Mucormycosis : A Review

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Abstract

Mucormycosis is a life threatening infection that occurs in patients who are immunocompromised because of diabetic ketoacidosis, neutropenia, increased serum levels of available iron and organ transplantation. Understanding the pathogenesis of mucormycosis and the host response to invading hyphae that ultimately can provide targets for the novel therapeutic interventions. The most common etiologic agent of mucormycosis is Rhizopusoryzae.[1]

Medical and surgical treatment shows unsuccessful because there was a delay in its diagnosis and institution of appropriate treatment[2].

INTRODUCTION

Mucormycosis are life-threatening fungal infections mostly occurring in hematology, solid organ transplant also in diabetic, seen in immuno competant patients having trauma or burn. Nosocomial or community outbreaks have also been described.

Mucormycosis is characterized by the host tissue infarction and necrosis that resulting from the vascular invasion by the hyphae starting with the specific interaction with endothelial cells. Most common clinical presentations are rhino-orbito-cerebral and pulmonary.

These infections are sometimes difficult to manage for several reasons. Firstly diagnosis is difficult because clinico-radiological similarities with the invasive aspergillosis and historical lack of diagnostic tools. [3]

CAUSES OF MUCORMYCOSIS

Rhizopusarrhizus species from the family of Mucoraceae, most commonly identified cause of mucormycosis in humans. Other fungal causes include mucor species, Cunninghamellabertholletia, Apophysomyceselegans, Absidia species, Saksenea species, Rhizomucorpusillus, Entomophthora species, Conidiobolus species and Basidiobolus species. [4]

Generally mucormycosis infection are not seen by many doctors because the fungal causes are not readily infectious. Usually infection develops because of some unusual circumstances like injuries that cause entry of fungi causing infection. [4]

PATHOGENESIS

Host defence

Both mononuclear and polymorphonuclear phagocytes of normal hosts kill the mucorales by the generation of the oxidative metabolites and the cationic peptides defensins. Clinical evidence shown that these phagocytes are the major host defence mechanism against mucormycosis. [5]

Fungal- Endothelial Interaction

The hallmark of mucormycosis infection is virtually uniform presence of extensive angioinvasion with the resultant vessel thrombosis and tissue necrosis. This angioinvasion is associated with ability of the organism to hematogenously disseminate from the original site of infection to the other target organs. So the damage of and penetration through endothelial cells lining blood vessels is likely have a critical step in organism's pathogenic stratergy. [5]

CLINICAL MANIFESTATION

Clinical hallmark of mucormycosis is vascular invasion resulting in thrombosis and tissue necrosis. [5]

Most cases, the infection is rapidly progressive and can results in death unless underlying risk factors are corrected and aggressive treatment with antifungal agents and surgical excision is instituted. Based on clinical presentation and anatomic site, invasive mucormycosis can be classified into 6 clinical forms (a)rhinocerebral (b) pulmonary (c)cutaneous (d) gastrointestinal (e)disseminated and (f) uncommon rare forms: endocarditis, osteomyelitis, pericoronitis, and renal infections. [6]

Most common sites are sinuses, lungs and skin. The overall mortality rate for the infection is 44% in diabetics, 35% in patients with underlying conditions and 66% in patient with malignancies [6].

PULMONARY MUCORMYCOSIS

Most often in neutropenic patients with cancer undergoing induction chemotherapy and those who have undergone HSCT and have GVHD. Mortality rate in patients is 76%, even higher in severely immunocompromised patients. Clinical features show similar features of pulmonary aspergillosis. [6]

RHINOCEREBRAL MUCORMYCOSIS

Most common form seen in diabetic patients. Also seen in underlying malignancies, recipi-

ents of hematopoietic stem cells or solid organ transplants.[6]

CUTANEOUS MUCORMYCOSIS

It is caused by direct inoculation of fungal spores in the skin, which may lead to disseminated disease. Based on its extent of infection classified as localized, deep extension and disseminated.[6]

GASTROINTESTINAL MUCORMYCOSIS

It is an uncommon form. And also diagnosis is also delayed so the mortality rate is 85%.[6]

DISSEMINATED MUCORMYCOSIS

Infection from one organ can spread hematogenously to other organs. Organ which is commonly associated is lung. Also occurs from alimentary tract, burns, and extensive cutaneous lesion.[6]

UNCOMMON FORMS

Other unusual forms include endocarditis, osteomyelitis, pericoronitis, and polynephritis. Iv drug use is a typical risk factor in endocarditis and traumatic inoculation or surgical intervention can lead to osteomyelitis.[6]

TREATMENT

Background treatment strategies

The successful treatment for this infection requires 4 steps: (a) early diagnosis, (b) reversal of underlying predisposing risk factors, if possible; (c) surgical debridement where applicable and (d) prompt antifungal therapy

EARLY DIAGNOSIS

The recent study from Chamilos et al. quantifies the benefit of the early initiation of the polyene antifungal therapy. They had reported that if treatment was initiated within 5 days of diagnosis of mucormycosis, the survival was markedly shows improvement compared to initiation of polyene therapy at >6days after diagnosis. Hence, establishing an early diagnosis is very critical for the initiation of antifungal therapy

The development of other diagnostic methods is also a major unmet need. Development of quantitative PCR systems is a promising area of ongoing research to enable more rapid diagnosis in the infection.

CT scanning of patients with rhino-cerbral disease is simply sinusitis, so the absence of deeper infection by CT scan does not rule out the infection. But MRI is more sensitive than CT scan for detecting orbital and central nervous system involvement.

CT scan are useful for early diagnosis of pulmonary mucormycosis, particularly in cancer patients[7].

REVERSAL OF UNDERLYING DISEASE

It is critical to reverse the underlying defects in host defense while treating patients with mucormycosis. Immunosuppressive medications, especially corticosteroids, should be dose reduced or can be stopped if it is possible.

Administration of iron can be avoided, because of its exacerbation of severity in animal models of mucormycosis. Also it is advisable to minimize blood transfusion, if it is feasible.[7]

SURGICAL MANAGEMENT

In some cases like blood vessel thrombosis and resulting tissue necrosis during mucormycosis can result in poor penetration of antifungal agents to the site of infection. In those cases debridement of necrotic tissues may be needed for the complete eradication of the infection

Recent studies says that surgery was found to be independent variable by logistic regression for the favourable outcome in patients with the infection.

Many cases of patients who did not under-

gone surgical treatment had a far higher mortality rate than who undergone surgery.[7]

ANTIFUNGAL THERAPY

First line monotherapy options

For decades Amphotericin B deoxycholate was the cornerstone of mucormycosis therapy. Lipid formulations of AmB are relatively less nephrotoxic and can be safely administered at higher doses for longer period of time than AmB..

Liposomal AmB therapy was associated with 67% survival rate, compared to 39% survival when patients with AmB therap. So now most experts prefer lipid polyenes rather than AmB as the treatment option.

Many available data shown that LAmB over amphotericin B lipid complex (ABLC) for the treatment of CNS mucormycosis.[7]

COMBINATION ANTIFUNGAL THERAPY

In heavily immunocompromised patients lack of clinical data therapy so combination of antifungals has become a common practise. These therapies has got synergistic effect and broader coverage. Shows synergistic effect between polyenes and echinocandins. Echinocandins have some invivo effect, through degradation of small amount of glucan on the cell wall of the fungus, with unmasking of immune epitopes, and facilitating phagocytosis[8].

SALVAGE THERAPY

Many salvage studies have suggested a response rate of approximately 40% for both posaconazole and with amphotericin B lipid complex

Increasing the dose of liposomal amphotericin B, adding an echinocandin or posaconazole and switching to posaconazole are reasonable strategies for the patients showing progressive infection on lipid amphotericin B therapy alone.[9]

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