormycosis and use has been increasingly reported when amphotericin B has had to be discontinued due to adverse side effects [7,8].

The following case report illustrates the challenges of managing rhinocerebral mucormycosis in diabetic patients with concurrent co-morbidities, limiting the use of medical therapies.

2. Case

A 62 year old man presented to hospital (day 0) with a one week history of left sided facial hyperaesthesia, retro-orbital discomfort and blurred vision. He had complained of suffering from a dull persistent headache for the past five weeks. He had a past medical history of insulin dependent type two diabetes, chronic kidney disease with stage 3 renal failure, hypertension, chronic

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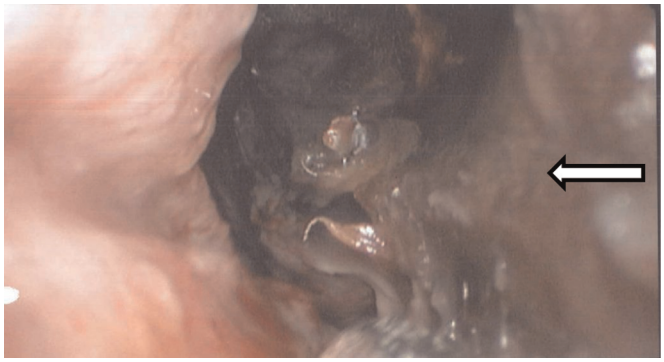

Fig. 1. Endoscopic photography of left nasal cavity demonstrating black eschar (dead tissue) indicated by the arrow on the left lateral nasal wall.

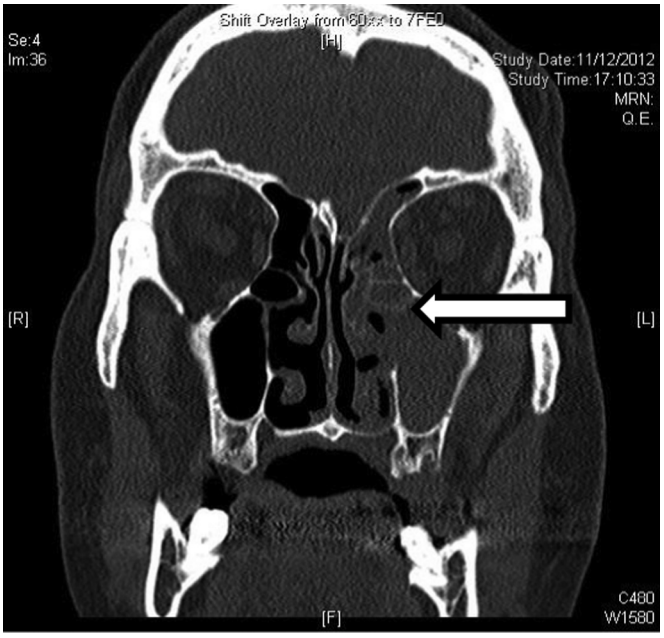

Fig. 2. Coronal CT image without contrast showing thickening of mucosa and opacification of left ethmoidal and maxillary sinuses (indicated by the arrow).

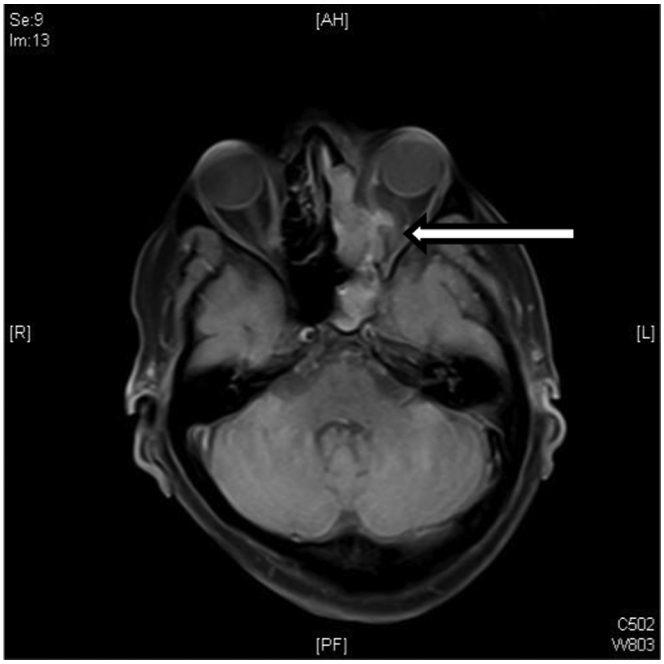

Fig. 3. Diffusion weighted MRI axial imaging showing extensive inflammatory changes in the left nasal cavity and paranasal sinuses with mass encroaching into left orbital plate (indicated by arrow).

pancreatitis and ischaemic heart disease.

Referral to the local ear, nose and throat (ENT) department was made on day +2, after the patient had been seen by the ophthalmology department due to progressive visual loss. On examination the patient was found to have complete ptosis of the left eye. The left pupil was found to be fixed and dilated with paralysis of cranial nerves III, IV and VI. Visual acuity in the left eye was reduced to counting fingers at one metre. Slit lamp examination of the left retina demonstrated a "cherry red spot" and cattle trucking sign, consistent with a central retinal artery occlusion and optic neuritis. Flexible nasal endoscopy revealed brown discharge and eschar on the lateral wall of the left nasal cavity (Fig. 1).

Laboratory results on admission (day 0) showed an elevated white cell count 31.7 ($\times 10^{9/l}$) and C-reactive protein 396 (mg/l0); Creatinine 354 (μmol/L) (elevated from baseline 271 μmol/L 4 months previously); blood sugars 14.3–25.5 (mmol/L) and potassium 6.0 (mmol/L), all of which were consistent with hyperglycemic hyperosmolar state, acute kidney injury (AKI) and hyperkalaemia.

An urgent computed tomography scan (CT) of the head was performed revealing mucosal thickening in the left ethmoid, maxillary and frontal sinuses with disease involving the medial wall of the left orbit, soft tissue swelling around left orbit with slight displacement of the medial extraocular muscles (Fig. 2).

Magnetic resonance imaging (MRI) scan showed collection/mass within the left ethmoidal air cells which had breached through the left orbital plate and encroached into the left orbit posteriorly (Fig. 3). At this stage there were no signs of intracranial spread of disease.

On day +2, upon assessment by the ENT consultant the patient underwent immediate and extensive débridement of all infected and necrotic tissue. Left infundibulectomy was performed opening up the ethmoid, maxillary and frontal sinuses for drainage of the sinuses and any collections. A left orbital decompression was performed by incising the orbital periosteum in an attempt to preserve the remaining vision.

Tissue samples from debridement macroscopically grew colonies of woolly, white and subsequently grey fungi, which grew with such rapidity they fitted with colloquial description of fungi as 'lid lifters' (Fig. 4). Microscopic examination showed broad hyphae with irregular branching and fungus was identified as *Rhizopus arrhizus* (Fig. 5). Diagnosis of *R. arrhizus* was made by the colonial appearance and microscopic structure-confirmed by the Public Health England Mycology Reference Laboratory, Myrtle Road Bristol.

The patient was commenced on antimicrobial therapy on day +2, which consisted of AmBisome 300 mg (3–5 mg/kg/day) intravenously and posaconazole 420 mg orally, twice daily. After a total of 6 days of treatment with intravenous AmBisome and posaconazole, treatment was discontinued on day +8 due to derangement of renal function and liver function test.

Post-operatively, the patient continued to experience worsening headache, nausea and paraesthesia over the left infra-orbital region. Serial MRI and CT scans were performed which showed extension of the disease process which now involved the left orbit and frontal sinus.

The patient's case was re-discussed with the local microbiology team who recommended salvage treatment with deferasirox. The patient received an oral dose of deferasirox 15 mg/kg however due to significant and rapidly worsening renal function, treatment was

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