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Review Article

MUCORMYCOSIS: PROGNOSIS, DIAGNOSIS AND THERAPY-CURRENT TRENDS

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ABSTRACT

Mucormycosis, an aggressive and potentially life-threatening fungal infection, presents multifaceted challenges in diagnosis, treatment, and prognosis. This review explores the diverse clinical spectrum of mucormycosis, encompassing its etiology rooted in environmental fungi, risk factors amplifying susceptibility, and intricate clinical manifestations affecting various organ systems. Diagnostic approaches, including imaging modalities and tissue biopsies, alongside management strategies such as antifungal therapy and surgical intervention, are delineated. Emphasizing the importance of an interprofessional approach, the abstract underscores the collaborative efforts of specialists from infectious diseases, otolaryngology, hematology/oncology, endocrinology, microbiology, and dedicated nursing and pharmacy support. Despite advancements, the prognosis for mucormycosis remains challenging, particularly without immune status restoration, urging further exploration and innovative approaches for improved patient outcomes.

Keywords :- Mucosis, Immunocompromised, Antifungal Agents, Cutaneous Infection.

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INTRODUCTION

Mucormycosis stands as an opportunistic fungal infection belonging to the zygomycete family, known for inducing various infection types. Typically, underlying conditions create a predisposition for hosts to succumb to this infection. These fungi, usually non-pathogenic in individuals with a robust immune system, turn into devastating opportunistic infections in immunocompromised patients. Clinical manifestations include pulmonary, gastrointestinal, cutaneous, encephalic, and rhinocerebral infections. It's essential to distinguish rhinocerebral from allergic fungal sinusitis, the latter being a localized, non-invasive overgrowth in immunocompetent individuals. Mucormycosis is characterized by tissue necrosis stemming from blood vessel invasion and subsequent thrombosis, often progressing rapidly. Prompt and aggressive surgical debridement, coupled with high-dose intravenous antifungal therapy, stands as the cornerstone of effective treatment. [1]

OCCURANCE AND RISKS

Among the species frequently identified in patients are Apophysomyces (A. variabilis), Cunninghamella (C. bertholletiae), Lichtheimia [Absidia] (L. corymbifera L. raosa), Mucor (M. circinelloides), Rhizopus (R. arrhizus (oryzae) R. microsporus), Rhizomucor (R. pusillus), and Saksenaea (S. vasiformis). These fungi are typically found in the environment and are harmless to immunocompetent individuals. However, in patients with compromised immune systems (e.g., transplant recipients, HIV patients, those on chronic steroids or disease-modifying anti-rheumatic medications, leukemia or other cancer patients), they can cause rapidly progressing necrotizing infections. Uncontrolled diabetes, especially in individuals with a history of diabetic ketoacidosis, also poses a risk [2, 3].

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Mucorales, heat-resistant fungi commonly found in soil and decaying matter, seldom cause diseases due to their low virulence. Among immunocompromised groups, Rhizopus is the prevalent fungal infection, although various Aspergillus species are also frequently encountered. The rise in mucormycosis cases is attributed to increased immunosuppression prevalence in the general population, stemming from improved survival rates in cancer and transplant patients, as well as wider use of immunosuppressive drugs for autoimmune conditions. Inhalation of air spores serves as the primary route of infection, depositing in the paranasal sinuses and lungs. Other less common routes involve ingestion or direct skin contact.

Risk factors encompass diabetes mellitus, malnutrition, malignancies like lymphomas and leukemias, renal failure, organ transplantation, burns, immunosuppressive therapy, cirrhosis, and AIDS. Additionally, diabetic ketoacidosis and dialysis, especially with the iron chelator deferoxamine, heighten susceptibility to mucormycosis. The most frequent clinical manifestation is rhinocerebral mucormycosis, where even with medical or surgical interventions, mortality remains high unless immune system function can be restored. [4]

TYPES OF MUCORMYCOSIS

Mucormycosis can affect various body systems, targeting sites like the lungs, central nervous system, paranasal sinuses, gastrointestinal tract, and skin. Its clinical presentations are diverse, typically marked by rapid progression, heavily influenced by the fungus's entry route and underlying conditions.

- **Rhinocerebral type**

This type of mucormycosis begins with spore inhalation into the paranasal sinuses, leading to blood vessel invasion. It initiates with nasal congestion or discharge and can progress to facial numbness, blurry vision, headaches, ocular pain, fever, and other symptoms. Intranasal lesions often present as painless ulcers with necrotic tissue, advancing swiftly, particularly in immunocompromised patients. Persistent nasal symptoms should prompt a biopsy to rule out mucormycosis, also known as "invasive fungal sinusitis - IFS."[5]

- **Pulmonary type**

This type of mucormycosis results from inhaling infectious material, causing rapidly progressive bilateral pneumonia. Common symptoms include fever, hemoptysis, breathing difficulties, and coughing, more prevalent in patients with hematological conditions. It may manifest as bronchitis, bronchopneumonia, or pulmonary embolism and can extend to nearby tissues or form cavitary lesions resembling tuberculosis or allergic fungal disease. [6]

- **Cutaneous type**

This type of mucormycosis appears as primary or secondary disease. Primary infections stem from direct inoculation, often seen in patients with burns or traumatic skin wounds. It initially presents as a single area of cellulitis, evolving into a necrotic lesion or other forms like abscesses, skin swelling, and necrosis. Symptoms may include nausea, vomiting, ulcers, thrombosis in the gastric, esophageal, or intestinal mucosa, resulting in diarrhea, hematemesis, and melena. Complications such as perforation and peritonitis might arise, with poor prognosis linked to bowel infarctions and hemorrhagic shock, albeit gastrointestinal symptoms are rare except in severely immunocompromised patients. [7]

- **Disseminated type**

This type of mucormycosis can arise from primary infections and presents nonspecific manifestations, complicating diagnosis. However, a metastatic skin lesion strongly suggests disseminated mucormycosis, signifying a poor prognosis. [8]

PHYSIOLOGY

Mucorales thrive in soil and decaying matter. In immunocompetent individuals, these spores entering the respiratory tract typically adhere to nasal mucus and are expelled through swallowing or sneezing. Should any mucous membrane have a wound, polymorphonuclear neutrophils play a crucial role by phagocytosing and eliminating fungal structures. Neutrophils serve as the primary defense against these infections, making individuals with neutropenia or neutrophil dysfunction particularly vulnerable. This vulnerability is evident in clinical cases among leukemia and bone marrow transplant patients.

Studies on Rhizopus arrhizus have revealed that ketone bodies in these patients are metabolized by a ketone reductase, enabling fungal survival in acidic conditions. Consequently, the fungi transition into hyphal forms within host tissues, infiltrating blood vessels extensively. This invasive angioinvasion leads to vessel thrombosis and tissue necrosis. Diabetic patients, often with poorly controlled diabetes and increased circulating glucose, create an environment conducive to rapid filamentous structure development. These structures initially bind to blood vessels and swiftly occlude them, resulting in extensive ischemic necrosis within days. Moreover, metabolic acidosis inhibits the chemotaxis of polymorphonuclear leukocytes, reduces phagocytic activity, and dampens local inflammatory responses in immunocompromised patients, compounding the challenges posed by other underlying diseases. [9]

The prognosis hinges on the promptness of therapeutic intervention and the level of the patient's underlying immunodeficiency. Mortality rates vary significantly, ranging from 25% to 87% contingent upon the infection site. Grave prognostic indicators encompass disseminated infection, renal impairment, central nervous system involvement, and insufficient response to medical treatment. The pivotal prognostic factor lies in reinstating a normal immune status. In instances where this isn't achievable, the prognosis remains uniformly grim. However, if immune competence can be temporarily or fully restored, the prognosis tends to improve. [10]

DIAGNOSIS

Routine blood tests seldom offer a definitive diagnosis but may reveal neutropenia, which correlates with increased risk. Imaging plays a crucial role in assessing the disease extent. Radiological studies are essential to investigate suspected mucormycosis sites—specifically, the brain, paranasal sinuses, lungs, and abdomen—tailored to clinical suspicions. In suspected rhinocerebral mucormycosis, initial intervention involves endoscopic assessment and sinus biopsy to detect tissue necrosis and gather samples. Characteristic hyphae in the tissue offer a presumptive diagnosis, often obtained most accurately by biopsying the middle turbinate. Computed tomography (CT) scans help evaluate adjacent structures like the eyes and brain, revealing findings such as soft tissue edema, sinus mucoperiosteal thickening, bone erosions, and orbital invasions. Immunosuppressed patients with respiratory symptoms may require a CT chest to explore potential pulmonary mucormycosis. Diagnosis is challenging as the infection mimics pneumonia. Chest radiographs may depict pleural effusion, nodules, consolidation, and ground-glass infiltrates. Bronchoalveolar lavage might reveal broad nonseptate hyphae. For suspected gastrointestinal mucormycosis (manifesting as abdominal pain or bleeding), a CT scan can assess colitis. Once confirmed, endoscopy with biopsy is warranted. Characteristic hyphae in the biopsy can suggest the diagnosis. [11]

TREATMENT AND MANAGEMENT

The standard approach to managing mucormycosis involves early diagnosis, addressing underlying risk factors and illnesses, surgical debridement, and prompt intravenous antifungal therapy, typically employing amphotericin B. This necessitates immediate management of hyperglycemia, acidosis, and discontinuation of immunosuppressive agents whenever feasible. Amphotericin B, particularly the lipid formulation, is the first-line treatment. It's administered intravenously in high doses once daily initially, starting at 5 mg/kg IV daily, with a maximum of 10 mg/kg IV. Treatment duration varies based on the patient's clinical condition. Urgent surgical debridement is crucial to curtail further infection spread. Aggressive removal of necrotic tissue is vital, often involving radical procedures like facial resections, partial pneumonectomy, or colectomy, depending on the affected site. Similar to managing necrotizing fasciitis, this demands highly aggressive surgical intervention, which may lead to significant morbidity. Unfortunately, outcomes remain very poor without immune status restoration, even with aggressive therapies and drastic surgeries. Posaconazole or isavuconazole stands as second-line therapy for mucormycosis. For salvage treatment, posaconazole at 200 mg IV four times daily is recommended. Combination therapy using amphotericin and posaconazole isn't supported by guidelines. Hyperbaric oxygen therapy serves as an adjunct. Elevated oxygen pressure enhances neutrophil activity against the fungus and aids in wound healing. [9, 11]

CONCLUSION

Mucormycosis poses a life-threatening fungal infection with markedly high mortality rates. Its management involves an interprofessional approach, including specialists in infectious diseases, otolaryngology, hematology/oncology, endocrinology, microbiology, specialty-trained nursing, and pharmacists aiding in therapeutic drug administration and monitoring. This collaborative effort across disciplines aims to achieve the best possible patient outcomes. Effective coordination among nurses and clinicians plays a pivotal role in achieving optimal results. However, despite prompt and thorough evaluation and treatment by the interprofessional team, the prognosis often remains unfavorable.

REFERENCES

1. Binder U, Maurer E, Lass-Flörl C. (2014). Mucormycosis-from the pathogens to the disease. *Clin Microbiol Infect*. 20(6), 60-6.
2. Lewis RE, Kontoyiannis DP. (2013). Epidemiology and treatment of mucormycosis. *Future Microbiol.* 8(9), 1163-75.
3. Thornton CR. (2020). Detection of the 'Big Five' mold killers of humans: Aspergillus, Fusarium, Lomentospora, Scedosporium and Mucormycetes. *Adv Appl Microbiol.* 110, 1-61.
4. Katragkou A, Walsh TJ, Roilides E. (2014). Why is mucormycosis more difficult to cure than more common mycoses? *Clin Microbiol Infect*. 20(6), 74-81.

5. Sahota R, Gambhir R, Anand S, Dixit A. (2017). Rhinocerebral Mucormycosis: Report of a Rare Case. *Ethiop J Health Sci.* 27(1), 85-90.
6. Lin E, Moua T, Limper AH. (2017).Pulmonary mucormycosis: clinical features and outcomes. *Infection.* 45(4), 443-448.
7. Castrejón-Pérez AD, Welsh EC, Miranda I, Ocampo-Candiani J, Welsh O. (2017). Cutaneous mucormycosis. *An Bras Dermatol*. 92(3), 304-311.
8. Kang JW, Kim JH. (2016). Dark necrotic mucosa in sinonasal mucormycosis. *Br J Hosp Med (Lond).* 77(1), 51.
9. Farmakiotis D, Kontoyiannis DP. (2016). Mucormycoses. *Infect Dis Clin North Am*. 30(1), 143-63.
10. Long B, Koyfman A. (2015). Mucormycosis: what emergency physicians need to know? *Am J Emerg Med*. 33(12), 1823-5.
11. Skiada A, Lass-Floerl C, Klimko N, Ibrahim A, Roilides E, Petrikkos G. (2018). Challenges in the diagnosis and treatment of mucormycosis. *Med Mycol*.01, 56(1), 93-101.

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