CASE REPORTS

STEROID INDUCED RHINOCEREBRAL MUCORMYCOSIS: REPORT OF A CASE

M.Huntürk ATİLLA, M.D., Fikret İLERİ, M.D., Ahmet KÖYBAŞIOĞLU, M.D., S.Sabri USLU, M.D., Leyla MEMİŞ*, M.D., M.Birol UĞUR, M.D., Erdoğan İNAL, M.D.

Gazi University, Faculty of Medicine, Departments of Otorhinoloryngology and Patology*, Ankara-Turkey

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SUMMARY: *Rhinocerebral mucormycosis is a potentially fatal fungal disease which may involve the nose, paranasal sinuses, orbit and central nervous system. Mucormycosis is most commonly seen in association with immunosuppression, diabetic acidosis, deferoxamine, steroid and cytotoxic therapy, severe burns, AIDS, renal disease, malignancy or haematalogical disorders. Current treatment consists of correction of the underlying disorder, aggressive debridment of the wound, in combination with intravenous amphotericin B.*

Key Words: *Rhinocerebral, Mucormycosis, Steroid.*

INTRODUCTION

Mucormycosis is an acute, often fatal, opportunistic infection caused by Mucoraceae family that includes Rhizopus, Mucor or Absidia species. These fungi can be isolated from the soil, dust, bread mold and are important in the decaying of organic material (1, 2). These organisms can lead to serious infections usually in patients with a predisposing factor. Immunocompromise, diabetes mellitus, hematologic malignancies, severe burns, renal disease, AIDS, deferoxamine, iatrogenic immune suppression after organ transplantation and chemotherapeutic agents are factors that can alter patients' general resistance and predispose to mucor (1, 3). Rhinocerebral mucormycosis originate in the nose and paranasal sinuses with regional spread to the orbit. Initially there is facial pain, fever, bloody nasal discharge, facial swelling and oedema. The disease progresses dramatically with facial cellulitis, gangrenous mucosal changes in the nose and paranasal sinuses, cranial nerve palsies, vision loss and proptosis. A rapid course can sometimes lead to intracranial extension and death (2, 4).

CASE REPORT

A 65-year-old female patient was diagnosed as chronic pruritus and lichen planus in another center and was treated with oral methyl prednisolone 60 mg per day in tapering doses for 20 days. At the end of the treatment, symptoms consisting of fever, swelling of the right eye, right sided nasal obstruction and nasal discharge manifested. The condition was diagnosed as orbital cellulitis and a treated with administration of Imipenem 500 mg per six hours for a week. The signs and symptoms worsened progressively despite treatment, and an ulcer on the hard palate on the right side with necrotic margins was observed on physical examination. Stupor and

loss of consciousness progressed to right hemiparesis and facial nerve paresis, and the patient was referred to our hospital for further evaluation. At the time of admission, she had grade III coma on the Glasgow scale, high fever and signs of sepsis. Physical examination revealed right-sided periorbital oedema and ecchymosis. Nasal examination showed presence of mucopurulent discharge. On oral examination, the ulcer on the hard palate was 4 x 4 cm in size with necrotic margins. The ulcers were covered with dead tissue and did not bleed on touch. Ophthalmic examination revealed proptosis, orbital cellulitis with ophthalmoplegia. Visual evaluation demonstrated total loss of vision in the right eye, with the absence of corneal reflex. A paranasal computerized tomography showed the presence of soft tissue density obliterating bilateral maxillary and ethmoid sinuses, bone destruction in the medial and lateral walls of maxillary sinus and ethmoid sinuses (Fig. 1A), orbital cellulitis and radioopaque densities in the retroorbital tissues (Fig. 1B). Magnetic Resonance İmaging-Angiography revealed no abnormalities.

Diagnosis was established by a biopsy of the palatal ulcer; histopathology revealed features compatible with mucormycosis.

Routine blood tests showed haemoglobin of 11.5 g/dl, white blood cell 9.400, count had a profile of polymorphs 61.8%, lymphocytes 30.5%, eosinophils 2%. Erythrocyte sedimentation rate was 29 mm/first hour, the fasting blood sugar was 100 mg/dl and the postprandial blood sugar was 135 mg/dl. Venereal disease research laboratory and human immunodeficiency virus tests were negative whereas hepatitis C virus antibody was found to be positive. IgG levels and T cell counts were found to be within the normal range. A chest X-ray did not demonstrate any abnormalities.

The initial treatment consisted of an early wide surgical resection of the affected tissues. This involved right medial maxillectomy, bilateral total sphenoethmoidectomy, resection of the right side of the hard plate, septum and orbital exenteration. After surgery, intravenous amphotericine B 50 mg per day was administered for three weeks. The patient's renal and liver functions were monitored periodically. On histopathologic examination, there were extensive areas of necrosis, hyalinized areas with the foci of fungal hyphea, microabscess formation and granulamatous reaction (Fig. 2A). The fungus was broad and rarely septate hyphea; the hyphea branched irregularly which was demonstrated better by hemotoxylin and eosin (HE) staining (Fig. 2B). These fungal hyphae invaded the blood vessels. There was also mycotic infiltration of the perivascular tissue. The diagnosis of rhinocerebral mucormycosis was made on the basis of appearance of hyphae.

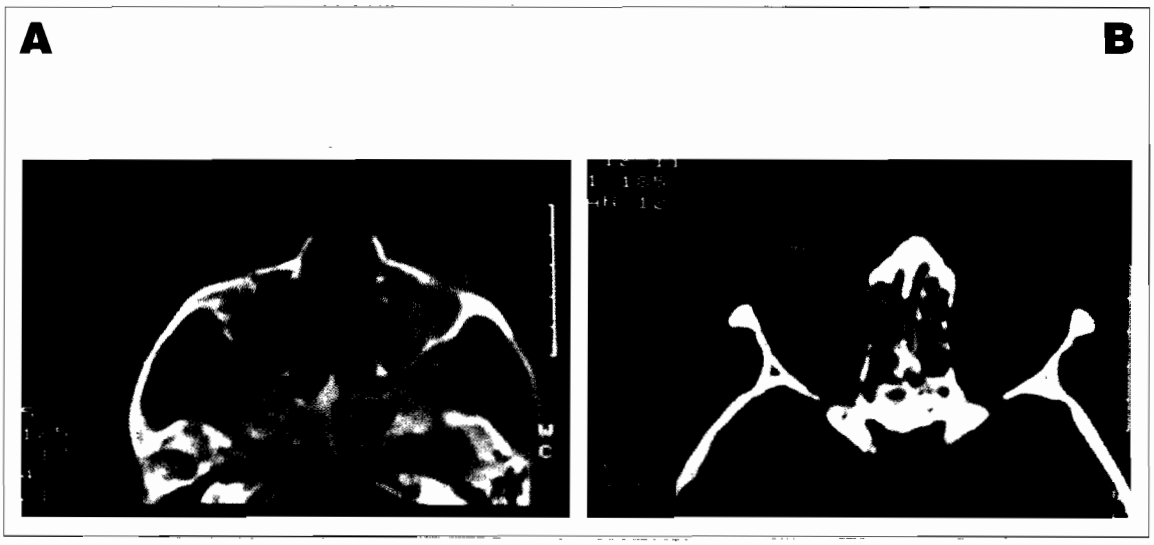

Fig. 1: Paranasal computerized tomography showing soft tissue density obliterating bilateral maxillary and ethmoid sinuses with bone destruction in the medial and lateral walls of maxillary sinus and ethmoid sinuses (A). Paranasal computerized tomography showing evidence of orbital cellulitis in the retroorbital tissues (B).

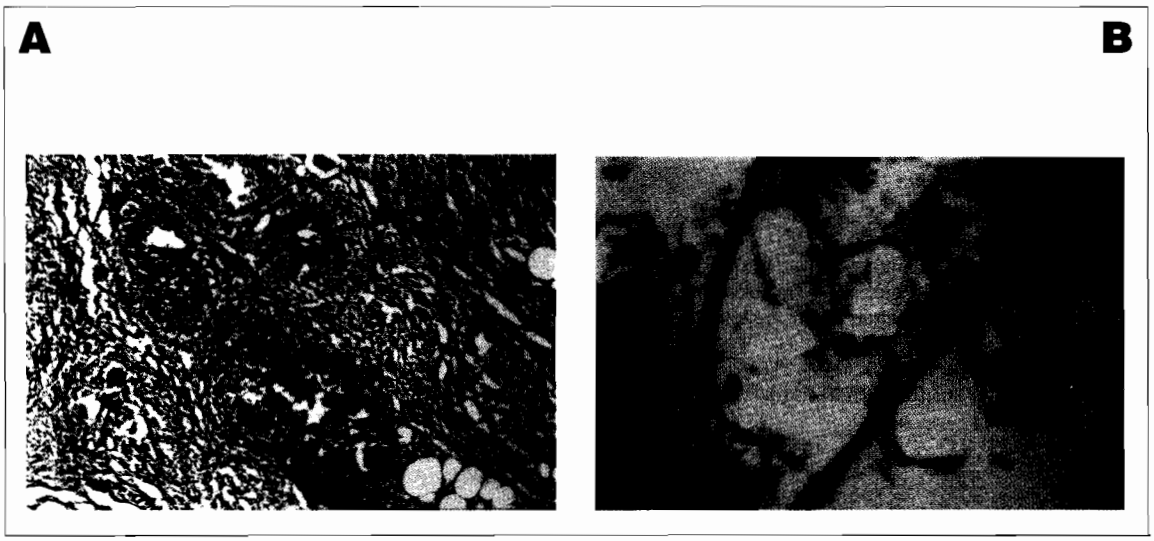

Fig. 2: Multiple granulomatous lesions with giant cells of the foreign body or Langhan's type and mixed inflammatory infiltration in periorbital soft tissues due to mucormycosis. HE x 200 (A). Mucormycosis: Hyphae irregulary branched in bone morrow.HE x 400 (B).

During the follow up period the condition of the patient worsened, fever and later signs of sepsis developed. The patient died in the second month of the follow up period.

DISCUSSION

Mucormycosis, an opportunistic infection caused by an organism of Mucoraceae family, has an acute, often fatal course. One of its forms, rhinocerebral mucormycosis, remains an aggressive disease with a very high mortality rate (1).

Serious underlying predisposing factors such as immunocompromise, poorly developed diabetes mellitus, hematological malignancies, anemia, malnutrition, severe burns, renal disease, AIDS, deferoxamine, iatrogenic immune suppression after organ transplantation and chemotherapeutic agents should be given high priority in management of this condition (1, 2, 5, 8). In our case, there was no diabetic or systemic immune problems, but prolonged systemic corticosteroid therapy for the treatment of chronic pruritis and lichen planus was the predisposing factor.

Treatment consists of correction of the underlying disorder and repeated surgical debridment of the wound in combination with intravenous amphotericin B. The treatment should include local wound care after surgery. Surgery should involve wide local excision and debridement of all devitalized oral, nasal, sinus and orbital tissues (1, 2, 5). Blitzer et al (4), after reviewing of 179 cases, concluded that orbital exenteration may be required if signs of retinal artery thrombosis, orbital apex necrosis or ocular invasion occur. In our case ocular invasion was marked and was demonstrated on the computerized tomography. The disease invaded the ethmoid, sphenoid sinuses, left maxillary sinus and the septum. During the surgical procedure, all the involved structures were excised.

The disease has a rapidly spreading character which progresses from the nose to the paranasal sinuses and the orbit. In a series by Peterson et al, factors that appear to be associated with poor outcome include *1.* immunosuppressive therapy, especially with organ transplantation *2.*orbital involvement *3.* diabetes with diabetic ketoacidosis *4.*significant underlying medical disease *5.*medical management alone. In diabetic patients there is a lower mortality rate than in immunosuppressed patients including steroid induced ones. The long term survival rates range from 66%6 to 85 %7 in the literature. In our case previous use of steroids, late referral to our department with extensive involvement especially into the orbit were probably the main factors leading to the fatal outcome. Early definitive diagnosis and effective treatment is of utmost importance for these patients because of

the rapidly progressive nature of the disease.

Correspondence to: M.Huntürk ATİLLA, M.D.
Gazi Üniversitesi Tıp Fakültesi
Kulak Burun Boğaz Anabilim Dalı
Beşevler
06500 ANKARA - TÜRKİYE
Phone : 312 - 214 11 00 / 6425

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