

## Invasive cranial mycosis our experiences

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### ABSTRACT

Fungi can cause serious cranial infections in immunocompromised and diabetic patients. Common pathogens mainly include *Aspergillus* and *Mucor*. These organisms cause tissue invasion and destruction of adjacent structures (e.g. orbit, ethmoid, sphenoid, maxillary & cavernous sinuses). Mortality and morbidity rate is high despite combined surgical, antifungal and antidiabetic treatment. We present our experience of six cases with such infection.

**Key words:** Mycosis, diabetes, Immunocompromised state, complete ophthalmoplegi

### INTRODUCTION

Acute invasive cranial mycosis is the most aggressive form of fungal infection. It is seen particularly in immunocompromised patients. Common causes of underlying immunosuppression include - Diabetes mellitus, especially those with ketoacidosis and neutropenic state. Clinical presentation mainly includes rapid development of fever, facial pain, nasal congestion and epistaxis. Extension into the orbit, cavernous sinus or intracranial compartment is frequent & results in deterioration in vision, proptosis and neurological deficits. The disease may also progress into vessels and result in systemic dissemination and increase morbidity and mortality.

We present our experience with six such patients of cranial fungal infections.

### CASE REPORTS

#### Case 1

A 56yr old male<sup>[1]</sup>, recently detected to have diabetes was

admitted in our institute in Hyperglycaemic Hyperosmolar State (serum osmolarity - 347meq/dl) with septicaemia and renal insufficiency. He was treated with intravenous insulin infusion and injectable antibiotics. Within 48 hrs, he became well hydrated and his sensorium improved. His sugars were well controlled. After 3 days, he complained of pain in right eye and right maxillary region. He also developed ptosis [Figure 1a] with complete ophthalmoplegia with dilated fixed pupil on the right side. CT scan head & orbit showed granulomas at right orbital apex. Some destruction of contiguous bone was also reported. He then developed black necrotic area adjacent to nose on right side and there was necrotic mass in right nasal cavity. Patient was taken for emergency surgery and debridement of necrotic mass was done. Mass showed broad, non-septated, ribbon



Figure 1a: Ptosis in case 1

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like hyphae with wide angled branching on fresh KOH mount [Figure 1b]. Culture later grew mucormycosis. Inj. amphotericin B was started.

Final impression was Hyperglycaemic Hyperosmolar State with Mucormycosis. Despite good control of sugars, adequate debridement and antifungal therapy, patient succumbed.

### Case 2

A 50yr old male<sup>[2]</sup>, who had Type2 Diabetes for last 4yrs was admitted in our institute in 2009. He was very irregular with his treatment and was on indigenous medications for past few days. He had history of frontal headache, dizziness, slurred speech and weakness on left half of body. Ten days back, he became inattentive. He was in Hyperglycaemic Hyperosmolar state with septicaemia. CT scan head revealed large (5-6cm) discrete, irregular peripheral ring- enhancing necrotic lesion in right frontoparietal region of brain causing mass effect & midline shift with

perifocal edema [Figure 2a]. Neurosurgical intervention was done and 8ml of thick viscous black fluid, which was mainly caseous, was aspirated. The material was analysed. Microscopic examination revealed Langerhans giant cells with moniliform septated hyphal elements and tentative diagnosis of chronic granulomatous inflammation with super added fungal infection was made. On culture growth was observed after 1 week & morphologically classified as *Rhinoctadiella* Mackenzie [Figure 2b]. For the management of the case,

insulin infusion was given along with injectable amphotericin B and Antitubercular drugs. Despite this therapy patient's condition continued to deteriorate & he succumbed within 2 weeks of diagnosis.

### Case-3

An elderly male<sup>[3-5]</sup> presented to our institute in 2009 with headache and loss of vision since one week. He had been taking steroids off & on for chronic dermatosis for past



Figure 1b: Microscopic picture of mucormycosis

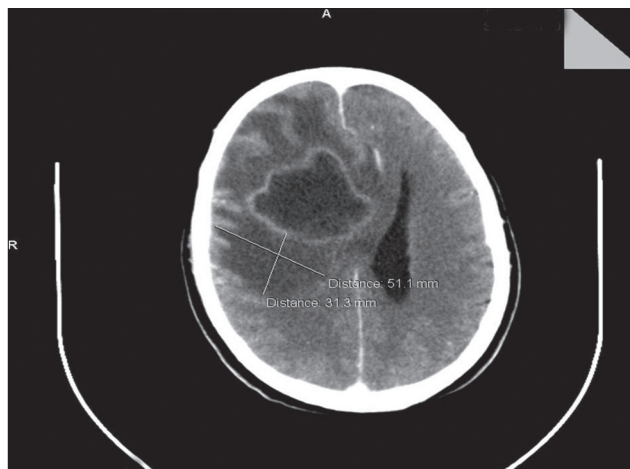


Figure 2a: Irregular peripheral ring - enhancing necrotic lesion

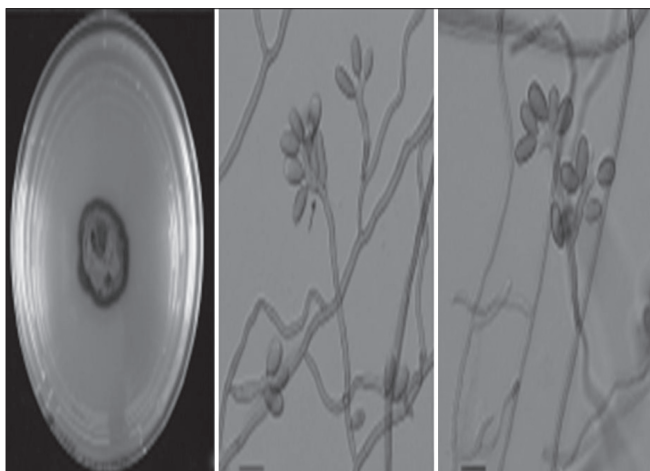


Figure 2b: Microscopic picture of *Rhinoctadiella*



Figure 3a: Periorbital swelling and ptosis

4-5 yrs, he was diagnosed with diabetes 4 months back & was prescribed oral antidiabetic drugs which he had stopped taking 15 days before presentation. He came to us in Diabetic Ketoacidosis with involvement of left eye. Examination of his left eye revealed [Figure 3a] periorbital swelling, complete ptosis and 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> 6<sup>th</sup> cranial nerve palsy was present. Nasal examination showed blackish firm deposit. Patient was put on antibiotics & insulin therapy. CT scan orbit and head showed soft tissue density in maxillary, anterior and posterior ethmoid air cells. KOH preparation of the nasal swab showed aseptate fungal hyphae, which were branching at right angles. Morphology was suggestive of mucor species [Figure 3b]. Intravenous amphotericin B was started and endoscopic nasal debridement was done. Patient's condition improved but he developed blindness in the left eye and was discharged with controlled sugars.

#### Case- 4

A 45 yr old female recently detected diabetic came to our institute in 2010 with fever, headache & swelling over left

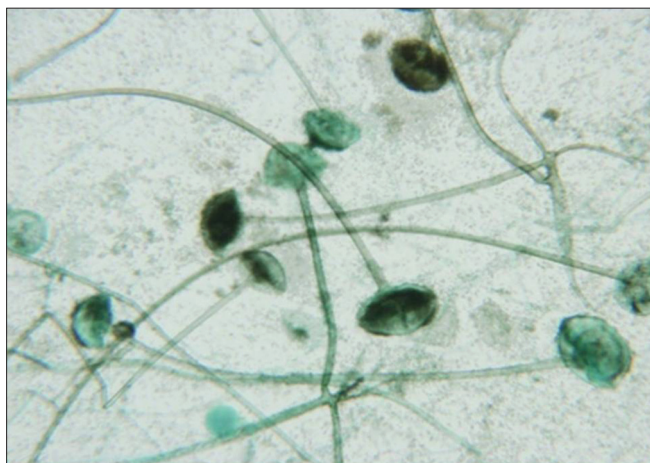


Figure 3b: Microscopic picture of mucormycosis



Figure 4b: Pseudohyphae and branching filaments

side of face since 10 days. She also had bleeding from right nostril since 3 days. Nasal endoscopy revealed bilateral crusting of nasal septum with white dots resembling mould. CT scan PNS showed concentric mucosal thickening in left maxillary sinus & soft tissue density in anterior & posterior ethmoid air cells and left sphenoidal sinus [Figure 4a]. Microscopic examination of nasal swab on KOH mount showed few budding yeast like cells with pseudohyphae and branching filaments [Figure 4b]. Culture of specimen from nasal scraping showed *Aspergillus flavus*. Patient was given insulin & itraconazole, local debridement was done. Patient responded to treatment and was discharged in good condition.

#### Case-5

A 55yr old male who was known case of T2DM, was admitted in our institute in 2011. He had history of trauma to face on left side. CT scan brain and face was done, which revealed fracture of whole left maxillary sinus, left ethmoid sinus & bilateral sphenoid sinus with left periorbital edema. His lab investigations showed high blood sugars and leucocytosis. Renal function and urine routine were normal. After some days, patient developed swelling over face which specially involved left side. Black area was present around left eye. Scraping was done, sent for KOH 10% mount. It showed fungal hyphae, which were non - septate. Culture grew Mucormycosis. He was put



Figure 4a: Mucosal thickening in sinuses



Figure 5: (a) Periorbital swelling and ptosis. (b) Reconstruction of face



on insulin infusion and injectable Amphotericin B. Later, extensive surgical debridement including enucleation of left eye ball and facial reconstruction of left side was done [Figure 5a and 5b]. Patient responded to treatment and was discharged after 6 weeks.

### Case-6

A 27yr old non-diabetic male was admitted in our institute in 2013 with chronic kidney disease (urea- 172.5mg% & creatinine- 8.5mg%), metabolic acidosis, septicemia and normocytic normochromic anaemia. He had noticed ptosis in right eye since one day [Figure 6a]. On examination, Ocular movements were restricted in right eye suggestive of involvement of 3<sup>rd</sup>, 4<sup>th</sup> and 6<sup>th</sup> cranial nerve and papilledema was present. Black discoloration was present over right nasal region. His right palate showed a white patch which later turned to black [Figure 6b]. MRI brain and orbit showed mucosal thickening in right maxillary and ethmoid sinus. Tissue was sent for culture and biopsy. Immediate 10% KOH mount was done, which came positive for fungal filaments [Figure 6c]. Culture report later confirmed Mucormycosis. Patient was put on haemodialysis. He did not give consent for debridement and further management. Unfortunately, the attendants took the patient home against medical advice [Table 1].

## DISCUSSION

All our patients had uncontrolled diabetes and/or acidic medium (metabolic acidosis in case six), who inhaled mucor or other fungi like aspergillus, rhinocladiella, developed sinusitis and which progressed to involve the orbital apex & vessels. This further continued to run its inexorable march, only to prove fatal in few of our patients despite our best efforts.

Mucormycosis is a serious fungal infection, which usually affects patients with immunocompromised state and



Figure 6a: Ptosis in right eye



Figure 6b: Black discoloration right side of nose and palate necrotic area

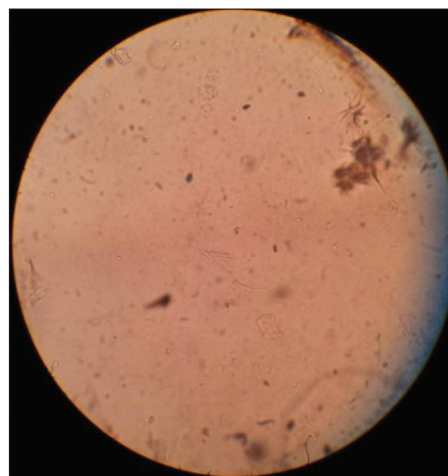


Figure 6c: Fungal hyphae in potassium hydroxide mount

Table 1: To summarize our experience

S. No.	Age	Gender	Risk factor	Fungus Isolated	Treatment given	Outcome
Case 1	56 yr	Male	Diabetes mellitus	Mucormycosis	I.V. insulin, Amphotericin B and surgical debridement	Fatal
Case 2	50 yr	Male	Diabetes mellitus	RHINOCLADIE LLA mackenziei	I.V. insulin, Amphotericin B and ATT	Fatal
Case 3	60yr	Male	Diabetes mellitus, corticosteroids	Mucormycosis	I.V. insulin and Amphotericin B	Blindness in left eye
Case 4	45yr	Female	Diabetes mellitus	Aspergillus flavus	I.V. insulin and Itraconazole	Patient improved
Case 5	60yr	Male	Diabetes mellitus	Mucormycosis	Surgical debridement, i.v insulin and i.v. amphotericin	Encucleation of left eye, hemifacial reconstruction. Improved
Case 6	27yr	MALE	Chronic Kiney disease and metabolic acidosis	Mucormycosis	Haemodialysis	LAMA

acidotic environment most suitable being Diabetic Ketoacidosis /Hyperglycaemic hyperosmolar state. When a patient in this type of setting fails to improve from Diabetic ketoacidosis/Hyperglycaemic hyperosmolar state within 48 hours, we should be vigilant to look for black discoloration of palate, nasal mucosa and ophthalmoplegia. Ptosis is a late sign and associated with grave prognosis. Most patient with diabetic ophthalmoplegia involving 3<sup>rd</sup> nerve, have pupillary sparing. Absence of pupillary sparing should alert us to look for serious pathology.

The three factors which influence outcome are reversal of underlying condition, aggressive surgical debridement and prolonged anti fungal therapy. In our experience, if patients are suspected and referred to maxillofacial surgeon early for extensive debridement, with good sugar control on insulin infusion and given injectable Amphotericin B for long, monitoring kidney function tests, the chances of survival improve. But most patients are picked up late, after development of ptosis and succumb despite best efforts.

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