

A Case Report

A Case Report: Rhino-Orbito-Cerebral Mucormycosis with visual impairment and cranial nerve palsies in a tertiary care hospital Sri Lanka.

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Abstract

Mucormycosis is an angioinvasive infection, especially among immunocompromised patients. There are several forms of the disease and rhino-orbito-cerebral mucormycosis is the commonest presentation globally, especially among patients with diabetes mellitus with or without ketoacidosis. We report a patient with rhino-orbito-cerebral mucormycosis involving multiple cranial nerve palsies.

A 70-year-old female patient with uncontrolled diabetes mellitus presented with left periorbital swelling and reduced vision on the same side along with epistaxis. On examination, she was found to have multiple cranial nerve palsies. She was managed as rhino-orbito-cerebral mucormycosis after performing several microbiological, histological, and radiological tests. The patient was discharged after 4 months of hospital stay.

Despite successful medical and surgical interventions, the patient died a week after being discharged from the hospital. Though we have no strong evidence, the disease itself, her co-morbidities, sepsis, and surgical trauma could have contributed to her death.

Introduction


Mucormycosis is a disease caused by fungi belonging to the order Mucorales. The most reported pathogens in this order are *Rhizopus* sp, *Mucor* sp, *Lichtheimia* sp, *Rhizomucor* sp, *Cunninghamella* sp, *Apophysomyces* sp, and *Saksenaea* sp.¹ Humans acquire the infection primarily by inhalation of sporangiospores, and occasionally by ingestion of contaminated food or traumatic inoculation.² This group of fungi is ubiquitous, and microscopic morphology appears as broad, aseptate or sparsely septate ribbon-like hyphae.³

There are several forms of the disease.⁴ Rhino-orbito-cerebral, pulmonary, gastrointestinal, cutaneous, renal, disseminated, and other miscellaneous forms such as infection of bones, heart, ear, parotid gland, uterus, urinary bladder, and lymph nodes. Of them, rhino-orbito-cerebral

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mucormycosis remains the most common clinical presentation globally and frequently presents in patients with diabetic ketoacidosis and uncontrolled diabetes mellitus.⁵ Other risk factors include malignancy, transplant recipients, corticosteroid therapy and neutropaenia. However, a considerable number of cases have been reported in patients without any underlying disease or risk factors.⁵

Diagnosis is made by observing fungal elements in direct smears and histological sections and growth in fungal culture.⁷ Management includes correction of underlying risk factors and prompt administration of antifungal agents and thorough surgical debridement. In all forms of the disease amphotericin B (deoxycholate or liposomal preparations) is the cornerstone of therapy. However, the disease is associated with high morbidity and mortality.^{5,6}

We report a case of rhino-orbito-cerebral mucormycosis presenting with visual impairment and multiple cranial nerve palsies. Even though mucormycosis is common in Sri Lanka owing to the high prevalence of diabetes mellitus and increasing number of immunosuppressed patients, there are only a few published case reports on multiple cranial nerve involvement locally.¹⁰

Case Report

A 70-year-old female patient with diabetes mellitus for 15 years, with microvascular complications and poor glycaemic control, presented with left periorbital swelling and reduced vision on the same side and epistaxis from the left nostril for 2 days.

On admission, GCS was 15/15, blood pressure 140/84 mmHg, and pulse rate 101bpm. She was found to have left medical 3rd nerve palsy. On day 3 of admission, she was found to have 2nd, 3rd, 4th, 5th, 6th, and 7th left cranial nerve palsies with left mastoid tenderness and chemosis.

On admission her capillary blood sugar was 348mg/dl. She was started on soluble and isophane insulin. However, as her capillary blood sugar levels fluctuated necessitating regular dose adjustments, she was subsequently changed to mixtard insulin. She was referred to the ENT unit with the suspicion of mucormycosis. Rigid nasal endoscopy showed blackish discolouration in the middle turbinate and unhealthy nasal mucosa with blood clots on the left side. Biopsy samples were taken and sent for histology and fungal studies.

Due to the high clinical suspicion of mucormycosis, she was started on IV liposomal amphotericin B (3mg/kg) on day 3 of admission. She also underwent left sided functional endoscopic sinus surgery (FESS) together with orbital decompression and right sided middle meatal antrostomy. She was found to have a necrosed left sided middle turbinate and unhealthy mucosa over the left sided inferior and middle turbinates, left sided maxillary sinus, left sided anterior and posterior ethmoids, and left sided frontal recess. There was fungal debris in the right sided maxillary sinus and unhealthy mucosa over the posterior wall of the right maxillary sinus. Non contrast MRI-brain with sinuses showed thickening of the left trigeminal nerve and invasive fungal disease suggestive of rhino-orbito-cranial mucormycosis. Histology using the Grocott methenamine silver stain (GMS) showed scattered broad, non-septate fungal hyphae, confirming the presence of fungi. Necrotic material obtained at FESS showed fungal filaments suggestive of zygomycetes (Fig. 1). Inoculation on Sabouraud dextrose agar supplemented with chloramphenicol and incubated at 26 °C and 37 °C yielded *Rhizopus* sp. (Fig. 2) after 3 days.

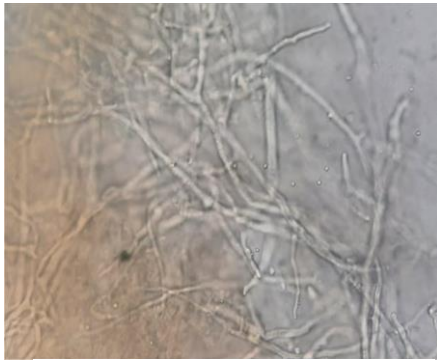


Figure 1: Direct microscopy showing broad, non-septate fungal hyphae



Figure 2: Culture isolate of *Rhizopus* sp. Gray colour cotton candy like colonies

As she had a blind eye and extensive involvement of orbital soft tissues, she underwent left sided eye exenteration 38 days after initiation of antifungal treatment together with right sided ethmoidectomy and sphenoidectomy (Fig. 3). This was followed by a forehead flap repair on



Figure 3: Patient following eye exenteration

the same day to cover the defect. Post-operative ICU care was given. There was close liaison with the endocrinology unit to achieve glycemic control.

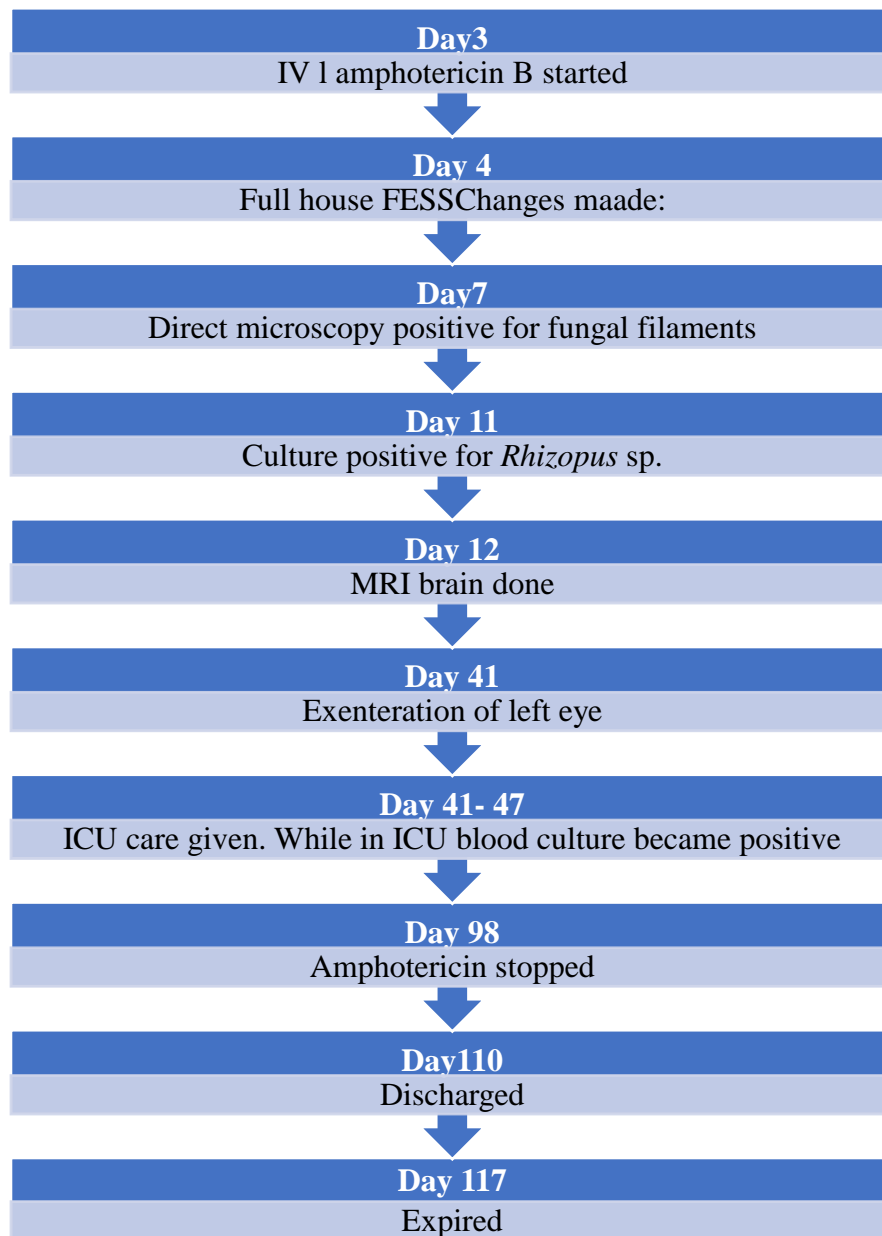
At the ICU, her peripheral blood culture became positive on post operative day 5 for *Pseudomonas* sp. and she was treated with IV meropenem 1g 8 hourly which was continued for 20 days. She was treated with IV liposomal amphotericin B followed by IV amphotericin B deoxycholate preparation for a total of 96 days.

Gradually the patient's clinical condition improved, during which repeated rigid nasal endoscopy and debridement of the residual fungal debris was carried out. Computed tomography done 40 days after eye exenteration showed radiological clearance of fungal masses. Follow up fungal culture and direct microscopy repeated four times over a 2-month period were negative.

After 4 months of hospital stay during which she was treated with a total of 1250 mg of IV liposomal amphotericin B over 25 days and a total of 3550mg of the deoxycholate preparation over 71 days, the patient was discharged. Her glycaemic control was assessed before discharge. She was discharged on mixtard insulin and oral antihyperglycemic drugs. One week after discharge, the patient expired at home.

The timeline of her illness is shown in Figure 4.

Timeline



Discussion

This patient presented with uncontrolled diabetes mellitus which is the commonest risk factor for rhino-orbito-cerebral mucormycosis, particularly in the Asian subcontinent.⁵ Dissemination to the central nervous system is associated with more than 80% mortality.¹

The foremost host immune defenses against mucormycosis are phagocytic mononuclear and polymorphonuclear cells.⁶ Generally, healthy people clear the spores by the action of phagocytosis. Patients with poorly controlled diabetes mellitus and diabetic ketoacidosis are more likely to develop the disease as their phagocytic function and chemotaxis is impaired.^{6,8}

Mucormycosis is an angio-invasive infection which results in thrombosis and tissue necrosis.⁶ Acute rhino-cerebral mucormycosis can aggressively spread to the orbits and cranium and in severe forms of the disease can cause chemosis, ptosis, proptosis, ophthalmoplegia, blindness

and multiple cranial nerve palsies, all of which were present in our patient. Definitive diagnosis can be made by histopathology and fungal studies. Early detection of cranial nerve involvement together with aggressive surgical and antifungal management can curtail the spread, thereby improving overall outcome of the patient.¹⁰

We treated her successfully with IV amphotericin B together with appropriate surgical interventions. Complications such as hypokalaemia and hypocalcaemia were managed as required with intravenous KCL and oral CaCO₃. However, despite successful medical and surgical interventions, the patient died a week after discharge from hospital. Though we have no strong evidence, the disease itself, her co-morbidities, sepsis, and surgical trauma could have contributed to her death.

Take home message:

Mucormycosis needs multidisciplinary management due to its complications as well as problems posed by the treatment. Delay in presentation is a challenge we need to overcome. Awareness among the public is the key.

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