Kulak Burun Bogaz Ihtis Derg
2005;15(1-2):40-44

CASE REPORT

Rhinocerebral mucormycosis: a report of two cases

Rinoserebral mukormikozis: İki olgu sunumu

İbrahim ERCAN, M.D.,[1] Burak Ömür ÇAKIR, M.D.,[1] Şenol CİVELEK, M.D.,[2] Suat TURGUT, M.D.[1]

Rhinocerebral mucormycosis is an aggressive fungal disease that involves the nose, paranasal sinuses, orbit and central nervous system. It may rapidly be fatal. This infection usually occurs secondary to immune suppression, diabetic ketoacidosis, and prolonged use of antibiotics, steroids, and cytotoxic drugs. Management of the condition consists of treatment of underlying disease and surgical debridement combined with intravenous amphotericin B. This paper presents two patients with rhinocerebral mucormycosis, both suffering from diabetes. Complete recovery was achieved in one patient with surgical debridement of necrotic tissue combined with systemic antifungal treatment, whereas in the other, the disease was complicated with subarachnoid hemorrhage and the patient died on the third day of treatment.

Key Words: Amphotericin B/therapeutic use; debridement; dermatomycoses/complications/therapy; diabetes complications; facial dermatoses; mucormycosis/pathology/therapy.

Rinoserebral mukormikozis burnu, paranazal sinüsleri, orbitayı ve merkezi sinir sistemini tutan agresif seyirli fungal bir hastalıktır ve çok kısa sürede hızla ölümcül olabilir. Bu enfeksiyon genellikle bağışıklık sisteminin baskılanmasına, diyabetik ketoasidoza ve uzun süreli antibiyotik, steroid ve sitotoksik ilaç kullanımına bağlı olarak gelişir. Esas tedavi, altta yatan hastalığın tedavisi ve cerrahi debridman ile birlikte intravenöz amfoterisin B kullanımından oluşur. Bu yazıda diyabetli iki hastada görülen rinoserebral mukormikozis sunuldu. Bir olguda, nekrotik dokuların cerrahi debridmanı ve sistemik antifungal tedavi ile tam iyileşme elde edildi. Diğer olgu ise, hastalığın subaraknoid kanama ile kötüleşmesi sonucu tedavinin üçüncü gününde yaşamını yitirdi.

Anahtar Sözcükler: Amfoterisin B/terapötik kullanım; debridman; dermatomikozis/komplikasyon/tedavi; diyabet komplikasyonları; yüz dermatozu; mukormikozis/patoloji/tedavi.

Mucormycosis is an acute, opportunistic infection. The agent belonging to class Zygomycetes (Phycomycetes) order Mucorales is a saprophytic fungus found in soil, bread mold and, rotten fruits and vegetables.[1] It can be cultured from the mouth, nasal airway and feces of the healthy individuals.[2]

Many predisposing factors have been reported. However, the most frequent one is the diabetes mellitus. The others are namely leukemia, lymphoma, AIDS, chemotherapy, severe burns, malnutrition and chronic renal failure. Impaired neutrophil function, neuropathies, and vascular insufficiency are

◆ *Departments of [1]Otolaryngology and [2]Pathology, Şişli Etfal Training Hospital (Şişli Etfal Eğitim ve Araştırma Hastanesi [1]KBB ve Baş-Boyun Cerrahisi Kliniği, [2]Patoloji Kliniği), İstanbul, Turkey.*

◆ *Received - December 30, 2003 (Dergiye geliş tarihi - 30 Aralık 2003). Request for revision - June 25, 2004 (Düzeltme isteği - 25 Haziran 2004). Accepted for publication - September 1, 2004 (Yayın için kabul tarihi - 1 Eylül 2004).*

◆ *Correspondence (İletişim adresi): Dr. Burak Çakır. Hızırbey Cad., Küme Sok., No: 5/13, 34732 Göztepe, İstanbul, Turkey. Tel: +90 212 - 231 22 09 / 1132-1134 Fax (Faks): +90 212 - 240 29 91 e-mail (e-posta): burak_cakir@hotmail.com*

* *Presented in the 2nd International Allergy Congress, October 4-8, 2000, Çeşme, İzmir, Turkey (2. Uluslararası Alerji Kongresi'nde sunulmuştur, 4-8 Ekim 2000, Çeşme, İzmir).*

known responsible for the tendency in diabetics. In ketoacidosis, acidic environment due to increased glucose and free iron levels enhance the fungal growth. On the other hand, mucormycosis can be seen in controlled diabetics, polytraumatized persons, and healthy subjects.[3]

The disease, which shows invasion along the elastic lamina of the blood vessels and consequent thrombosis and tissue necrosis, has many systemic manifestations. Rhinoorbital and rhinocerebral forms are most severe. Ones rhinocerebral form of mucormycosis distributes headache, rhinorrhea, and black-necrotic intra nasal and intra oral mass formations. Progression may lead to orbital cellulitis, orbital apex syndrome, cavernous sinus syndrome, and central nervous system involvement. Extension to the central nervous system may lead to death.

Diagnosis is based on histopathologic study. Presence of invasion and subsequent tissue reaction is worthy for diagnosis rather than the mere presence of this ubiquitous organism. Culture is used to identify specific species.[4] Presence of fungus may be showed by PAS or methenamine silver staining.[2] Radiographic findings are sinus opacification without liquid level, nodular thickening on sinus wall and focal bone erosion. In early stage the diseases may mimic innocent sinusitis and care must be taken on the diabetic or immune compromised patients suffering from sinusitis.

Mucormycosis may be confused with malignancy because of extensive necrosis. Pyogenic orbital cellulitis, syphilis, tuberculosis, lethal midline granuloma, Wegener granulomatosis, aspergillosis, and other systemic mycoses have been considered in differential diagnosis.[2] Early diagnosis of the underlying disease as soon as possible, intravenous Amphotericin B as an antifungal therapy, and surgical debridement of necrotic tissue are essentials for the effective treatment of mucormycosis. Surgical debridement may prevents extension of the disease to central nervous system. Moreover, debridement increases the survival rates up to 50%. Importance of potassium iodide and hyperbaric oxygen in the treatment have been emphasized.[2] The reported survival rates of mucormycosis in literature are between 21% and 70%. Highest mortality rate has been seen on non-diabetic patients. Overall survivals for all forms of mucor have ranged from 6% to 73%.[4] Since the oral signs are seen as the first clinical manifestations of the disease it must alert otorhinolaryngologists for early diagnosis.

CASE REPORT

Case 1 – A 71-year-old diabetic female presented with swelling of the left side of the face and left periorbital region (Fig. 1). Hyperemia of the left periorbital region, desquamation of the cheek, loss of vision of the left eye and purulent drainage to the month for 20 days were major complaints. Additionally, she had left sided facial paralysis. Otorhinolaryngological examination revealed edema and hyperemia on the skin of left maxillary region including the left periorbital region. A dark colored crust of two-centimeter in diameter was noticed in the center of this lesion. In addition to left sided facial paralysis, the third, fourth, ophthalmic branch of fifth and sixth cranial nerves were also paralyzed. On ophthalmologic examination left vision loss accomparised with total ophthalmoplegia was detected. Asymmetric expansion in cavernous sinus on coronal sectional T1 weighted MR imaging was noticed (Fig. 2). Insulin treatment was started when blood glucose level was found as 436 mg/dl. Following regulation of blood glucose level total FESS was performed. In operation, increased pus drainage was observed in left middle meatus by pressing the globe. Necrotic soft tissue and bone was removed from left middle meatus and ethmoid sinuses. The diagnosis of mucormycosis was estab-

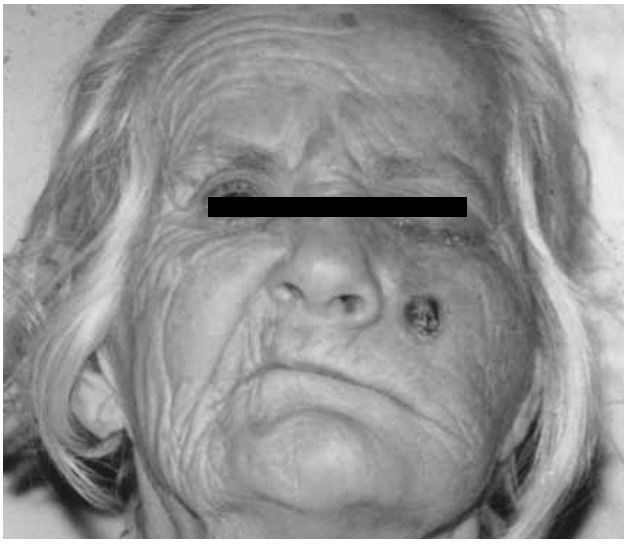

Fig. 1 – *Preoperative appearance of the Case 1.*

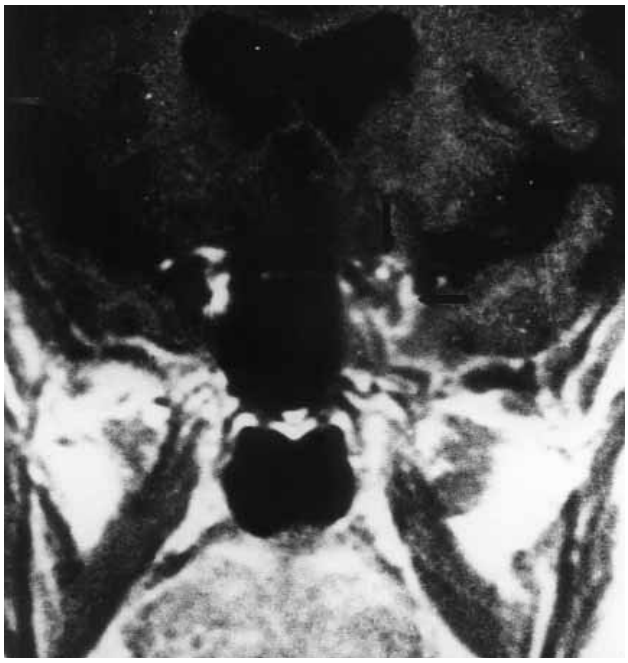

Fig. 2 – *Asymmetric expansion in cavernous sinus (arrows) in coronal sectional T1 weighted MR (Case 1).*

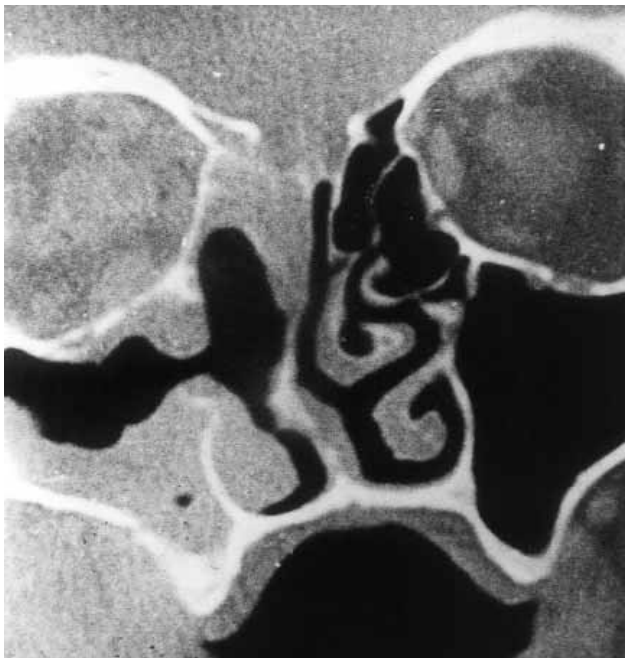

Fig. 3 – *Nodular thickening in soft tissue density in maxillary sinus in coronal CT with contrast agent (Case 1).*

lished by staining of surgical specimen with Periodic Acid-Schift (PAS). A histopathological sections showed extensive areas of necrosis and broad, unseptate or barely septate hyphae, which are typical features of mucormycosis. Liposomal Amphotericin B with the dosage of 1mg/kg was started intravenously. On coronal enhanced control CT, nodular thickening in soft tissue density in maxillary sinus was detected (Fig. 3). Because there is no improvement in the symptoms of the left cheek and orbital such as loss of visual perception on the 26th day of admission a 2nd surgery was performed. In this second operation periorbital and retroorbital purulent material were exposed and drained by orbital exenteration. In histopathological examination Mucor spores and hyphae stained with PAS were noticed in peripheric nerve section (Fig. 4). Amphotericin B treatment was stopped on 58th day of treatment and patient was discharged with complete recovery of inflammatory symptoms. 1-year follow up shows the patient is still doing well.

Case 2 – A 48-year-old male administered to the hospital with complaints of left sided facial pain that has started after a tooth removal 2 months before, and swelling of left periorbital region with loss of vision for 15 days. He was a diabetic patient for 22 years and had chronic renal failure requiring hemodialysis for 1 year. Based on anterior rhinoscopic and endoscopic nasal examination, mucosal edema, purulent discharge and secretion in both nasal cavities were noticed. Physical examina-

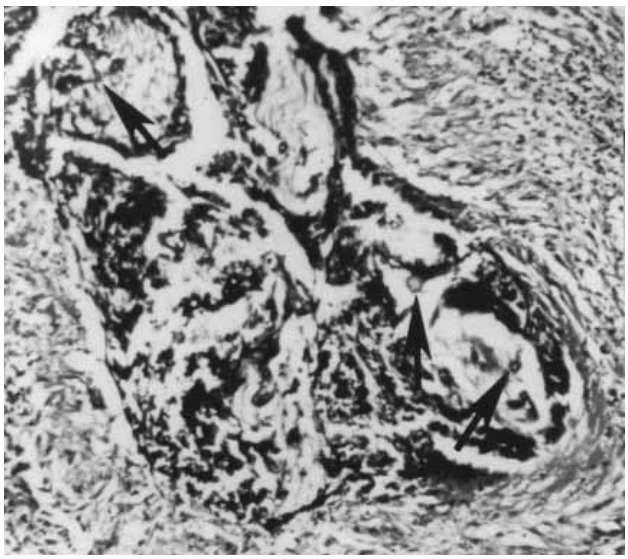

Fig. 4 – *Mucor spor (indicated by arrows) and hyphae stained with PAS were seen in peripheric nerve section (Case 1) (PAS x 100).*

tion revealed left sided facial swelling, hyperemia and edema in periorbital region. Total ophtalmoplegia was detected in left blind eye. Laboratory values included blood glucose level, 530 mg/dl; BUN, 73 mg/dl; creatinin, 2.6 mg/dl; hemoglobin, 6.8 g/dl; white blood cells, 12600/ml. Paranasal inflammation involving optic nerve and retrobulber region was seen on cranial and orbital computed tomography (Fig. 5) and magnetic resonance imaging scans. There was no growth in culture of material which taken from the left middle meatus in Saboroud media. Diagnosis of mucormycosis was confirmed by histochemical study in biopsy material with PAS staining, showing characteristic feature of branching non-septate or rarely septate hyphae. Amphoteracin B (1mg/kg) administration began intravenously as the first step treatment. Unfortunately, the patient died of subarachnoid hemorrhage on the third day of treatment.

DISCUSSION

Cerebral mucormycosis is first described by Platauf[15] in French medical literature in 1885. However Gregory et al.[6] was the first one who mentioned about cerebral mucormycosis in English medical literature in 1943. Rhinocerebral mucormycosis described by Baker in 1957 is a different type of invasive sinusitis.[7] Yohai et al.[8] had reviewed 208 patients in literature since 1970. They observed that fever (44%), nasal secretion /black necrotic tissue in the nose (38%) periorbital or facial edema (34%), visual changes (30%), headache (25%), and facial pain (22%) were typical symptoms of the disease. In our two cases one sided visual loss, nasal secretions/black necrotic tissue in the nose, and periorbital and facial edema were seen. Feeley et al.[9] reported a case with paranasal sinuses and septum involved. It has also been reported that in advanced stage, orbital apex syndrome, cavernous sinus syndrome and central nervous system involvement could be seen.[4,10] In our first case, ophthalmoplegialogy was detected and. asymmetric expansion in cavernous sinus on coronal sectional T1 weighted MR imaging was noticed. In second case, paranasal inflammation involving optic nerve and retrobulber region was seen on cranial and orbital computed tomography.

The diagnosis of the disease, which mimics malignancy clinical, is based on histopathologic study. Culture is used to identify specific species. Another fungal infection seen in paranasal sinuses is aspergillosis. This infection generally invades vessel walls, causing thrombosis, arteritis, and tearing of arterial wall.[7] Like mucormycosis it may extend into orbit and cranial cavity.[4,11] Peterson et al.[4] analyzed their 28 cases between 1955 and 1995. Eighteen patients, or 64%, had D.M., 5 (18%) had hematological malignancies, and remaining 5 (18%) were on steroid treatment or they were immunocompromised. They were divided into three treatment groups; 1. Medical management; 2. Medical and surgical management without orbital decompression; and 3. Medical and surgical management with orbital decompression. They found mortality rates in group one 60%, in-group two 21%, and in group three 25%. They concluded that orbital involvement causes higher mortality rate in general but orbital exenteration was not mandatory in all patients with evidence of orbital disease. Both of our patients had diabetes mellitus which was the most predisposing factor. The patient who had also chronic renal failure that was another predisposing factor died despite of the treatment. Early diagnosis and having had less predisposing factor may be good prognostic signs. Surgical debridement can

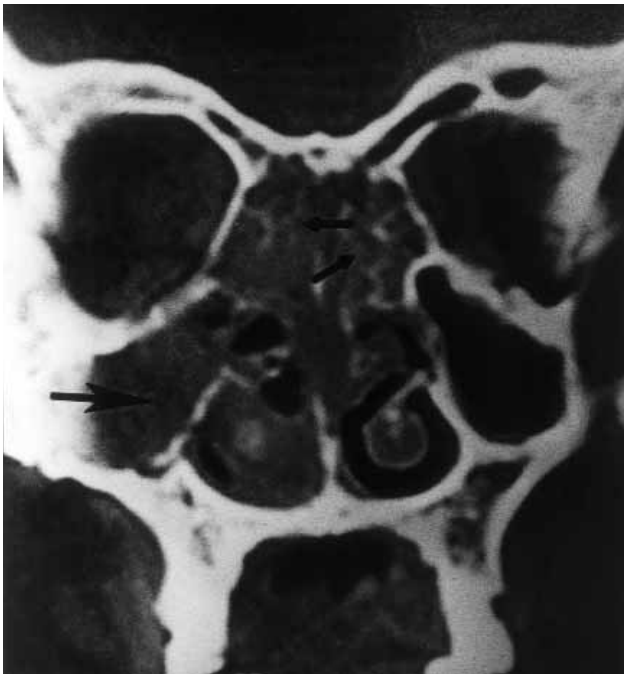

Fig. 5 – *Punctuate erosions in ethmoid cells (thin arrows) and soft tissue density filling bilateral ethmoid sinuses, left maxillary sinus (thick arrow), and inferior meatus coronal sectional CT with contrast agent (Case 2).*

prevent intracranial spread.[12] In addition to treatment modalities of the disease, potassium iodide[13] and hyperbaric oxygen are newly recommended.[8,14,16] Survival of rhinocerebral mucormycosis varies between 22% and 70%.[17]

In conclusion, invasive fungal disease should be kept in mind in differential diagnosis of paranasal sinus pathologies and after establishing the diagnosis especially in the diabetic and immunocompromised patients. The infection must be treated effectively by administration of immediate long term antifungal chemotherapy and surgical debridement as soon as possible.

REFERENCES

1. Hafız G, Aktaş E, Uluğ T, Başerer N, Tınaz M, Ergen M, Kılıç H. Rinoserebral mukormukozis. Türk Otolarengoloji Arşivi 1999;37:46-50.
2. Damante JH, Fleury RN. Oral and rhinoorbital mucormycosis: case report. J Oral Maxillofac Surg 1998;56:267-71.
3. Erkan M, Ceroğlu S, Cantürk M, Kandemir O. Rinoserebral mukormukozis. KBB Postası 1993;2:7-9.
4. Peterson KL, Wang M, Canalis RF, Abemayor E. Rhinocerebral mucormycosis: evolution of the disease and treatment options. Laryngoscope 1997;107:855-62.
5. Boelaert JR. Mucormycosis (zygomycosis): is there news for the clinician? J Infect 1994;28 Suppl 1:1-6.
6. Gregory JE, Golden A, Haymaker W. Mucormycosis of the central nervous system. Bull Johns Hopkins Hosp 1943;73:405-15.
7. deShazo RD, O'Brien M, Chapin K, Soto-Aguilar M, Gardner L, Swain R. A new classification and diagnostic criteria for invasive fungal sinusitis. Arch Otolaryngol Head Neck Surg 1997;123:1181-8.
8. Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino-orbital-cerebral mucormycosis. Surv Ophthalmol 1994;39:3-22.
9. Feeley MA, Righi PD, Davis TE, Greist A. Mucormycosis of the paranasal sinuses and septum. Otolaryngol Head Neck Surg 1999;120:750.
10. Coşkun H, Hızalan İ, Erişen L, Helvacı S, Baul O, Onan S. Rinoserebral mukormikozis, 2 olgu sunumu. In: XXVI. Ulusal Türk Otorinolarengoloji ve Baş Boyun Cerrahisi Kongresi (Özet Kitabı); 22-26 Eylül 2001; Antalya, Türkiye; 2001. s. 89-90.
11. Bhattacharyya AK, Deshpande AR, Nayak SR, Kirtane MV, Ingle MV, Vora IM. Rhinocerebral mucormycosis: an unusual case presentation. J Laryngol Otol 1992;106:48-9.
12. Özaksoy D, Günbay MU, Güneri A, Ceryan K, İkiz AO, Özen E ve ark. Dört olgu nedeniyle Rinoserebral mukormukozis: Klinik, radyolojik bulgular ve tedavi. Dokuz Eylül Üniversitesi Tıp Fakültesi Dergisi 1992;6:69-73.
13. Verma KK, Pandhi RK. Subcutaneous mucormycosis in a non-immunocompromised patient treated with potassium iodide. Acta Derm Venereol 1994;74:215-6.
14. Nussbaum ES, Hall WA. Rhinocerebral mucormycosis: changing patterns of disease. Surg Neurol 1994;41:152-6.
15. Platauf AP. Mycosis mucorina. Virchows Archiv: An International Journal of Pathology 1885;102:543-64.
16. Mazurat RD, Goldman BM. Prosthodontic rehabilitation of a patient with mucormycosis. J Can Dent Assoc 1992;58:571-3.
17. Blitzer A, Lawson W, Meyers BR, Biller HF. Patient survival factors in paranasal sinus mucormycosis. Laryngoscope 1980;90:635-48.