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A Brief Review of Mucormycosis: Report of Five Cases

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Case Series

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ABSTRACT

Mucormycosis is an emerging and slowly rising fatal infectious disease in most countries. It is the third most common invasive mycosis after candidiasis and aspergillosis. Hematologic malignancies notably acute myeloblastic leukemia (AML) and diabetes mellitus (DM) especially when uncontrolled or there is ketoacidosis are the most common predisposing conditions. Clinical manifestations vary according to the organ involved. Based on anatomic localization, mucormycosis can be classified as one of 6 forms: Rhinocerebral, Pulmonary, Cutaneous, Gastrointestinal, Disseminated and Uncommon presentations.
The mortality rate is often very high. Early diagnosis and aggressive treatment are the cornerstone

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of management. Here we report 5 cases of mucormycosis in patients admitted to Imam Reza hospital, the tertiary referral center in Northwest of Iran. We will also have a brief review of this fungal infection.

Keywords: Mucor; mucormycosis; diabetes mellitus; sinusitis.

1. INTRODUCTION

Mucormycosis (also called zygomycosis) is a rare infection caused by organisms that belong to a group of fungi called Mucoromycotina in the order Mucorales (CDC). Here we report 5 cases of mucormycosis admitted to our center in recent years. All of them had uncontrolled Diabetes Mellitus as the background disease. All had rhinocerebral infection. Altered consciousness was noted in most of our patients. All patients have undergone various forms of surgical operations most of them extensive.

2. CASE 1

The patient was an 83-year-old female with Rheumatoid Arthritis (RA). She had received corticosteroids recently. Following corticosteroid use she had developed polydipsia and polyuria with a high blood sugar. She had been admitted to the local hospital and received insulin. A few days after discharge she had developed xerostomia and necrotic lesions on the hard palate. The lesions had rapidly spread to the adjacent areas including nose, paranasal sinuses and eyes. There was extensive necrosis with a black eschar on hard palate, upper part of the face. The pt was ill and toxic. She received Amphotericin B for Mucur and Imipenem, Vancomycin and Ciprofloxacin for concomitant bacterial sinusitis. Unfortunately she died of severe disease.

3. CASE 2

A 60 year old female who had diabetes for 6 years and was under treatment with oral antidiabetics and basal insulin with a poor control. Her HbA1c was 10%. Following an upper respiratory infection she had developed headache, swelling and erythema of the right eye which was painful. It was accompanied by proptosis of the eye and paresthesia of surrounding area. A biopsy was done which confirmed mucormycosis. Computing Tomography (CT) scan showed sinusitis, extensive necrosis of the paranasal sinuses and orbit. Involvement of orbit and paranasal sinuses including frontal and sphenoidal sinuses. She received Amphotericin B for two months and lives an active life.

4. CASE 3

The pt was a 57 year old male with diabetes of 15 years duration under treatment with oral antidiabetics. His diabetes control was very poor with a hemoglobin A1c (HbA1c) of 11. 3%. He had received fluconazole for one month prior to admission. Swelling of the left side of the face with erythema and paresthesia of that area had begun 40 days ago. It had a progressive course. On CT and MRI exam there was pansinusitis and involvement of left maxilla and ethmoidal sinus. On examination there was left facial nerve paralysis and perforation of nasal septum. The patient received Amphotericin B and ampicillin/ Sulbactam for bacterial coinfection and had a good outcome.

5. CASE 4

A 59 year old male with Type 2 Diabetes Mellitus (T2DM) on oral antidiabetics with an HbA1c of 9. 8% presented with a two week history of facial paresthesia and ptosis of Right Eye. He was treated for a presumed diagnosis of Bell`s palsy. He was subsequently diagnosed as having mucormycosis. A biopsy provided strong evidence of mucor infection. The infection was very invasive, invading surrounding bones cavities and extending to cavernous sinus causing ophthalmoplegia. He underwent several endoscopic operations and received Amphotericin B for 2 months. He is alive but unfortunately has lost his left eye vision.

6. CASE 5

This patient was a 70 year old man and newly diagnosed T2DM and Chronic obstructive pulmonary disease (COPD) who received oral antidiabetics and inhaled Fluticasone. His HbA1c was 10.3%. He had dry coughs, headache and fever from 10 days ago and had developed left Facial paresthesia, ptosis and then sudden blindness. There was pansinusitis subperiosteal

abscess in the left Orbit in the CT. A biopsy was done which showed mucormycosis. He underwent several endoscopic and open operations. He received Amphotericin B and antibiotics for 2 months. He left our hospital on his own responsibility and died two weeks later.

7. DISCUSSION

Mucormycosis has emerged as a catastrophic infectious condition afflicting many patients with certain disease conditions. Mucormycosis and entomophthoramycosis were previously encompassed by the term zygomycosis [1]. Changes in high-level taxonomy in reference to molecular phylogenetic analyses have, however, led to the class name Zygomycota being replaced by Glomeromycota [2].

In this new classification, all the agents of mucormycosis have been placed under the subphylum Mucormycotina and the agents of entomophthoramycosis are now in the subphylum Entomophthoramycotina. Since the phylum Zygomycota no longer exists, the disease name zygomycosis has become obsolete. Mucormycotina are characterised by large, ribbon-like hyphae with only occasional septae (aseptate fungi).

Many case series studies have been published in recent years, most cases were reported by Rodent et al which comprised 929 cases from 1885 to 2004. In his study DM was the most common predisposing condition comprising 36%, hematologic malignancies 21%, solid organ transplantation/ malignancy 7%, deferoxamine therapy 6%, autoimmune diseases and corticosteroid use 1%, trauma or no underlying conditions 9% [1].

Other large series were reported by Skiada et al and Chakrabarti et al. [3] from Europe and India respectively. In both of them hematologic malignancies and diabetes mellitus were the most common predisposing conditions [1].

In developed countries, such as the USA, France, and Austria, mucormycosis mainly occurs in transplant recipients and neutropenic patients, although in France the frequency is rising among patients with diabetes mellitus [4].

In India the frequency has risen from 13 cases per year in 1990–99 to 36 cases per year in 2000–04, and 50 cases per year in 2006–07, and the highest-risk group is patients with uncontrolled diabetes [3].

Other conditions including but not limited to are iron overload, major trauma, prolonged use of corticosteroids, illicit intravenous drug use, neonatal prematurity and malnourishment, use of antifungal agents with no activity against mucor such as Voriconazole and Caspofungin, immunosupressive or corticosteroid use, extensive burns and trauma [1,2,5].

8. PATHOPHYSIOLOGY

Any condition in which there is neutrophilic or phagocytic dysfunction or iron overload is a predisposing condition for growth of the fungus. Mucor has a unique ketone reductase system which enables it to utilize ketones as a source of energy [6,7]. Mucor has a strong tendency to invade any kind of vessel including arteries, veins and lymphatics. When these vessels are invaded by the fungus, thrombi are formed leading to tissue ischemia and acidosis, conditions most favored by the organism [6,7].

Spread to adjacent organs and dissemination via blood stream leads to catastrophe and death of the patient in most cases.

9. DIAGNOSIS

Clinical suspicion should prompt aggressive and emergent treatment. Most cases are treated upon clinical suspicion. However, laboratory diagnosis is possible. Tissue diagnosis is the standard.

Histopathologic examination of surgical specimens can confirm the clinical diagnosis with the appearance of right-angle branching aseptate hyphae, which are considered typical of mucor species, along with evidence of angioinvasion and tissue necrosis [2,5,6]. Fungal cultures can provide further confirmation. However, a large number of false negative results have been reported compared to direct histopathological examination [5].

10. CLINICAL MANIFESTATIONS

Clinical manifestations differ according to the organ involved and from patient to patient. Symptoms are mostly of acute presentation and progress rapidly. Patients are ill or toxic and systemic signs and symptoms present, although local signs and symptoms predominate. If not

addressed promptly, the patient will deteriorate rapidly and catastrophe will ensue.

Rhinocerebral mucor mostly presents acutely and in a fashion similar to sinusitis and periorbital cellulitis [5]. Patients complain of pain and paresthesia around the orbit. Fever resistant to medications is present to varying degrees. Edema is soft, cool and non-tender in contrast to the edema of cellulitis which is taut, warm and tender [6]. In some patients there is a history of dental manipulation by dentists and the infection begins from the hard palate spreading to sinuses and orbits. Proptosis, ptosis, loss of vision, often complete ophthalmoplegia or “frozen eye” and severe ocular congestion occurs. During following hours a black necrotic eschar pathognomonic of the disease develops. Infection invades bones, spreading to Central Nervous System (CNS) or para nasal sinuses and palate occurs via orbital apex or cribriform plate respectively. Vascular invasion leads to widespread dissemination and various forms of cerebral vascular involvement. Vascular aneurysms develope and cavernous sinus is involved producing characteristic signs and symptoms of headache and ophthalmoplegia [1,2,5,6].

10.1 Cutaneous Mucor

Cutaneous mucor is the result of direct contamination or rarely spread from deep organs. It often involves burn patient and may be localized or spread to deep tissues.

10.2 Pulmonary Mucor

Symptoms are non -specific and include resistant fever, cough and sputum production, chest pain and hemoptysis [1].

10.3 Gastrointestinal Mucor

Gastrointestinal (GI) Mucor is an uncommon disease and usually diagnosed postmortem. It is may be acquired by contaminated food such as dried bread. Stomach is the most common site of infection but any part of GI tract may be involved. Signs and symptoms are non specific and catastrophic complications may ensue including peritonitis, perforation and massive hemorrhage.

10.4 Disseminated Mucor

Disseminated mucor is the most fatal form. Any organ involved can spread the organism, the most common one being the lungs. Severe iron overload and profound immunosupression predispose to dissemination [1]. Signs and symptoms are variable but a metastatic cutaneous lesion is an important clue to the diagnosis.

10.5 Uncommon Forms of Mucor

Any organ in the body may be infected by mucor. Osteomyelitis, peritonitis, endocarditis and pyelonephritis have been reported. IV drug use, trauma and intraperitoneal catheters are typical predisposing factors.

11. TREATMENT

Early diagnosis and initiation of antifungal drugs along with aggressive surgical debridement of necrotic tissues are the key to successful treatment. Mortality, however, is high approaching 90% in GI, disseminated and stem cell recipients. Diabetic patients, in contrast, have more favorable outcome [2]. Delay in diagnosis and treatment is associated with poor outcome.

12. ANTIFUNGAL DRUGS

Amphotericin B is the most effective drug and the most commonly used one [1,2,5,6]. Two forms exist, deoxycholate and liposomal. Liposomal form is lipid soluble and enters the CNS more efficiently. It reduces fungal burden more robustly and has a more favorable safety profile. Liposomal amphotericin B has been shown to have more survival benefit compared to the deoxycholate [2].

Posaconazole, a triazole, and capsofungin are other antifungal drugs used alone or more commonly in combination with Amphotericin B. In combination, they are more effective [2].

Statins, colistin, iron chelators and granulocyte transfusion have been used all with variable success [2].

Overall, Amphotericin B and extensive surgical debridement have resulted in most favorable outcomes and therefore is the cornerstone of the treatment [8]. The other ones being used as per case.

13. CONCLUSION

Mucormycosis is a fatal and devastating disease mostly seen in diabetics. Periorbital edema, paresthesia, severe sinusitis, rapidly progressive invasive infection and ultimately death are the usual picture. Early, aggressive and invasive treatment is the key to successful management.

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this case series.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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