CASE REPORTS

Rhino Cerebral Mucormycosis – A Case Report

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Summary

A 42-year-old man who was on long term steroid therapy for bone marrow failure developed left orbital swelling and blindness along with prolonged fever. Neurological examination revealed proptosis of the left eyeball with complete ptosis and periorbital edema. There was ulceration of both lips with crust formation. There was total ophthalmoplegia with dilated pupil on left side. There was impairment of sensation over the distribution of trigeminal nerve. Fundoscopy showed papilloedema on the left side. Left sided orbital debridement and exenteration was done. The pathological diagnosis was mucormycosis. Systemic administration of amphotericin B was started immediately. On 25th day of starting therapy the patient suddenly started to deteriorate and died on the next day possibly due to rapid extension of the disease. Rhino cerebral mucormycosis is a rapidly progressive fatal disease. Successful treatment seems to be based on early diagnosis, control of underlying disease, radical surgical resection, and systemic administration of amphotericin B. Mucormycosis should be considered as differential diagnosis of orbital cellulitis or orbital apex syndrome.

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Introduction:

Mucormycosis (Zygomycoosis) is an opportunistic fungal infection caused by filamentous fungus of the order mucorale,[1-2] the rhino-cerebral being the commonest one. The site of onset is the nasal mucosa and the disease extends rapidly to the palate, orbit and brain. Risk factors for mucormycosis include hematological malignancy, namely leukemia and lymphoma, diabetes mellitus especially those with ketoacidosis[2]. The use of steroids and immunosuppressive agents in bone marrow and solid organ transplantation[3], broad-spectrum antibiotics and cytotoxic chemotherapy, and dialysis for uraemic patients, particularly with desferrioxamine therapy, are also known predisposing causes[1,4-5]. Thus, the infection is often an indication of a serious predisposing condition. Malnutrition in children in developing countries also carries a risk of mucormycosis with gastrointestinal involvement, and cerebral mucormycosis has been reported in intravenous drug user via the hematogenous route[5]. Mucormycosis has very high mortality rate of at least 50%[6]. Pulmonary and gastrointestinal disease has an even higher mortality rate due to late diagnosis. Lethal mucormycosis has been described in an otherwise healthy man[7-9]. Here, a case of rhino-cerebral mucormycosis in a patient on steroid therapy for bone marrow failure is presented. Possibly this is the second case reported from Bangladesh[10].

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Case Report:

A 42 year old machine man of a daily newspaper weighing 60 kg presented with progressively increasing fever, anorexia and weakness for 15 days. He was treated with a 10 days course of ciprofloxacin along with antipyretics without any response. When he was hospitalized he was found moderately anaemic. There was no lympadenopathy. Liver and spleen were not palpable. Systemic examination revealed no abnormal findings. Laboratory examinations revealed: Hemoglobin 8 gm/dl, ESR 135 mm in first hour, WBC count 1000/cumm, with neutrophil 26% and lymphocyte 68%, platelet count 60000/cumm, and peripheral blood film showing pancytopenia. He was not diabetic and fasting and post prandial blood sugar were 5.6 and 7.9 mmol/l respectively. His liver and kidney function tests were within normal limits. Urine analysis revealed no abnormality and blood culture revealed no growth. Bone marrow study revealed dry tab. Later on trephine biopsy of bone marrow showed evidences of progressive marrow failure. He was started Inj. Dexamethasone 2mg IV six hourly along with Inj. Ceftriaxone and Inj. Gentamicin. Five units of blood were transfused.

After two weeks when the patient was transferred to Bangabandhu Sheikh Mujib Medical University Hospital he was still febrile but complaining of discharge from nose that was initially clear but later becoming blackish. Subsequently, he started to feel mild pain in left eye with dimness of vision. Very shortly he developed swelling of left orbit and completely lost his vision. He was also complaining of loss of sensation over left side of face. He didn't loose consciousness. He was found mildly anaemic, febrile (temperature 39^0C), non-icteric and there was no significant lymphadenopathy. His thyroid and testes were normal.

There was proptosis of the left eyeball with complete ptosis and periorbital edema (Figure-I). Both the lips were ulcerated with crust formation. There was complete ophthalmoplegia with dilated pupil on the left side. There was impairment of sensation over the distribution of trigeminal nerve. Fundoscopy showed dilated fixed pupil, diffuse retinal edema, and multiple hemorrhagic spots in the fundus associated with papilloedema on the left side. The patient was fully conscious and well oriented. Examination of nose and nasopharynx under general anesthesia revealed red and necrotic turbinate with extensive crusting over the left nasal cavity. There was no evidence of nasopharyngeal carcinoma. After removal of the crust, tissue under the crust was taken for histopathological and mycological study. MRI of the brain showed left-sided proptosis with ethmoidal sinusitis. CT scan of nose and paranasal sinuses showed evidence of inflammatory lesions involving left retro-orbit, left side of the face, and left maxillary, ethmoidal and cavernous sinus. During this period of illness he was on steroid in various doses and routes; and he was taking prednisolone 30 mg daily when he was hospitalized. After admission in the hospital his hematological profile was as follows: WBC count 12,000/cu mm with neurtrophil 90% and lymphocyte 08%, hemoglobin 13 gm/dl, ESR in first hour 05 mm, platelet count 200 x 10^9/l, peripheral blood film showing neutrophilic leuocytosis. Isotope bone scan was normal. Fasting and postprandial blood sugar, liver function and renal function tests were within normal limits. Histopathology of tissue obtained from nasal mucosa showed fungi with broad aseptate hyphae, branching at right angles and forming terminal spore (Fig.-2). These were also present within blood vessels (Fig.-3). Culture of the tissue in Sabourd's Agar (SDA) media yielded growth of mucor on the frothy day which was further confirmed under microscope (Figure 4). Injection Amphotericin B 100 mg mixed with 500ml of dextrose in aqua per day was started. A team of otolaryngologist, ophthalmologist and neurosurgeon did surgical exploration. All the sinuses were cleared of the crusts. Left-sided orbital debridement and exenteration was done and ethmoidal sinus was also removed (Figure 5). The tissue obtained also showed the presence of the fungi, characteristics of mucor both on culture and histologically. After starting the antifungal therapy the patient was improving well. He started to feel sensation in the left side of face. The drug showed no side effects. His blood count, renal and hepatic functions were also

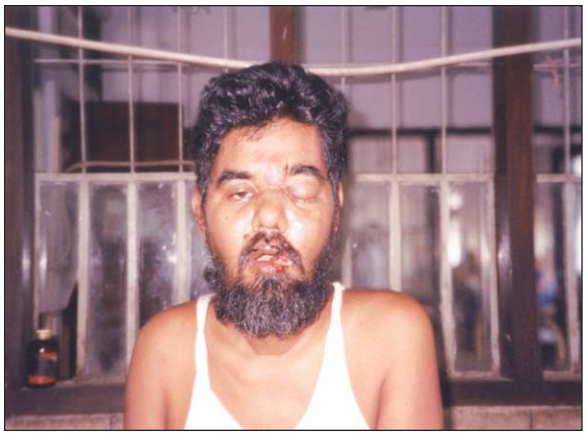

Fig.-1 : *Clinical view of the patient's face*

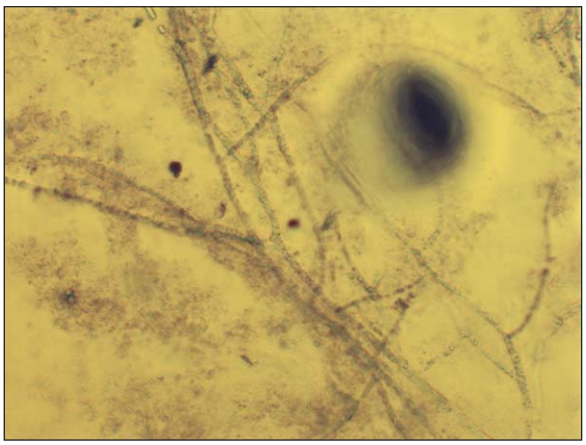

Fig.-2 : *Nasal tissue stained with lactophenol blue showing aseptate ribbon like branching hypae many are at right angle.*

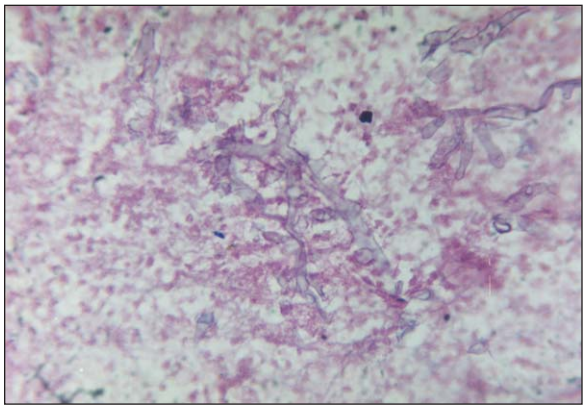

Fig.-3 : *Hypae invading the blood vessel*

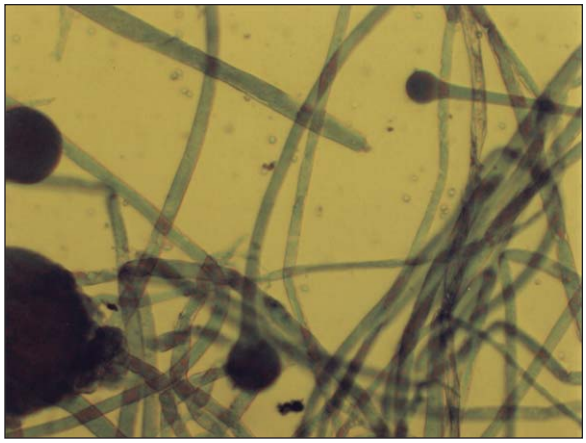

Fig.-4 : *Growth of mucor in Sabourd's Agar Media and stained in lactophenol blue.*

Fig.-5 : *Necrotic tissue material after debridement.*

within normal limits. On the 25th day of starting Amphotericin the patient started to deteriorate with acute respiratory distress. At that time his ECG, serum CPK, serum electrolytes were within normal limits. Emergency chest X-ray PA view showed patchy infiltrate on both lung fields. Arterial blood gas analysis showed mild hypoaxemia with normal carbon-dioxide. Parenteral Ceftriaxone 2 gm was given. On the following day the patient expired.

Discussion:

Mucormycosis has growing importance because of the increasing population of immunocompromised patients. Due to the high mortality and morbidity rates of the fungal infection in this group of patients, a high index of suspicion is warranted in the relevant clinical situation. Early diagnosis by an aggressive investigative approach to obtain tissue biopsy and early surgical intervention, combined with systemic antifungal therapy will optimize the treatment outcome[11]. Correction of the underlying risk factors is essential to achieve a cure. This patient suffered from rhino-cerebral mucormycosis, commonly referred as mucormycosis, the infection spreading from the left maxillary and ethmoidal sinus to the left orbit. The term rhino-cerebral indicate sinus involvement but does not always means that central nervous system involvement has occurred[12]. The immunodeficiency caused by prolonged steroid therapy on the setting of progressive marrow failure favored the growth of such opportunistic fungus in this case. Mucormycosis can present either as craniofacial mucormycosis which manifest as low grade fever later turning to high grade, dull sinus pain, nasal congestion with thin bloody nasal discharge, and unilateral generalized reduction of ocular motion, chemosis and proptosis. Invasion of globe and ophthalmic artery may lead to blindness. Haematogenous spread may occur to brain or lung or other organs. It may affect the gastrointestinal system causing multiple ulcers, which may perforate. This opportunistic mucor commonly attack patients suffering from severely debilitating disease like uncontrolled diabetes mellitus, patient with organ transplantation taking immunosuppressive drug, hematological malignancy, steroid therapy, uraemia, or receiving long term desferrioxamine therapy. Its presentation can be confused with those of sinusitis, carotid or cavernous sinus thrombosis or even viral infection and is often missed at early presentation[13-14].

Classical predisposing factors, typical clinical pictures and isolation of the specific mucor fungus

from the smear and histopathological section of the tissue are sufficient for diagnosis of the case. If any patient presents with the above features at the background of immunosuppression, as in this case, mucormycosis should be suspected strongly. Amphotericin B is the most reliable antifungal agent that is effective against mucormycosis. The usual recommended dose is 1 mg/kg/day, but a higher dose of 1.5 mg/kg/day was used for the reported case because of the serious infection[15]. The duration of treatment is three to six weeks. But the patient died on the 25th day of starting therapy, even after withdrawal of steroid much earlier, surgical debridement and good hematological condition.

Mucormycosis has a very high mortality rate. There is no report of survivors of mucormycosis before the availability of Amphotericin B in 1950s. Mortality rate among the patients with invasive sinus disease without cerebral involvement may be as high as 50-80%. If infection spreads to the brain case fatality rate may exceed 80%[12]. Deaths in this case in spite of early diagnosis and institution of Amphotericine B in higher doses might be due to extension of the disease due to inadequate debridement. Ferry et al described 11 deaths out of 16 after treatment with surgical debridement along with intravenous Amphotericin B[16].

So, a high index of suspicion is needed, in appropriate clinical settings, to diagnose and aggressively treat mucormycosis in view of the high mortality rate for susceptible patients.

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