

Retrieved from the jaws of death – A successfully managed case of rhino-cerebral mucormycosis despite healthcare constraints due to economic turmoil

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Abstract

Rhino- orbital-cerebral mucormycosis is a rapidly progressive life-threatening fungal infection which primarily affects the nose, paranasal sinuses and orbit. It is an opportunistic fungal infection caused by fungi of order Mucorales. They are a group of ubiquitous fungi which grow on decaying vegetation and a wide variety of organic compounds, and they pose a huge threat to life by direct invasion of the vital structures in the body. Early identification and treatment of this disease is therefore of paramount importance for a better outcome. We report a case of a 65-year-old man with a background history of poorly controlled type 2 diabetes mellitus, hypertension and chronic kidney disease, who presented with a diffuse headache of 5 days along with left sided facial oedema, redness of left eye and visual disturbance. Imaging studies revealed sinusitis involving multiple sinuses and the nasal mucosal biopsy showed fungal hyphae. Considering the clinical presentation and the overall findings from the investigations a diagnosis of rhino-cerebral mucormycosis was made. Medical management was done with administration of intravenous Amphotericin B and IV itraconazole along with other supportive medication. Patient had a successful recovery after a lengthy hospital stay which included surgical debridement of affected tissues and the medical treatment even with challenges faced due to unavailability of drugs due to economic constraints on health.

Key words: rhino-cerebral mucormycosis, Amphotericin B, fungal sinusitis, economic turmoil, Itraconazole

Introduction

Rhino-cerebral mucormycosis is a rare filamentous fungal infection which is primarily a disease of the immunocompromised patient with altered host defence mechanisms.(1) It still remains as a disease with high mortality.(2) Therefore, high degree of clinical suspicion in the early stages is of paramount importance for the timely and warranted aggressive management of mucormycosis. The most commonly

reported pathogens in mucormycosis are *Rhizopus spp*, *Lichtheimia spp*, *Mucor spp* and *Rhizomucor spp*. Based on the anatomical site, the clinical manifestations are mainly in rhino-cerebral, pulmonary, cutaneous and gastrointestinal sites. There are other anatomical sites that are rarely involved in this disease such as the heart, bone, peritoneal cavity and kidneys which cause endocarditis, osteomyelitis, peritonitis and renal infection respectively.

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Case presentation

A 65-year old man, who has a background history of type 2 diabetes mellitus, hypertension, and chronic kidney disease stage 3 presented with a diffuse headache of 5 days along with left sided facial oedema, redness of left eye and visual disturbance of the affected eye.

He was in his normal health until 5 days before presentation, and then he gradually developed a diffuse nonspecific headache which worsened in severity over time. He did not have any similar headache in the past or any clear predisposing cause for the headache. The headache was not associated with autonomic symptoms such as nausea, vomiting, tearing and he did not have photophobia or phonophobia.

Following the onset of the headache, he gradually developed left sided facial oedema including the ipsilateral periorbital region. The painful facial swelling progressively worsened over the course of 5 days. The aching pain was moderate in severity and did not respond to paracetamol.

A few days later he developed numbness over the affected area and also noted the deviation of the mouth to the unaffected side with inability to open the left eye. The opposite side of the face including the right eye was completely spared.

He was diagnosed with type 2 diabetes mellitus 6 years back. Since then, he was on oral hypoglycaemics with irregular clinic follow up and poor drug compliance. He was diagnosed with chronic kidney disease stage 3 a few years back, but was lost to follow-up. He has not undergone routine screenings for complications of diabetes. He did not have any significant past medical problems which required in-hospital care. He was diagnosed with hypertension along with diabetes however defaulted treatment due to treatment barriers posed by his poor socio-economic state. He was treated for severe SARs Cov-2 pneumonia 10 months back with high dose steroids. The drugs were tapered over a course of 2 weeks duration and he had not been on any medication thereafter.

On examination he was overweight with a BMI of 27.2 kgm². He was ill looking, conscious and rational with a GCS of 15/15. He was febrile with a temperature of 101°F. He was not pale or icteric. Significant left facial swelling was noted. There was no generalised lymphadenopathy. His oral hygiene was unsatisfactory and unhealthy white and brown

plaques were noted on the left upper palate. No skin rashes noted. Fundal examination was normal, and showed no features of papilledema. No features of meningism were noted. Cardiovascular, respiratory and abdominal examinations were unremarkable.

Neurological assessment revealed a visual acuity of 6/60 in the left eye while it was 6/36 in the right eye. The left side pupil was dilated with left eye complete ptosis. Proptosis and chemosis were also noted. Complete ophthalmoplegia was noted on the left side. There was a sensory loss on the left side of the face signifying the involvement of the ophthalmic & maxillary branches of the trigeminal nerve. The left corneal reflex was absent and ipsilateral lower motor neuron type facial nerve palsy was noted. Rest of the cranial nerve examination of the left side was normal while no cranial nerve pathology was detected on the right side. All four limbs were neurologically normal and there were no cerebellar signs.

Considering this presentation, initial differentials were periorbital cellulitis, intra orbital cellulitis, cavernous sinus thrombosis, rapidly growing orbital tumour or rhino-cerebral mucormycosis. Series of investigations were carried out in pursuit of establishing one of these diagnoses (table 1).

Based on the targeted investigations the diagnosis of rhino-cerebral mucormycosis was made. This patient was managed with a multidisciplinary team. He was started on intravenous Amphotericin B along with other measures to optimise his glycaemic status. After a prolonged hospital stay with multiple surgical procedures, several antimicrobials and rehabilitation the patient recovered completely.

Discussion

Rhino-cerebral mucormycosis is a fulminant fungal infection usually caused by the microorganisms of the family *Mucoraceae* and class *Zygomycetes*.⁽¹⁾ The factors which influence the development of this disease include immunocompromised states such as poorly controlled diabetes mellitus, malnutrition, post organ transplant, patients on high dose immunosuppressive medication, patients with acquired immunodeficiency syndromes, malignancies etc.⁽¹⁾

This patient had a background history of poorly controlled diabetes mellitus, chronic kidney disease stage 3 and hypertension with irregular clinic follow up. In addition he was treated with high dose corticosteroids. This is in keeping with the natural history of rhino-cerebral mucormycosis which is

Table 1 - Investigations

Investigation		Results	Normal range
Full blood count	Haemoglobin (g/dL)	10.6	11-13
	White cells (× 10 ⁹ /L)	7.3	4.5 – 11
	Platelets (x 10 ⁹ /L)	236	150 – 400
	Neutrophils %	58	50-70
	Lymphocytes %	38	20-40
Serum electrolytes	Serum potassium (mmol/L)	4.3	3.5 – 5.5
	Serum sodium (mmol/L)	131	135 – 145
Inflammatory markers	C Reactive Protein (mg/dl)	255	<5
Renal functions	Serum Creatinine (μmol/L)	208	52-92
CSF analysis	Protein (mg/dl)	114	15-45
	Glucose (mg/dl)	130	
	Polymorphs (/cumm)	30	
	Lymphocytes (/cumm)	05	
	Red blood cells (/cumm)	30	
	Cytology	Lymphocytes ++	
	HSV antigen/antibody	Not detected	
Infective screening	Blood Culture	Negative	
	Urine Culture	Negative	
Blood picture	Normochromic normocytic anaemia		
Nasal Mucosal Biopsy	Direct Smear – Fungal Hyphae Noted		
CECT Brain & Paranasal Sinuses	<ul style="list-style-type: none">• Left side pre septal soft tissue cellulitis• Mild sinusitis involving left frontal, bilateral ethmoid, maxillary and sphenoid sinuses		
MRI Brain, Orbit, Paranasal sinuses & MRV	<ul style="list-style-type: none">• Left orbital cellulitis• Sinusitis involving the bilateral maxillary, sphenoid & ethmoid sinuses		

essentially a disease of the immunocompromised host.

Mucormycosis has a wide spectrum of clinical presentations and it most commonly targets the Rhino-Orbital-cerebral area(2) as in this case.

Patients suffering with this condition classically present with periorbital facial pain, facial cellulitis, proptosis, headache, acute visual loss, nasal ulceration and stuffiness etc.(3) Majority of these symptoms were present in this case as well. Prolonged fever is a frequently associated symptom

even though it was not seen in this case.(4) The most commonly involved sinuses are the ethmoid and maxillary sinuses which was the case here as well, along with other sinuses frontal and sphenoid sinuses.(5)

In the acute setting the mimickers of these symptoms include sinusitis or periorbital cellulitis.(1) The only disease specific finding for mucormycosis is blackened necrotic eschars of nasal mucosa or palate.(1) This was present in this case as brown plaques in the hard palate. Formations of these eschars represent a progressive disease which has already reached to the stage of vessel thrombosis and tissue infarction and it's an early sign of disease extension beyond the sinuses.(1)

Investigations used to identify this disease include radiological studies such as Magnetic Resonance Imaging (MRI), Computed tomography (CT) and direct histological assessment of the surgical specimens. In the initial stages the value of these imaging modalities is minimal because of the thickening of the mucosal layer of the sinus, but they are useful in evaluating disease progression as the clinical symptoms may not be directly comparable to disease progression.

Management principles used in treating patients with this disease include early diagnosis, reversing the underlying predisposing factors and prompt antifungal treatment coupled with surgical debridement where necessary.(5) Multidisciplinary and multimodal approach is of utmost importance in addressing patients suffering with this disease.(6) Amphotericin B is the drug of choice for initial therapy and commonly a lipid-based formula is used to deliver a higher dose with less nephrotoxicity. Use of other drugs like Posaconazole, Echinocandin in combination with Amphotericin is also practised in different parts of the world, but the benefits of these protocols are yet to be proven. Combination therapy and its efficacy is an area which needs further evaluation.

Pharmacological therapy was initiated with limited doses of IV liposomal Amphotericin B limited in the first few days. During the pharmacotherapy our patient faced a new challenge due to prevailing economic turmoil spilling on to the health sector. The hospital ran out of Liposomal Amphotericin B and given the severity of the patients' condition, with the help of the microbiologist, we decided to use IV Itraconazole which was available at the time. Unfortunately, the facilities were not available to calculate the MIC of the organism. Although

itraconazole is not a second line choice for treatment for mucormycosis itraconazole has been used successfully to treat some patients.(7) And we observed that our patient did not worsen clinically during treatment with itraconazole. He was later put on IV Liposomal Amphotericin B when it was available. Therefore, when the first or second choice treatment is not available, there may be a place for IV itraconazole in treatment of advanced mucormycosis.

Surgical methods are also considered as an effective treatment modality in the management of mucormycosis. Aggressive surgical debridement of involved tissues should be considered in the case of poor response to medical therapy. It is known to improve survival rates. The complications associated with surgical debulking include disfigurement due to removal of necrotic tissues as it may require removal of the palate, nasal cartilage, and the orbit.



Figure 1 - White brown plaques on the hard palate



Figure 2 - Macroscopic appearance of the fungal culture

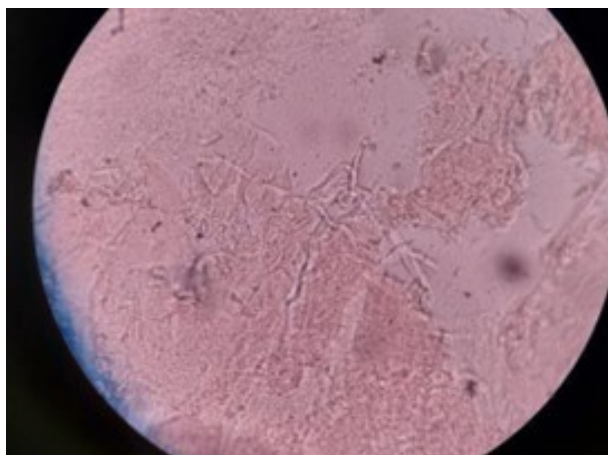


Figure 3 - Direct smear of sample showing fungal hyphae

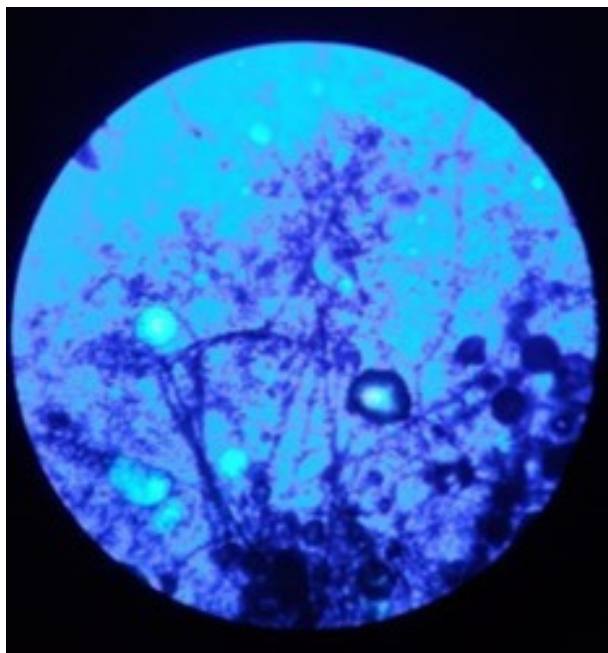


Figure 4 - Lactophenol cotton blue staining showing fungal hyphae

Conclusion

High degree of clinical suspicion as well as early medical and if needed surgical interventions are required in the management of patients with Rhino-cerebral mucormycosis. As it is a potentially life threatening or life altering infection, these measures will help to minimise the morbidity and mortality of this condition and will ultimately help to achieve better outcomes for the patient.

And in resource poor settings, even though the first line treatment is not always feasible, there may be cheaper and more achievable options where the

patient as well as the health system may benefit.

Declarations

Author contributions

History taking, examination, necessary investigations, management, daily monitoring of the patient & writing of the manuscript was done by AN Wijethunge. W Uluwattage supervised the management of this case and Bhagya Piyasiri, R.S.Kodithuwakku, WMDN Weerasinghe, J.H.T Dileka, I U Halpita were major contributors in writing the manuscript. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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