Rhinocerebral Mucormycosis in Diabetes：A Case Report

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Abstract

Rhinocerebral mucormycosis is a rare life-threatening infection caused by fungi from the order Mucorales. The disease occurs mostly in association with diabetic ketoacidosis. Because of its rapid progression and high mortality, early recognition and aggressive treatment offer the only chance to increase the survival rate. A case of rhinocerebral mucormycosis in a diabetic female patient typically
presenting as fever, left periorbital pain and nasal eschar is reported. The clinical manifestations, diagnosis, and treatment of rhinocerebral mucormycosis are discussed.
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Key Words：Rhinocerebral mucormycosis, Diabetic ketoacidosis

Rhinocerebral mucormycosis is a rare life-threatening infection caused primarily by fungi from the order Mucorales. This disease is mostly encountered among immunologically incompetent patients. This acute fulminant fungal infection spreads promptly from the paranasal sinus and orbital regions to the brain in a few days. The mortality rate in patients with systemic mucormycosis is as high as 50%, while in patients with cerebral involvement, it exceeds 80% 1. Because of its rapid progression and high mortality, early recognition and aggressive treatment offer the only chance to increase the survival rate. We repor-
ted a diabetic female patient who presented with early typical symptoms and expired due to severe extensive rhinocerebral mucormycosis. The clinical manifestations, diagnosis and results of treatment are discussed and the literature regarding rhinocerebral mucormycosis is reviewed.

Case Report

A 64 year-old female patient has ten-year history of diabetic mellitus, coronary artery disease and hypertension. She took glipizide and metformin re-gularly but her blood sugar control was poor (HbA1c 10.9%). Before transfered to our institution, she had

low-grade fever, lethargy and left periorbital pain was treated with oral antibiotics for two days. On transfer to our emergency department, she was febrile (39.1℃) and physical examination revealed left periorbital swelling, and small black necrotic spot over her nose. A complete blood count showed leukocytosis (WBC 31,000/mm3 with segmented neutrophil 87%). The patient's blood sugar level was high (655 mg/dl) and she had acidosis (pH7.30). The presence of ketones was noted on urinary analysis. Initially, a diagnosis of diabetic ketoacidosis and facial cellulitis was made. Despite two days of treatment with intravenous antibiotics and intensive insulin therapy, intermittent spiking fever persisted and the left periorbital swelling progressively extended to the right side. She also developed an obvious left sided ptosis accompanied by ocular palsy, blindness and absence of pupillary response. A black eschar involving almost entire nose with a dark grain discharge deve-loped from the nasal cavity. And her consciousness rapidly deteriorated. A computed tomographic (CT) scan revealed obliteration of bilateral maxillary, ethmoid, frontal and sphenoid sinuses. Left medial orbital fat thickness with exophthalmus and left mastoiditis developing to adjacent soft tissue were seen (Figs.1, 2). Small biopsy samples obtained from the nasal eschar showed the picture of mucormycosis with some foci of non-sepatate fungal hyphae (10 to 25 micrometer in diameter), and hyphal branches ty-pically at right angles (Fig. 3). There was formation of thick-walled chlamydoconcidia at the ends of the hyphae (Fig. 4). Sinus culture and blood culture reports were negative. An antifungal regimen including amphotericin B 1mg/Kg/day was initiated. Ophthalmology and otolaryngology were consulted urgently. Extensive surgical debridment was suggested but refused by her family. The patient continued to receive treatment with intravenous amphotericin B and strong antibiotics. However, her consciousness continued to decline and clinical condition showed progressive deterioration. The patient finally expired three weeks after admission.

Discussion

Mucormycosis is a fungal infection caused by a member of the family Mucoraceae. Rhizopus, Mucor, Absidia are the most common isolated from patients with mucormycosis. Rhizopus is responsible for 60% of all cases of mucormycosis, and 90% of rhinocerebral mucormycosis 2. The fungi are found in soil, bread, mold, rotten fruits and vegetables. It is repor-ted that there are six major clinical symptoms of mucormycosis, presenting as rhinocerebral, pulmonary, gastrointestinal, disseminated, cutaneous and miscellaneous 3.The most common and fatal is rhinocerebral involvement. Though mucormycosis is ubiquitous and grows rapidly, it seldom strikes in immunologically competent patients. Therefore, if an infection with mucormycosis occurs, it usually indicates a serious underlying medical condition. The risk factors for developing rhinocerebral mucormycosis include severe burn, acquired

immune deficiency syndrome (AIDS), immunosuppressive medications, leukemia, diabetic mellitus, and organ transplantation 4. About 70% to 80% of these patients have diabetes mellitus. As is reported in our case, most diabetics who develop rhinocerebral mucormycosis (RCM) are in poor metabolic control with complicating ketoacidosis 5. It is suggested that fungal organism grows in ketotic patients because acidosis disrupts iron binding to transferring and the result increases in free iron then promotes growth of the fungus. At the same time, high blood sugar level may also alter the immunologic capability to resist mucormycosis through reduction of WBC chemotaxis and the abi-
lity of macrophages 6.

As seen in our case, diabetic patients with poor controlled blood sugar who develop rhinocerebral mucormycosis typically present with malaise, retro-orbital headache, fever, and occasionally dark, blood-tinged rhinorrhea. Originally the oral and nasal ca-

vities may reveal a black eschar on the plate, septum or turbinate that may then involve the orbit via the communicating foramina and venous channel 7. Unilateral ptosis and pupillary dilatation imply involvement of cranial nerve V and VII. Because the disease provokes diffuse tissue necrosis, the fungi can easily invade the wall of blood vessels, leading to thrombosis and tissue ischemia 8. Therefore, it is not uncommon to find the infection spreading to the ca-vernous sinus or the central nervous system. The deterioration in mental status is an ominous sign, often heralding intracerebral extension of the disease process. All of these symptoms may develop over a period of several days or may occur as a fulminating process within hours 2. Imaging studies are important to evaluate the extent of the disease. CT of patients with rhinocerebral mucormycosis shows opacification of the paranasal sinus and thickening of the sinus mucosa and bone destruction without an air-fluid level. In addition, when the orbit is invaded, increased density of the orbital fat and venous engorgement may be seen 9. Magnetic resonance imaging (MRI) can demonstrate soft tissue lesions better, especially in diagnosis of cavernous sinus thrombosis. We suggested the patient to accept MRI examination but the patient's family refused. Biopsy of the affected tissue is required to confirm the infection. On histologic section, these organisms are characterized by wide, non-septate hyphae with right-angled branching 10. Cultures are still the standard means of diagnosis. But even positive histologic findings, routine sinus cultures and blood cultures are rarely positive.

Treatment of rhinocerebral mucormycosis should consist of prompt control of hyperglycemia and ketoacidosis, aggressive surgical debridment of involved tissue,

and administration of parentenal amphotericin B. Amphotericin B has potential renal toxicity and its dosage should be individually adjusted between 0.5mg/Kg/day and 1.0mg/Kg/day, based on the body weight and renal function of the patients 11. A total cumulative dosage of 2 to 4g is generally advocated. Hyperbaric oxygen(HBO) treatments should also be considered for those patients with aggressive infections. A few studies have shown that HBO has direct in vitro fungistatic activity and reduce tissue hypoxia, which may reverse the hypoxic acidosis that helps the fungi to proliferate 12. Blitzer and Lawson found that in their review of 170 cases of RCM, 63% of untreated diabetics died as compared with 17% mortality rate when therapy included aggressive surgery and amphotericin B administration 5. The importance of surgery is pronounced when no surgical treatment or only biopsy was performed the mortality rate is as high as 58% 5.

Conclusion

Rhinocerebral mucormycosis is an acute opportunistic mycosis that predominantly occurs in the patients with diabetes . The clinic physician may see patients with RCM in its earliest stages masquerading as other less serious diseases. Early diagnosis, aggressive surgical debridment, high dose amphotericin B and good control of blood sugar are the most important factors to decrease the morbidity and mortality from this fungal disease.

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糖尿病人鼻竇大腦之白黴菌病感染：病例報告

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摘　　要

鼻竇大腦白黴菌病是一種稀少且致命的黴菌感染，罹患這一危險感染者多有糖尿病控制不良合併酮酸中毒，因爲這一類感染病情進展快速且高死亡率，早期診斷積極治療才能有效提高病人存活機會。我們報告一糖尿病女性病患至急診求治，表現出發燒、左臉頰紅腫疼痛、鼻部有黑色焦痂等典型白黴菌感染症狀，討論鼻竇大腦白黴菌病之臨床表徵、診斷方法及治療預後，並作相關文獻回顧。

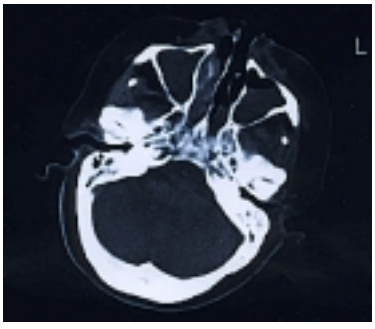

Fig.1. CT scan showing opacification of bilateral maxillary, ethmoid and

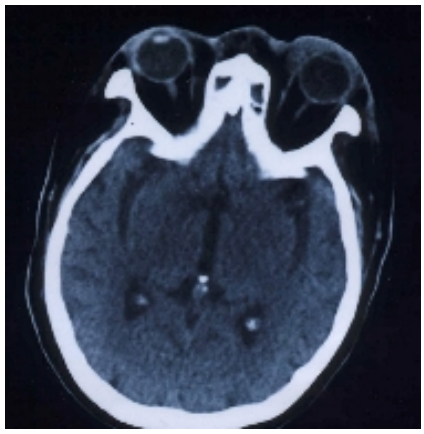

Fig.2. CT scan showing left orbital fat thickness with exophthalmus

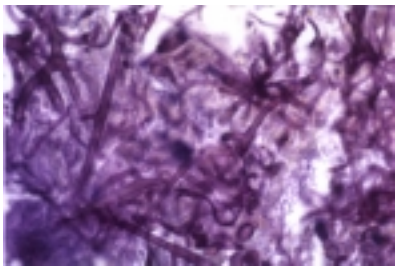

Fig.3. Photomicrograph showing wide non-sepatate fungal hyphae with right-angled branching (PAS stain, x 400 original)

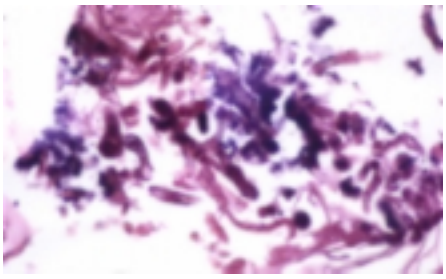

Fig.4. Photomicrograph showing terminal chlamydoconcidia at some of hyphae (H&E stain, x400 original)