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RHINO-CEREBRAL MUCORMYCOSIS: A CASE REPORT

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ABSTRACT Rhino-cerebral mucormycosis is a rare, invasive fungal infection caused by fungi of the order Mucorale and class of mucormycets. It is one of the diseases that remain poorly understood with high mortality rate. Presently, the triad of clinician's awareness prompt initiation of treatment and timely surgical intervention is the effective way of managing the disease. We report a case of 52 year old female with diabetes mellitus with history of fever, peri-orbital oedema, ptosis, opthalmoplegia and ulcers in hard palate. Patient was diagnosed to have Rhino-cerebral mucormycosis with cavernous sinus extension. She was treated with intravenous Amphotericin B, insulin, Functional endoscopic sinus surgery (FESS) and debridement. She was given intravenous antifungal therapy followed by oral antifungal. Patient showed significant improvement.

KEYWORDS : Rhino-cerebral mucormycosis, Diabetes mellitus, opthalmoplegia, Amphotericin B

INTRODUCTION:

Mucomycosis is a rare, invasive, life threatening fungal infection caused by fungi of the order Mucorale and class of mucormycets. It's ubiquitous in nature and abundant in our environment. It is highly concentrated near construction activities, decaying vegetables and organic material, soils etc. Mucorale's growth is favored in tropical countries as temperature and humidity supports sporulation. Inhalations of spores infect humans.[1,2] The sites of pre-dilection for this infection are the nose and para-nasal sinuses, it progresses to involve the orbit and at times in the intracranial structures such as the cavernous sinus and the cerebral hemispheres.[3] Rhino-orbito-cerebral mucomycosis mainly occurs in immuno-compromised patients. Poorly controlled diabetics, immune-suppression, hematological malignancy and iron over load are some of the conditions which predispose patients to the development of this disease.[4] The fungi are vaso-invasive and locally destructive but their main pathogenic mechanism is growth along the blood vessels, invasion of the lumen and formation of mycotic thrombi which are said to lead to mycotic emboli.[4,5] Within the orbit, the mucorea cause extensive invasion on the extra ocular muscles and may lead to ophthalmoplegia and can form progression in cavernous sinus.[7] We are report a case of rhino-cerebral mucomycosis.

CASE REPORT:

A 52 year female admitted with history of fever along with chills for last 7-8 days, swelling, weakness and numbness on right side of face for last 3-4 days. On examination patient was conscious oriented, afebrile, vitals were stable, no meningeal sign, ptosis of right eye, right side lid oedema, right eye external and internal opthalmoplegia (3^{rd},4^{th},6^{th} nerves) with vision of 6/6 (Table.1), right maxillary tenderness right LMN (lower motor neuron) facial palsy (Figure 1),and ulcers over hard palate (Figure 2).

Figure1: Right sided ptosis with periorbital edema and right sided facial palsy

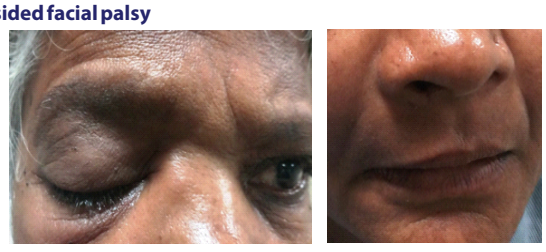


Figure 2: Ulcers and Perforation in the right anterior region of the hard palate

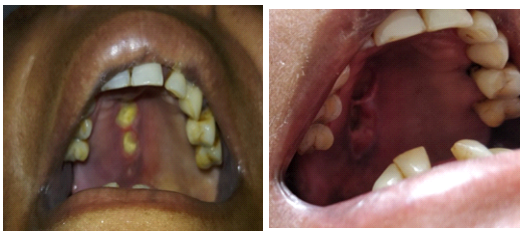


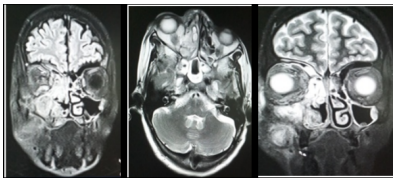
Table 1: Examination and comparison of right and left eye

	Right	Left
Tenderness	Absent	Absent
Eyelids	Ptosis Periorbital oedema: present Temperature : normal	Normal
Vision	Normal	Normal
Pupils	Fixed	Normal, reacting to light
Extra ocular movements	Total restriction in all direction	Full and free in all direction

Table 2: Patient laboratory reports

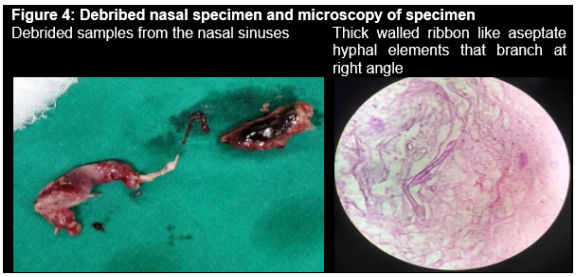
Random blood sugar	343 mg/dl,
Urine ketone bodies	Negative
Serum creatinine	0.9 mg/dl
Haemoglobin	10.4gm%
Total leukocyte count	23700/µl
Erythrocyte sedimentation rate	60 at the end of 1 hour
C- reactive protein titers	Positive

Figure 3: MRI Brain with PNS contrast: T2 weighted image shows hyperintense region in right maxillary sinus, ethmoidal sinus, sphenoid sinus with subtle erosions of bone extending to right nasal cavity, hard palate, floor of orbit, with right cavernous sinus invasion.

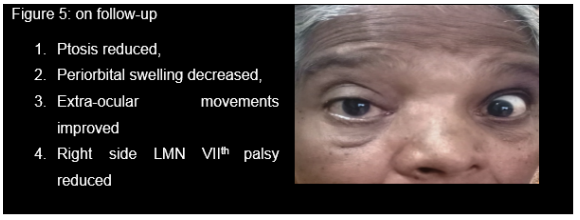


Based on history, clinical findings and investigations (Table 2) patient was diagnosed to be Rhino-cerebral mucormycosis with cavernous sinus extension. Patient was started on antibiotics, insulin, and Amphotericin B. Surgical intervention in the form of functional endoscopic sinus surgery (FESS) and debridement was done. Sample was sent for histopathology, KOH mount, fungal culture and antibiotic sensitivity. KOH mount was negative for fungal elements. Histopathology report revealed thick walled ribbon like aseptate hyphal elements that branch at right angle which confirmed the diagnosis of mucormycosis (Figure 4).

Figure 4: Debrided nasal specimen and microscopy of specimen



After surgical intervention (FESS) and medical therapy patient has showed significant improvement in cranial nerve palsies with decreased periorbiatal swelling. Patient was given Amphotericin B for 15 days. Patient was discharged on tablet Itraconazole. Healing plates for hard palate ulcers were given for further healing and support. On one month of follow-up improvement was seen with ptosis reduced, periorbital swelling decreased, extra-ocular movement improved and right side LMN (VIIth) palsy reduced (Figure 5).



DISCUSSION:

Rhino-cerebral mucormycosis is rare an opportunistic fungal infection caused by fungal spores which are ubiquitous in nature. In India, diabetic patient outnumbers other risk factors for getting mucormycosis. Many of the diabetic patients are unaware about diabetic status and presented with mucormycosis.[6]

Sites of mucormycosis lesion are rhino-orbital-cerebral mucormycosis involving paranasal sinuses, orbit with intracranial extension, pulmonary, cutaneous, gastrointestinal, disseminated and others like isolated renal in immune-competent host, brain abscess, endocarditis in IV drug users etc. High index of suspicion is required for the diagnosis of mucormycosis, mainly due to non-specific clinical features and culture which can be sterile in up to 50% of cases due to aseptate fungus being damaged during tissue handling in laboratory.[5,6]

The infection usually results from entry through nose and spreading to para-nasal sinuses.[8,9]

The infection can be divided into 3 stages:

Stage 1: It occurs after inhaled spores infect the para-nasal sinus. Necrotic lesion usually appears on nasal mucosa, turbinate and hard palate. It causes nasal discharge and nasal blockade and progressive formation of necrotic eschar on the mucosa of the nose, most frequently on the middle and inferior turbinate. Epistaxis can be a sign in this stage.

Stage 2: Orbito-facial infection occurs by either direct extension through nose and maxillary sinus or through the blood vessels. Signs and symptoms can be facial pain, facial anesthesia, prostosis, orbital edema and facial cellulitis and complete opthalmoplegia.

Stage 3: Infections spreads intracranially via the cribriform plate or orbital apex. By the time orbital involvement becomes manifest 80% of the patients already have meningieal involvement. Intracranial extension can cause meningitis, cerebritis, infarction, abscess formation, cavernous vein thrombosis and internal carotid thrombosis. Neurological manifestations are usually nonspecific but focal sign of cavernous sinus or internal carotid artery thrombus may be present.[10,11]

The definitive laboratory diagnosis of rhino-cerebral mucormycosis requires tissue diagnosis. The classical histological appearance is large, broad, non-sepate hyphae with right angle branching and distinct vascular invasion.

Treatment principles include:

1. Early diagnosis.
2. Reversal or control of precipitating cause like correction of diabetic ketoacidosis, minimization of immunosuppressions if possible etc.
3. Antifungal therapy: Amphotericin B, Posaconazole, Isavuconazole
4. surgical debridement/ excision of lesion
5. Adjuvant therapy: Hyperbaric oxygen, Deferasirox, Caspofungin statins.[9]

At present, antifungal therapy and aggressive surgical intervention are used to treat mucormycosis. Based on retrospective clinical studies, amphotericin B is currently used as the first-line antifungal agent. Several case reports have documented that patients with rhino-cerebral mucormycosis were successfully treated by amphotericin B.[10,11] Unfortunately, despite antifungal therapy and disfiguring surgical debridement, the overall mortality of mucormycosis patients remains high and approaches 40% in diabetic patients with rhino-cerebral mucormycosis.[2]

In present case mucormycosis being one of the first differential diagnoses. Patient was diagnosed early with clinical presentation and investigation. Amphotericin B along with surgical debridement (FESS) was done early. Histopathology report relived the diagnosis of mucormycosis. Improvement was seen 10 days of Amphotericin B therapy along with surgery. Inj. Amphotericin B was given for 15 days followed by tab. Itraconazole on discharge. Patient blood sugar levels were well controlled. Patient improved significantly on follow-up. The supportive healing plates were advised for ulcers. A similar case series was reported by Rasoul Mohammadi et al in 2015, all 3 cases had hyperglycemic state, were diagnosed as rhino-cerebral mucormycosis. All patients were treated similarly with antifungal therapy and surgical debridement.[12] Similarly Ya-Chun Hsiao et al in 2002 reported a case of 64 year female patient with type 2 Diabetes mellitus with ketoacidosis diagnosed as rhino-cerebral mucormycosis and was treated with antifungal therapy and surgical debridement.[13]

CONCLUSIONS:

Mucormycosis has been reported from various parts of the world. Rhino-cerebral mucormycosis although a rare entity, should be kept in mind when handling cases with orbital cellulites, cavernous sinus thrombosis and invasive sinusitis, especially in patients with immunocompramised state including diabetes mellitus. Early diagnosis, surgical excision, appropriate debridement, suitable antifungal therapy, and treating the underlying co-morbidity will result in better outcome of the disease and better survival rate.

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