

รายงานผู้ป่วย

A Case Report

Rhino-Orbital-Cerebral Mucormycosis with Diabetic Ketoacidosis

โรคเชื้อรา Mucormycosis ของ จมูก เบ้าตา และสมอง ร่วมกับภาวะเลือดเป็นกรดในเบาหวาน

กฤษดา รอดประเสริฐ พ.บ.,

ว.ว. ประสาทวิทยา

กลุ่มงานอายุรกรรม

โรงพยาบาลราชบุรี จ.ราชบุรี

Kritsada Rodprasert, M.D.

Thai Board of Neurology

Division of Medicine

Ratchaburi Hospital, Ratchaburi Province

ABSTRACT

Mucormycosis often develops in immunocompromised patients, particularly in patient with diabetic ketoacidosis. Unless early diagnosis and treatment is established mucormycosis leading rapidly to death.

A 54-years-old male was admitted to the hospital with a severe diabetic ketoacidosis. His clinical status improved in 3 days as a result of aggressive medical treatment. He has complained fever with right periorbital pain on the 7th day and had a swelling of his right cheek, facial edema, a black eschar on the palate and nasal cavity, proptosis in association with visual disturbance and total ophthalmoplegia in a short time.

CT scan revealed nearly total fluid filled at right maxillary sinus and little amount of air content, mucosal swelling right frontal and posterior ethmoid sinuses within invasion to right orbit, proptosis right globe without retrobulbar mass lesion, mucosal thickening right nasal cavity and small hypodensity lesion at right frontal lobe about 1 x 1.4 x 1.5 cm.

Excessive surgical treatment was performed and amphotericin-B 1 mg/kg/day. Small biopsy samples obtained from nasal eschar showed mucormycosis. However, his consciousness continued to decline and clinical condition show progressive deterioration. The patient finally expired six weeks after admission. Because of its rapid progression and high mortality.

Keywords : Rhino-orbital-cerebral Mucormycosis, Diabetic ketoacidosis

บทคัดย่อ

โรคเชื้อรา *Mucormycosis* มักพบในผู้ป่วยที่มีภูมิคุ้มกันต่ำ โดยเฉพาะภาวะเลือดเป็นกรดในเบาหวาน การวินิจฉัยและรักษาที่ล่าช้าทำให้อัตราการเสียชีวิตสูงขึ้น

รายงานผู้ป่วยชายไทย อายุ 54 ปี มาโรงพยาบาลแล้วได้รับการวินิจฉัยว่าเป็นภาวะเลือดเป็นกรดในเบาหวาน อาการผู้ป่วยดีขึ้นในวันที่ 3 หลังจากการรักษา ต่อมาไข้ ปวดบวมแดงที่เบ้าตา หน้า และแก้มข้างขวา แผลดำในเพดานปาก และจมูก ตาโปน อัมพาตของการกลอกตาข้างขวา ในวันที่ 7 ร่วมกับการตรวจเอกซเรย์ทาง CT พบหนองที่ไซนัส Maxillary การอักเสบของจมูก ไซนัส Frontal และ ethmoid ด้านหลัง ลามไปที่เบ้าตาขวา ทำให้มีตาขวาโปนออกมา ร่วมกับก้อนขนาด 1 x 1.4 x 1.5 ซม. ที่สมอง, Frontal ด้านขวา เมื่อรวมกับการตรวจทางชิ้นเนื้อพยาธิของแผลดำจากจมูก จึงได้รับการวินิจฉัยว่า โรคเชื้อรา *Mucormycosis* ของจมูก เบ้าตา และสมอง ร่วมกับภาวะเลือดเป็นกรดในเบาหวาน (Rhino-orbital-cerebral *Mucormycosis* with Diabetic ketoacidosis) จึงได้ให้การรักษาทางยาและผ่าตัดเพื่อระบายหนองและเนื้อดำ ต่อมาผู้ป่วยอาการรับรู้ทางสติลดลงจนกระทั่งผู้ป่วยเสียชีวิตในสัปดาห์ที่ 6

Rhino-orbital-cerebral 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. I reported a diabetic male patient who presented with typical symptoms and expired due to severe extensive Rhino-orbital-cerebral mucormycosis. The clinical manifestations, diagnosis and results of treatment are discussed and the literature regarding Rhino-orbital-cerebral *Mucormycosis* is reviewed.

Case Report

A 54-years-old man was admitted to the hospital,

the patients blood sugar level was high (979 mg/dl) and he had acidosis (pH 6.9). The presence of ketones was noted on serum. Initially, a diagnosis of diabetic ketoacidosis was made. His clinical status improved in 3 days as a result of treatment with intensive insulin therapy. He has complained fever with right periorbital pain on the 7th day and had a swelling of his right cheek, facial edema, a black eschar on the palate and nasal cavity, proptosis in association with visual disturbance and total ophthalmoplegia in a short time.

CT scan revealed nearly total fluid filled at right maxillary sinus and little amount of air content, mucosal swelling right frontal and posterior ethmoid sinuses within invasion to right orbit, proptosis right orbit, proptosis right globe without retrobulbar mass lesion (Fig. 1, 2), mucosal thickening right nasal cavity and small hypodensity lesion at right frontal lobe about 1 x 1.4 x 1.5 cm (Fig. 3, 4). Excessive surgical treatment was performed and amphotericin - B 1 mg/kg/day.

Small biopsy samples obtained from nasal eschar showed mucormycosis. However, his consciousness con-

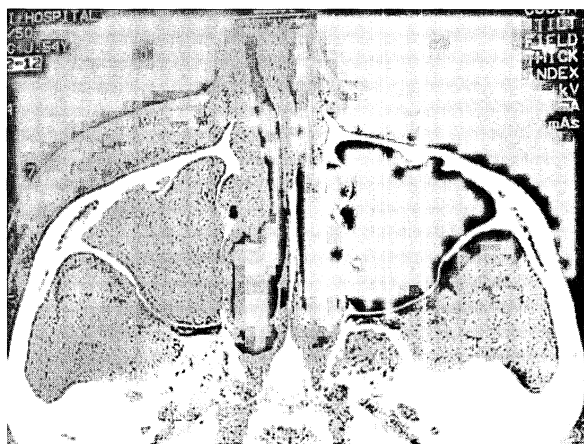


Fig. 1 CT scan showing nearly total fluid filled at right maxillary sinus and little amount of air content

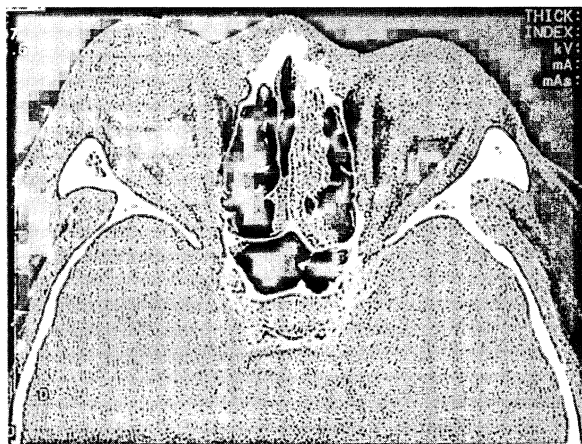


Fig. 2 CT scan showing proptosis right globe without retrobulbar mass



Fig. 3 CT scan showing mucosal thickening right nasal cavity



Fig. 4 CT scan showing small hypodensity lesion at right frontal lobe about 1 x 1.4 x 1.5 cm

tinued to decline and clinical condition show progressive deterioration. The patient finally expired six weeks after admission. Because of its rapid progression and high mortality.

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 reported 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 rhino-orbital-cerebral mucormycosis 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 transferrin 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 ability of macrophages.⁶

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

nous 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.

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.

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 rhino-orbital-cerebral mucormycosis should consist of prompt control of hyperglycemia and ketoacidosis, aggressive surgical debridement of involved tissue and administration of parenteral amphotericin B. Amphotericin B has potential renal toxicity and its dosage should be individually adjusted between 0.5 mg/Kg/day and 1.0 mg/Kg/day, based on the body weight and renal function of the patients.¹¹ A total cumulative dosage of 2 to 4 g 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, 63% of untreated diabetics died as compared with 17% mortality rate when therapy included aggressive surgery and amphotericin B administration. The importance of surgery is pronounced when no surgical treatment or only biopsy was performed the mortality rate is as high as 58%.

Discussion

Rhino-orbital-cerebral mucormycosis is an acute opportunistic mycosis that predominantly occurs in the patients with diabetes. The clinic physician may see patients earliest stages masquerading as other less serious diseases. Early diagnosis, aggressive surgical debridement, 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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