Mucormycosis; Clinical Manifestation, Diagnosis and Management; Study of Nine Cases

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ABSTRACT
Mucormycosis is an uncommon infection that afflicts severely immunocompromised patients and those with poorly controlled diabetes mellitus. In a retrospective study we evaluated nine cases of mucormycosis in several tertiary care hospitals in Tehran, Iran during several years. Clinical manifestations, diagnosis including laboratory and radiologic study, management including surgical and medical interventions were evaluated.

Keywords: Mucormycosis, Diagnosis and Management

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INTRODUCTION
Mucormycosis is an uncommon infection that afflicts severely immunocompromised patients and those with poorly controlled diabetes mellitus. A recent increase in the incidence of mucormycosis at many transplant centers has been linked to the introduction and widespread use of voriconazole prophylaxis in these high-risk populations [1]. It is a rapidly progressive fungal infection which usually occurs in immunocompromised individuals, and is characterized by soft tissue destruction and invasion of blood vessels [2]. It can produce an aggressive and sometimes fatal soft tissue infection seen most commonly in immunocompromised individuals. Eradication consists of surgical resection and antifungal chemotherapy [3]. Several conditions such as hematologic malignancy (leukemia, lymphoma, myeloma), solid organ transplantation, diabetes mellitus, corticosteroid therapy, or chemotherapy predispose patients to infection [4].

MATERIALS AND METHODS
In a retrospective study we evaluated nine cases of mucormycosis in several tertiary care hospitals in Tehran, Iran during several years. Clinical manifestations, diagnosis including laboratory and radiologic study, management including surgical and medical interventions were evaluated.

RESULTS
In this study there were six cases of rhinocerebral mucormycosis, one case of pulmonary mucormycosis, one case of pelvic mucormycosis and one case of isolated cerebral mucormycosis. Four cases (44.5%) had past medical history of diabetes mellitus (DM), one case (11.1%) had history of DM, SLE (systemic lupus erythematosus) and immunosuppressant therapy for SLE, in one case (11.1%) DM was detected for the first time after presentation of mucormycosis and the patient did not know about her diabetes mellitus. In one case (11.1%) the only risk factor was pregnancy. In two cases (22.2%) no risk factor for mucormycosis were found.

All of six cases with rhinocerebral mucormycosis were presented with swelling and erythema of periorbital area, ptosis, chemosis and decreased vision. Paranasal CT scan showed multiple sinuses involvement in all 6 cases. Brain CT scan with contrast showed subdural effusion in left parietal lobe with hypodense area in left
involved organ in favor of brain abscess and adjacent ischemia in case 1, enhancement of tentorium in favor of basal cistern arachnoiditis in case 2. Brain CT scan was normal in cases 3 and 4. Brain CT scan of case 5 showed subdural effusion in left parietal lobe. Brain MRI showed frontal lobe cerebritis in case 6. For all six patients surgical debridement of involved sinuses was performed and necrotic tissue was respected. Exenteration of involved eye was performed in cases 1, 2 and 5. For all of them amphotericin B started. Case 1 developed brain abscess. Vancomycin, cefazidime and meronidazole was added to amphotericin B, but the patient’s level of consciousness decreased after two days and expired. Case 2 developed meningitis that confirmed by lumbar puncture. Vancomycin and meropenem was added but level of consciousness decreased and the patient expired. Case 3 and 4 responded to amphotericin B and Erythema and edema of periorbita, area disappeared and general condition improved. Case 5 who developed brain abscess did not respond to medical and surgical treatment and expired. Case 6 with cerebritis did not respond to vancomycin and meropenem and amphotericin B and expired. One of our patients was a 32 year-old pregnant woman who developed fever after cesarean section. Sonography of abdomenopelvis showed a large mass in pelvic area. Magnetic resonance imaging (MRI) of pelvis with and without contrast was done that demonstrated septated nonenhancing cyst like lesion in right anterior aspect of pelvis with compression on bladder. With impression of malignancy and for better evaluation the mass excised and was evaluated pathologically. The result of pathology was negative for malignancy and showed broad nonseptated hyphal elements in favor of mucormycosis. The result of culture confirmed the diagnosis. Intravenous Amphotericin B started for her without improvement. The patient’s fever continued and her condition did not change. Amphotericin B discontinued and Posaconazole started. Fever disappeared and general condition gradually improved. Course of posaconazole completed and the patient was discharged from hospital with good condition and follow up.

One of our patients was a 33 year-old woman with dental infection with no response to antibiotic therapy. She developed sinus involvement extending to orbit thereafter. Paraclinical evaluation was done and showed changes in favor of mucormycosis. Exenteration of globe was done. Pathologic study showed hyphae of mucor that confirmed by culture. The patient also developed pulmonary symptoms. Bronchoalveolar lavage showed mucoral in smear and culture. Posaconazole started for her with good response.

The case 9 was a 46 year-old woman known case of diabetes mellitus with chief complaint of headache, fever and swelling of right posterior auricular area with erythema and hotness. Brain CT scan was performed that showed a brain abscess in right temporoparietal lobe. Smear of drained abscess showed broad nonseptated hyphal and culture result was mucoral agent. Amphotericin B was started. Despite several days after amphotericin B infusion, fever continued and ESR did not changed. Amphotericin B discontinued and posaconazole was started. Fever disappeared and ESR decreased and the patient was discharged with good general condition.

For all of patients smear and culture was performed and diagnosis of mucormycosis was confirmed. Table 1 shows summary of clinical manifestation, treatment and outcome of our patients.

<table>
<thead>
<tr>
<th>Case number</th>
<th>Involved organ</th>
<th>Risk factor</th>
<th>treatment</th>
<th>surgery</th>
<th>culture confirmation</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rhinocerebral</td>
<td>None</td>
<td>Amphotericin B</td>
<td>Yes</td>
<td>Yes</td>
<td>Expired</td>
</tr>
<tr>
<td>2</td>
<td>Rhinocerebral</td>
<td>DM</td>
<td>Amphotericin B</td>
<td>Yes</td>
<td>Yes</td>
<td>Expired</td>
</tr>
<tr>
<td>3</td>
<td>Rhinocerebral</td>
<td>DM</td>
<td>Amphotericin B</td>
<td>Yes</td>
<td>Yes</td>
<td>Survived</td>
</tr>
<tr>
<td>4</td>
<td>Rhinocerebral</td>
<td>DM</td>
<td>Amphotericin B</td>
<td>Yes</td>
<td>Yes</td>
<td>Survived</td>
</tr>
<tr>
<td>5</td>
<td>Rhinocerebral</td>
<td>DM</td>
<td>Amphotericin B</td>
<td>Yes</td>
<td>Yes</td>
<td>Expired</td>
</tr>
<tr>
<td>6</td>
<td>Rhinocerebral</td>
<td>DM, SLE, immunosuppression</td>
<td>Amphotericin B</td>
<td>Yes</td>
<td>Yes</td>
<td>Expired</td>
</tr>
<tr>
<td>7</td>
<td>Pelvis</td>
<td>Pregnancy</td>
<td>Posaconazole</td>
<td>Yes</td>
<td>Yes</td>
<td>Survived</td>
</tr>
<tr>
<td>8</td>
<td>Lung</td>
<td>None</td>
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<td>Yes</td>
<td>Yes</td>
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</tr>
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<td>9</td>
<td>CNS</td>
<td>DM</td>
<td>Posaconazole</td>
<td>Yes</td>
<td>Yes</td>
<td>Survived</td>
</tr>
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</table>

**DISCUSSION**

Mucormycosis is an increasingly frequent life-threatening infection caused by opportunistic fungal organisms of the class Zygomycetes. The pathognomonic feature is the presence of invasive aseptate mycelia that are larger than other filamentous fungi with the hyphae exhibiting right angle and haphazard branching. Usually classified as rhinocerebral, disseminated, and cutaneous types; this classification serves as important predictor of pathogenesis and outcome. These occur mostly in immunosuppressed patients including individuals with diabetes and patients with organ transplants and hematologic malignancies [5]. In fact it usually occurs among patients with poorly controlled diabetes mellitus (especially those with...
Mucormycosis can involve systems such as rhinocerebral [7], pulmonary [8], gastrointestinal [9], cardiac [10], and also skin [11], face [12], sino-orbital [13] and nasal cartilage [14]. Early diagnosis of mucormycosis is essential for efficacious anti-fungal treatment and prevention of irreversible spread of mucormycosis to vital organs [15]. The diagnosis of mucormycosis can only be confirmed by pathological and mycological examination of biopsy specimens. These requirements conflict with the need for urgent treatment with surgical debridement, amphotericin B and control of the underlying pathology (16). The keys to successful therapy include suspicion of the diagnosis and early recognition of the signs and symptoms, correction of underlying medical disorders such as ketoacidosis, and aggressive medical and surgical intervention [17]. Standard therapy for invasive mucormycosis includes parenteral amphotericin B in combination with radical debridement of infected tissues. Early diagnosis and treatment are of paramount importance. Unfortunately, long-term survival is poor owing to the prohibitive morbidity and mortality rates associated with the medical and surgical therapies. Posaconazole is a novel, extended-spectrum triazole oral antifungal agent with documented success in the treatment of patients with invasive mucormycosis [18]. A poor prognosis is primarily related with uncontrolled underlying disease. Surgical debridement is essential for a good prognosis, but timely intervention and complete aggressive debridement are not always needed in all patients. The patient who had slowly progressive disease also survived after conventional medical management and limited surgical debridement [19].

REFERENCES


**CITATION OF THIS ARTICLE**