



## A REVIEW ON - MUCORMYCOSIS

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### ABSTRACT

Due to the limited diagnostic tools and treatment options, mucormycosis is difficult to control the infection. Mucormycosis is the third most invasive fungal disease after candidiasis and aspergillosis. It is caused by zygomycosis fungi. The most important species that causes mucormycosis is Rhizopus. The incidence of mucormycosis is approximately 1.7 cases per 1,000,000 inhabitants per year. The clinical diagnosis of mucormycosis is difficult and is usually made in the late stages of the disease or after death. The treatment of mucormycosis requires timely diagnosis, correction of predisposing factors, surgical resection or cleansing as part of source control and appropriate antifungal treatment. Liposome amphotericin B is the drug of choice in this situation. The overall mortality rate of mucormycosis is about 40%.

**KEYWORDS:** Mucormycosis, Types, Treatments, Amphotericin-B, Covid-19.

### INTRODUCTION

Mucormycosis (zygomycosis) is a serious and life-threatening fungal infection that is rarely diagnosed. Many different fungi can cause mucormycosis; Mucormycosis fungal infection is the main cause; therefore, many researchers use the term mucormycosis rather than zygomycosis. Zygomycetes are divided into two orders, Mucorales and Entomophthora. Members of these two orders have very different infections. In general, members of the Mucorales cause acute vascular invasive infections in immunosuppressed patients with a mortality rate of more than 60%. [1] Complications of mucormycosis can be serious: blindness, organ dysfunction, loss of body tissue due to infection and debridement, and death.

## HISTORY

In 1885, the German pathologist Paltauf reported the first case of mucormycosis and described it as mucormycosis. [2] In the 1980s and 1990s, mucormycosis appeared more and more in immunosuppressed individuals. [3] Based on the prevalence rate, a study conducted in France reported an annual increase of 74%. [4] Mucosal infections have reportedly occurred worldwide and the possibility of seasonal changes. [5]

## GENERAL PRINCIPAL

As mentioned earlier, the clinical hallmark of mucormycosis is vascular invasion resulting in thrombosis and tissue infarction/necrosis. Mucormycosis almost always occurs in patients with defective host defenses and/or increased serum iron available, although rare cases have been reported in apparently normal hosts. In most cases, the infection is relentlessly progressive and results in death unless treatment with a combination of surgical debridement and antifungal therapy is initiated promptly. [6-8]

## PATHOPHYSIOLOGY

Mucorales is present in soil and decomposing materials. In people with normal immune function, Mucorales spores that reach the respiratory tract adhere to the nasal mucus and are eliminated by swallowing or sneezing. If there is any wound on the mucosa, polymorph nuclear neutrophils cells engulf and destroy the fungal structure. Neutrophils are the host against these infections; therefore, people with neutropenia or neutrophil dysfunction are at the highest risk. This is common clinically in leukemia patients and bone marrow transplant patients, and they are at the highest risk.

Research on *Rhizopus* rhizome showed that the ketone bodies in these patients re-educate ketones to metabolize so that they can survive under acidic conditions; therefore, fungi develop into hyphae in host tissues and then invade blood vessels. This extensive vascular invasion can lead to vascular thrombosis and tissue necrosis. Diabetic patients often suffer from clinically uncontrollable diabetes and an increase in the amount of circulating glucose, which provides excellent conditions for the rapid development of filamentous structures. These structures first join the blood vessels and then penetrate the blood vessels, which are completely blocked within a few days. Causes extensive avascular necrosis area.

Furthermore, metabolic acidosis prevents polymorph nuclear leukocyte chemo taxis, reducing the activity of phagocytic cells and reducing the local inflammatory response in patients whose immune systems have been compromised by one or more diseases. [9, 10]

## TYPES OF MUCORMYCOSIS

- Rhinocerebral (sinus and brain) mucormycosis- is a sinus infection that can spread to the brain. This form of mucormycosis is more common in uncontrolled diabetic patients and kidney transplant patients.
- Pulmonary (pulmonary) mucormycosis- is the most common type of mucormycosis in cancer patients and organ transplant or stem cell transplant patients.

- Gastrointestinal mucormycosis- is more common in young children than adults, especially premature babies and low-birth-weight babies under 1 month, who have received antibiotics, surgery, or medication, which reduces the body's resistance germs and diseases.
- Cutaneous (skin) mucormycosis: - occurs after a fungus enters the body through a break in the skin (for example, after surgery, burns, or other types of skin trauma). This is the most common mucormycosis in people with an unweakened immune system.
- Disseminated mucormycosis- occurs when the infection is spread through the bloodstream and affects other parts of the body. Infections most often affect the brain, but they can also affect other organs, such as the spleen, heart, and skin. [11-14]

### **RISK FACTORS FOR MUCORMYCOSIS**

- Risk factors for mucormycosis include any debilitating disease processes, especially diseases that can damage blood flow to tissues.
- Typical examples are patients with uncontrolled diabetes and foot ulcers, where dirt or debris can easily reach damaged tissues.
- Patients with burns, malignant tumors, immunosuppressed patients, splenectomy patients and wounds (usually severe) contaminated by soil or ambient water are at increased risk of mucormycosis.
- Therefore, as a group of people injured in environmental disasters, the risk of contracting this disease is high. [15-17]

### **SIGN AND SYMPTOMS IN MUCORMYCOSIS**

Mucormycosis may show the fever, headache, redness and swelling of the skin of the nose and sinuses, black crusts in the eyes, vision problems, and swelling of the eyes, facial pain, and cough sometimes accompanied by bloody discharge or black liquid, shortness of breath and diffuse abdomen. pain., Bloody vomit, sometimes black vomit, abdominal distension, flank pain, ulcers with a dark center and light edges, and changes in mental status.[18-21]

### **COMPLICATIONS**

The complications of mucormycosis can be subdivided into complications caused by the disease itself and complications caused by antifungal therapy. Complications associated with the disease are cavernous sinus thrombosis, disseminated infection, per orbital destruction, palate ulcers, osteomyelitis, and death.

## DIFFERENTIAL DIAGNOSIS

The differential diagnosis of mucormycosis includes maxillary sinus tumor, maxillary sinus aspergillosis, soft tissue infarction, soft tissue radiation necrosis, and other deep fungal infections. [22]

## TREATMENT

Successful treatment of mucormycosis includes rapid and accurate diagnosis, surgical debridement and administration, auxiliary application of hyperbaric oxygen, recombinant cytokine, or granulocyte infusion and prosthetic obdurate. According to Spellberg et al., Currently available monotherapy has a high mortality rate, especially for patients with hematological diseases, so it is recommended to opt for "combination therapy" for mucormycosis. Antifungal therapy includes AmB Dexycholate, AmB liposomes (510 mg / kg), AmB lipid complex, AmB colloidal dispersion, posaconazole (400 mg twice daily), and treatment of central diseases. Second-line treatment includes a combination of caspofungin and AmB lipid and a mixture of AmB lipid and posaconazole, the combination with Deferasirox is not recommended. The starting dose of Amphotericin B is 1 mg, which is slowly injected into the vein within 10-15 minutes at first and then given once a day based on body weight for the next 14 days. It may need to last longer. Isaconazole and posaconazole are alternatives. [23-27]

## COVID-19-ASSOCIATED MUCORMYCOSIS

During the COVID19 pandemic in India, this disease is becoming another major health emergency. The Government of India reported that as of May 25, 2021, more than 11,700 people are being treated for mucormycosis. Many Indian media refer to it as the "black fungus" because this fungus causes a black discoloration of dead and dying tissues. Even before the COVID19 pandemic, the incidence of mucormycosis in India was estimated to be about 70 times higher than in other parts of the world. [28] [29] Due to the rapid increase in the number of cases, many Indian state governments have declared it an epidemic. [30] The number of cases of mucormycosis, aspergillosis, and candidiasis related to COVID19 immunosuppressive therapy were reported during the 2020 and 2021 COVID19 pandemics in India. [31] [32] a review of the association between mucormycosis and COVID19 in early 2021 reported 8 cases of mucormycosis: 3 cases in the United States, 2 cases in India, and 1 case in Brazil, Italy, and the United Kingdom. [32] The most common underlying disease is diabetes. [32] Most people are hospitalized with severe respiratory problems caused by COVID19, recover, and develop mucormycosis within 10 to 14 days after receiving COVID19 treatment. . Five renal function tests are abnormal, three affect the sinuses, eyes and brain, three affect the lungs, one affects the gastrointestinal tract, and one affects extensively. [32] In two of the seven deaths, the diagnosis of mucormycosis was made after death. [32] The fact that the three had no traditional risk factors led the author to question the use of steroids and immunosuppressive drugs. [32] In May 2021, the BBC reported an increase in cases in India. [33] In May 2021, the Medical Research Council of India issued guidelines for the identification and treatment of COVID19-related mucormycosis. [34] As of June 8, 2021, more than 28,252 people from 28 states have been confirmed to have mucormycosis, and hundreds of people have died. Of these cases, 86% (24,370) had a history of sarscov2 infection, and 62.3% (17,301) had diabetes. [35]

## CONCLUSION

To summarize, mucormycosis is a disease that is typically aggressive and has a high fatality rate. Clinicians are still having difficulty diagnosing this condition. However, given the disease's high mortality rate, (I) early and rapid identification, (ii) recovery from predisposing factors, and (iii) early intervention with surgical debridement and therapeutic medications are the only options for improving the situation.

## REFERENCES

1. Herbrecht R, Letscher-Bru V, Bowden RA et al. Treatment of 21 cases of invasive mucormycosis with amphotericin colloidal dispersion. *Eur J Clin Microbiol Infect Dis* 2001;20:460–6
2. Mohammad R, Nazeri M, Sayedayn SM, Ehteram H. A successful treatment of rhino cerebral mucormycosis due to *Rhizopus oryzae*. *Journal of research in medical sciences: The Official Journal of Isfahan University of Medical Sciences*, 2014; 19(1): 72.
3. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, Sein M, Sein T, Chiou CC, Chu JH, Kontoyiannis DP. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clinical Infectious Diseases*, 2005; 41(5): 634-53.
4. Bitar D, Van Cauteren D, Lanternier F et al. Increasing incidence of zygomycosis (mucor-mycosis), France, 1997–2006. *Emerg Infect Dis.*, 2009; 15: 1395–1401.
5. Petrikos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. *Clinical Infectious Diseases*, 2012; 54(suppl\_1): S23-34.
6. Larsen, K., C. von Buchwald, B. Ellefsen, and D. Francis. 2003. Unexpected expansive paranasal sinus mucormycosis. *ORL J. Otorhinolaryngol. Relat. Spec.* 65:57-60
7. Lee, F.Y., S.B. Mosad, and K. A. Adal. 1999. Pulmonary mucormycosis: the last 30 years. *Arch. Intern. Med.* 159:1301-1309
8. A. Skiada, H. Sambatakou, A. Toskas, G. Vaiopoulos, M. Giannopoulou, and N. Katsilambros. 2003. Mucormycosis: ten-year experience at a tertiary-care center in Greece. *Eur. J. Clin. Microbiol. Infect. Dis.* 22:753-756
9. Katragkou A, Walsh TJ, Roilides E. Why is mucormycosis more difficult to cure than more common mycoses? *Clin Microbiol Infect.* 2014 Jun; 20 Suppl 6:74-81.
10. Lin E, Moua T, Limper AH. Pulmonary mucormycosis: clinical features and outcomes. *Infection.* 2017 Aug; 45(4):443-448.
11. Song Y, Qiao J, Giovanni G, Liu G, Yang H, Wu J, and Chen J. Mucormycosis in renal transplant recipients: review of 174 reported cases. *BMC Infect Dis.* 2017 Apr; 17(1): 283.

12. Abdalla A, Adelman D, Fahal A, Verbrugh H, Van Belkum A, De Hoog S. Environmental occurrence of *Madurella mycetomatis*, the major agent of human eumycetoma in Sudan external icon. *J Clin Microbiol*. 2002 Mar; 40(3): 1031–1036.
13. Vallabhaneni S, Mody RK. Gastrointestinal mucormycosis in neonates: a review external icon. *Current Fungal Infect Rep*. 2015.
14. Francis JR, Villanueva P, Bryant P, Blyth CC. Mucormycosis in children: review and recommendations for management external icon. *J Pediatric Infect Dis Soc*. 2018 May 15; 7(2):159-164
15. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases external icon. *Clin Infect Dis*. 2005 Sep 1; 41(5):634-53.
16. Petrikos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis external icon. *Clin Infect Dis*. 2012 Feb; 54 Suppl 1:S23-34.
17. Walsh TJ, Gamaletsou MN, McGinnis MR, Hayden RT, Kontoyiannis DP. Early clinical and laboratory diagnosis of invasive pulmonary, extra pulmonary, and disseminated mucormycosis (zygomycosis) external icon. *Clin Infect Dis*. 2012 Feb; 54 Suppl 1:S55-60.
18. Petrikos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis external icon. *Clin Infect Dis*. 2012 Feb; 54 Suppl 1:S23-34.
19. Lewis RE, Kontoyiannis DP. Epidemiology and treatment of mucormycosis external icon. *Future Microbiol*. 2013 Sep; 8(9):1163-75.
20. Spellberg B, Edwards Jr. J, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation, and management external icon. *Clin Microbiol Rev*. 2005 Jul; 18(3):556-69.
21. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease external icon. *Clin Microbiol Rev* 2000; 13:236-301.
22. Sciubba JJ, Regezi JA, Rogers RS. PDQ oral disease: diagnosis and treatment. *PMPH-USA*; 2002.
23. Spellberg B, Ibrahim A, Rolides E, Lewis RE, Lortholary O, Petrikos G, Kontoyiannis DP, Walsh TJ. Combination therapy for mucormycosis: why, what, and how. *Clinical infectious diseases*, 2012; 54(suppl 1): S73-8.
24. Skiada A, Lanternier F, Groll AH, Pagano L, Zimmerli S, Hambrecht R, Lortholary O, Petrikos GL. Diagnosis and treatment of mucormycosis in patients with hematological malignancies: guidelines from the 3rd European Conference on Infections in Leukemia (ECIL 3). *Hematological*, 2013; 98(4): 492-504.

25. Sipsas N, Gamaletsou M, Anastasopoulou A, Kontoyiannis D. Therapy of mucormycosis. *Journal of Fungi*, 2018; 4(3): 90.
26. BNF (80 Ed).BMJ group and the pharmaceutical press. September 2021-March 2021.p.629-635.ISBN 978-0-85711-369-6
27. M.C. Donald, Philip J. (September 10, 2018). "What is the role of isavuconazole (Cresemba) in the treatment of mucormycosis (zygomycosis)?" [Www.medscape.com](http://www.medscape.com). Retrieved May 25, 2021.
28. Dyer, Owen (May 13, 2021). *J (Clinical Research Ed.)*. **373**: n1238. doi ;10.1136/bmj.n1238. ISSN 1756-1833. PMID 33985993.
29. Lan Schwartz "Covid-19: India sees record deaths as 'black fungus' spreads fear". BM, Arunaloke Chakrabarti (June 2, 2021). "'Black fungus' is creating a whole other health emergency for Covid-stricken India". *The Guardian*. Retrieved June 3, 2021.
30. Delhi/Jaipur/Lucknow May 19, Dev Ankur Wadhawan Pankaj Jain Samarth Shrivastava Kumar Kunal New; May 19, 2021 UPDATED; *Fist*, 2021 17:51. "Rajasthan declares black fungus an epidemic; cases pile up in several states | 10 points". *India Today*. Retrieved May 20, 2021.
31. *Quarterly Current Affairs Vol. 4 - October to December 2020 for Competitive Exams*. **4**. Disha Publications. 2020. p. 173. ISBN 978-93-90486-29-8.
32. Garg, Deepak; Muthu, Valliappan; Sehgal, Inderpaul Singh; Ramachandran, Raja; Kaur, Harsimran; Bhalla, Ashish; Puri, Goverdhan D.; Chakrabarti, Arunaloke; Agarwal, Ritesh (May 1, 2021). "Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature". *Mycopathologia*. **186** (2): 289–298. doi; 10.1007/s11046-021-00528-2 (inactive May 25, 2021). ISSN 1573-0832. PMC 7862973. PMID 33544266.
33. Biswas, Soutik (May 9, 2021). "Mucormycosis: The 'black fungus' maiming Covid patients in India". *BBC News*. British Broadcasting Corporation. Retrieved May 11, 2021.
34. "ICMR releases diagnosis and management guidelines for COVID-19-associated Mucormycosis". First post. May 17, 2021.
35. "28,252 cases of black fungus detected so far, says Centre". *Mint*. Retrieved June 9, 2021.