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A Concise Review on Mucormycosis

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Abstract

Mucormycosis is a serious life-threatening angioinvasive infection caused due to mucormycosis. It is a very rare disease but occurs in patients who are immunocompromised which is because of neutropenia, diabetic ketoacidosis, increase serum level of available iron, and organ transplantation. For this reason, the doctor needed a high index of distrust to diagnose a malady in anyone case even if these risk factors are present in patients. Mucormycosis is categorized into rhinocerebral, cutaneous, pulmonary, gastrointestinal, and disseminated types. Even though by giving aggressive treatment, the overall mortality rate is high. In this addendum, we overview the latest knowledge on toxic properties taken by the very general etiology of mucormycosis, *Rhizopus oryzae*, because patients are highly susceptible to mucormycosis. The purpose and main aim of this review are to overview and fatality of mucormycosis, types, etiology, epidemiology, pathophysiology, pathogenesis, host defense against mucormycosis, iron uptake, and mucormycosis pathogenesis, risk factor, diagnosis, and treatment methods.

Keywords: Diabetes mellitus, Diagnosis, Mucormycosis, Risk factors

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Introduction

Mucormycosis is also called zygomycosis. The American pathologist Baker R.D. coined the term mucormycosis, which can be defined as a dangerous mycosis attributable to representatives of the mucous membranes and zygotes.[1] Mucormycosis is increasingly common in immunocompromised people. There are reports of a significant increase in mucormycosis throughout the country during hospitalization and after discharge from COVID-19 patients.

Types of Mucormycosis

Mucormycosis infection in humans is of two types: (1) Superficial and visceral and (2) localized and disseminated. Superficial forms appear on the nails, outer ear, and skin. The visceral types manifest themselves as a type of rhinocerebral, pulmonary, and gastrointestinal types.

Rhinocerebral Mucormycosis

Rhinocerebral mucormycosis is caused by filamentous fungi. The infection begins in the sinuses, resulting in subsequent inhalation of spores, which expands toward the cerebrum and then to the sinuses, nose, eyes, and affected people.[2] Clinically, non-encephalopathy presents with orbital headache, tingling, fever, facial pain, hypothermia, nasal congestion, and black discharge. Mucormycosis initially mimics bacterial sinusitis. Subsequent symptoms result in damage to the orbital nerves and blood vessels, including double vision, loss of vision, and loss of consciousness. Non-cerebral disorders are commonly found in patients with diabetes, especially ketoacidosis, malignant neoplasms associated with neutropenia, and solid organ transplants. Cellulite of the face and swelling of the orbit in rhinoceros brain disease progress. Necrotic scabs with purulent black discharge in the nasal cavity, soft palate, and face. Protrusion, chemosis, ptosis, and ophthalmoplegia show retro-orbital dilation. Cranial nerves such as V and VII are most often affected by non-cerebral diseases.[3] Black necrotic mounds are a sign of mucormycosis in Figure 1; however, the absence of these data cannot eliminate the possibility of developing mucositis. Fever is intermittent and may be up to half absent. The leukocyte total normally increases when a person's bone marrow is functioning. Patients may develop a slowly progressive form of nasal-orbital-cerebral mucositis lasting more than 4 weeks with signs and symptoms. Harrill *et al*., a study of 18 cases of chronic mucositis identified an average of 7 months, showed that the duration of symptoms persists. About 67% of patients were diabetic and 83% had signs of coronary artery thrombosis. However, the overall survival was 83%. The use of intravenous drugs puts the patient at risk of isolated cerebral mucormycosis. Effective treatment comprises advance identification, the rectification of major reversible diseases, antimycotic treatment, and abscission removal. Mortality in rhino-orbitocerebral mucormycosis is about 30–69%. Sometimes, nebulized amphotericin B is used as an adjuvant to surgical, endovenous vesicle amphotericin B in sinus mucormycosis.

Cutaneous Disease

Cutaneous mycosis is caused by direct ingestion regarding conidiospore within the skin and causes disseminated diseases. Skin mucositis is categorized in compliance with a degree of

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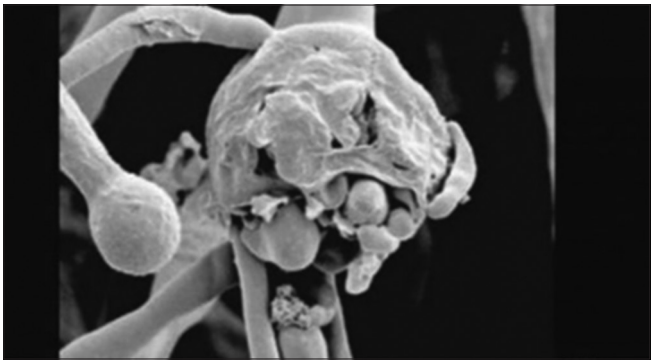

Figure 1: Structure of Mucormycosis

infection. Clinical symptoms of dermatosis include cellulite, erythema, induration, dermal necrosis, and black stone. Patients with skin conditions may possess one past regarding trauma or maybe exposure toward polluted clinical devices such as dressings. Rarely, the disease occurs near the area concerning catheterization or injection of insulin or illegal drugs. "Predisposition includes diabetes, leukemia, and organ transplants." Mucormycosis of the skin is the least associated form of infection. Diabetes occurred in 26% of cases of cutaneous, 67% of cases of non-cerebral, 21% of cases of general, and 20% of cases of the lung. Leukemia and/ either thrombocytopenia remain to begin in 16 cases of skin, 16% of cases of the nasal cerebral lesion, 42% disseminated cases, and 48% of cases of pulmonary disease. Cutaneous mucositis could be apparent as a tinea capital. It can manifest as pimples, vesicles, swelling, gangrene ulcers, genital-like lesions, gangrene, or necrotizing cellulitis. Dermatological observations are needed to assemble the diagnosis. Staining of fungal cultures and wound swabs is insensitive and can lead to erroneous microbiological results.[4]

Pulmonary Disease

Pulmonary mycosis is radiographically similar to chlamydiosis. The pair of contaminations lean to occupy arteries and veins which cause thrombosis. Radiographic signs include infiltration, wedge consolidation, nodules, cavitation, mycelium, and flap collapse. Pulmonary mucormycosis is clinically non-specific and manifests itself such as dyspnea, hemoptysis, fever, chest pain, cough, and necrosis. It is commonly seen inside sufferers among blood cancer, neutropenia, and bone marrow transpose and is often associated with sinus involvement. In rare cases, especially with diabetes, mycosis of the lungs can manifest itself as damage to the trachea or bronchi.[5]

Gastrointestinal Disease

Infections of the lining related to the alimentary canal may take place all over inside the digestive system, but usually affect the ileum, stomach, and large intestine. Clinical signs are non-specific and involve stomachache, windiness, gastric perforation, gastrointestinal bleeding, nausea, and vomiting. Occlusion or bloody stools may also appear. Some patients are prone to palpitations, rupture, and peritonitis. This is especially true for malnourished premature babies, diabetes, organ transplants, blood cancers, and premature babies who have previously taken corticosteroids. Drinking alcoholic beverages, fermented porridge, and the absorption of pathogens from foods including curdled milk and dry baked goods can cause gastrointestinal mucinosis. One-third of gastrointestinal mucormycosis occurs in infants.[6]

Disseminated Disease

With disseminated mucormycosis, the infection can be transmitted blood flow from one institution toward another. Mucositis is a common disease of the pleura, ossein, heart, kidneys, brain, liver, spleen, and other organs. Burns and extensive skin lesions can also occur. This occurs especially in sufferers among ferrous overwhelm receiving certain deferoxamine (DFO), severe immunosuppression in allogeneic stem cell recipients, neutropenia, acute leukemia, and corticosteroid usage. Patients with neutropenia, leukemia, or lymphoma make up seniority about tolerance including disseminated mucormycosis. Other risk factors for prevalence are organ transplantation, chemotherapy, corticosteroids, and DFO therapy.[7]

An Abnormal Constitute about Zygomycosis

Endocarditis is mainly due to artificial cocks, in addition, to bringing about arterial thrombosis, utilization of intravenous drugs is a risk factor. Osteomyelitis occurs after surgery or traumatic vaccination and occurs in the tibia, femur, humerus, calcaneus, scapula, metacarpal bones, phalanges, and sternum.

Etiology

Swallowing or inhaling spores cause mucormycosis. It contagious malady occurs due to mold order Mucorales and the class of Zygomycetes. *Apophysomyces (Anabaena variabilis), Cunninghamella (Cunninghamella bertholletiae), Mucor (Mucor circinelloides),* and *Rhizopus (Rhizopus arrhizus* [*oryzae*] and *Rhizopus microsporus)* are the greatest frequently secluded species from *S. vasiform*. There is a frequent territory animal that serves as unaffected by an immunocompetent human. Patients with significant immunodeficiency (e.g., HIV, transplant recipients, patients taking chronic steroids or disease-controlling antihypertensive drugs, sufferers including myeloid/other cancers, patients having cuts, and burns) can develop rapidly progressive necrotic infections. People with uncontrolled diabetes, especially such having a history of diabetic ketoacidosis, are also at a higher risk. It is incursive zygomycosis originated by *Actinomycetes elegance*. The genus Basidiobolus usually causes chronic subcutaneous infections of the thighs, buttocks, and/or trunk, and rarely an alimentary canal. Subdivision Conidiobolus give rise to chronic infections of the nasal sheath along with hypodermis as far as nares and face.[8]

Epidemiology

In recent years, the epidemiology of onychomycosis has changed with an increase in morbidity, exposure to current causes, and vulnerable populations. This growth was felt throughout the world but was particularly strong in the Asian continent. Although diabetes outweighs all other risk factors in Asia, post-tuberculosis and chronic renal failure have emerged as new risk groups. Most human diseases are produced due to inhalation of airborne fungal sporangia or direct infection by the body of damaged skin or mucous membranes. Mucorales are mostly

ubiquitous, but their exact ecology is uncertain and is found in heat resistant and decaying organic matter. Mucormycosis is a disease that has been documented all over the world. There may be seasonal fluctuations in mucosal infections. In high-risk patients in whom, for example, in sufferers who collect syngeneic bone marrow transplantation, mucositis has spread from 2 to 3%. There is also a transition from the dawn of society to the onset of illness in the hospital. In hospitals, mucic acid is used in a variety of hospital procedures, including iatrogenic immunosuppression and antifungal prophylaxis, medicated dressings, and intravenous catheters and even voice suppressors. An unexpected increase in zygomycosis had observed in transplant centers.[9]

Pathophysiology

People can get fungal infection by breathing in microscopic spores from the environment. Most people breathe in spores every day without getting sick. However, people with weakened immune systems or lung diseases are at a higher risk of developing health problems. When the mucous membrane is damaged, polymorphonuclear neutrophils destroy the phagocytes of the fungus. Neutrophils are the host's defense against this infection. Thus, patient with thrombocytopenia is at greater risk. Clinically, this is the highest risk in patients with leukemia and bone marrow transplant. Research on *R. arrhizus* has shown that the ketone bodies present in these patients are metabolized by ketone reductase, allowing them to survive in the acidic stipulation. In this way, the fungus forms mycelium in the host tissue and then penetrates the blood vessels. Diabetic patients usually have clinically uncontrolled diabetes mellitus and elevated levels of circulating glucose, which initially creates vascularized fibrous structures. This causes large area ischemia. Metabolic acidosis also prevents polymorphonuclear leukocyte chemotaxis, decreases phagocytic activity, and decreases local inflammatory responses in patients who are immunodeficient.[10]

Virulence Traits and Pathogenesis

Phagocytes and heterophils perform the main part in the immune defense against the pathogens of mucormycosis. Thus, prolonged neutropenia is one of the greater threat elements to the evolution of this disease. In addition, therapeutic interventions such originate working fault into phagocyte and leukocyte (e.g., corticosteroid therapy) are extra threat components toward mucormycosis. According to Casadevall and Pirofski, "Quantitative and qualitative indicators of toxicity depend on host factors, microbial factors, environmental factors, social factors, and interactions between themselves." This concept is especially relevant when considering opportunistic pathogens such as fungi. Diabetes itself can impair neutrophil function and contribute toward this seriousness regarding zygomycosis into sufferer having hyperglycemia. Uncountable major malady recorded atop while susceptibility to mucormycosis is associated with ferrous excess by caused of excess tissue iron increased serum delivery chains or elevated levels of undelivered iron. Iron is required for Mucorales, which can enhance heightening and expansion connected with mycelium *in vitro* or increase pathogenicity *in vivo*. Hemodialysis tolerant feasted by ferrous heterocyclic compound DFO is particularly at risk of mucormycosis, and Boelaert *et al*. found a high mortality rate (89% of patients) inside 46 tolerant which establish serious mucormycosis during DFO treatment. *Rhizopus oryzae* is the very common organism isolated from a patient with mucormycosis which is responsible for ~70% of the full instance of zygomycosis.[11]

Host Defense

Mononucleate and granular leukocytes of normal hosts produce aerobic glucuronide, protonated endorphin defensins to kill Mucorales. Clinical evidence suggests a well-known scavenger cell serves as the primary hostess protection method in opposition to mucormycosis. For example, there are various people with neutropenia and phagocytic dysfunction which is on the greater possibility of developing myxomatosis. Furthermore, typical hosts' mononucleate and granular leukocytes destroy Mucorales besides constructing aerobic glucuronide and protonated peptides known as defensins. In contradict, patients with acquired immune deficiency syndrome do rarely showing toward a greater chance of onychomycosis. This is shown by the current research that contagion of neutrophils to *R. oryzae* hyphae activates declaration attributed to damage such as receptor-2 and strong expression of the inflammatory gene as a result of quick induction of the NF-B pathway gene. Due to the hyperglycemia and low pH encountered into tolerance with hyperglycemia, phagocytes become dysfunctional and disrupt chemotaxis and intracellular death, which is impaired by oxidizing and non-oxidizing methods. These clinical observations show that mucormycosis does not develop even in immune animals that inhale Mucorales sporangiospores. In animals with immunodeficient corticosteroids, death occurs due to progressive pulmonary infection and hematogenous spread. The exact mechanisms of phagocyte destruction in ketoacidosis, diabetes, and corticosteroids remain unknown. Moreover, phagocytic infirmity is singly unable to describe superior occurrence about onychomycosis in patients with DKA, since the frequency of mycoses inside such sufferer does higher than in infections caused by other pathogens.[12]

Role of Iron

Zygomycetes have toxic factors that can cause disease in the body. One such characteristic could absorb ferrous out of entertainer. In mammalian hosts, iron binds to transport proteins, for example, lactoferrin. This sequestration prevents harmful results about free iron. This strategy of restricting the accessibility of ferrous is also an important universal mechanism of host defense against microorganisms, especially Mucorales, since *R. oryzae* grows poorly on normal exogenous serum-free glands. Hypersensitivity to onychomycosis in a sick person has increased plasma iron levels. They obsolete familiar for 20 years that patients taking iron chelator DFO have a significantly increased incidence of invasive mucormycosis. Role of iron metabolism in the pathogenesis of mucormycosis suggests the possibility of utilizing effective iron chelators as adjunctive antifungal therapy against *R. oryzae*. They used DFO as siderophores to provide the fungi with previously unavailable iron. *Rhizopus* sp. It can store 8–40 times more ferrous provided through deferral compare to *Aspergillus fumigatus* or *Candida albicans*, which increases the absorption of iron by *Rhizopus* spp. Linear correlation with serum increases. Animal model data also highlight the extreme iron requirement for the pathogenicity of *Rhizopus*, since the intake of desperate increases endurance charge about *Rhizopus* spp. infected animals. People with diabetic ketoacidosis are appearing in a higher chance of non-cerebral mucormycosis. Many data support the conclusion that serum iron levels are elevated in patients with

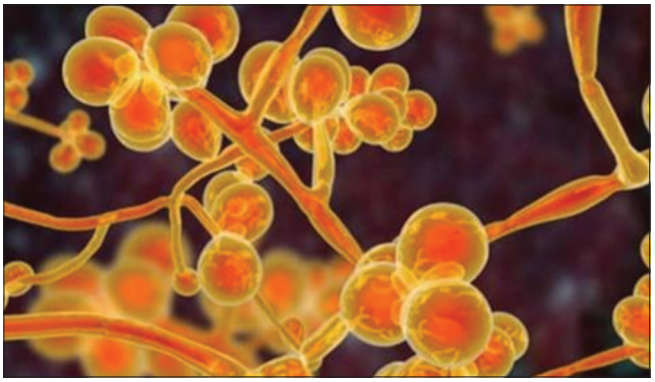

Figure 2: Structure of yellow fungus

the liberation related to ferrous through protein-binding contiguity to the acidic environment which may induce acidosis. DFO removes iron from transferrin and binds to the substrate through inducible receptors, and iron is conveyed within corpuscle due to the active reduction of the ferric form toward the greater solvable structure of iron. According to these results, the use of DFO worsened the survival of guinea pigs infected with *Rhizopus*, but not guinea pigs infected with *C. albicans*. In addition, *in vitro* studies of the absorption of radiolabeled serum iron by DFO showed that *Rhizopus* can absorb 8 and 40 times more iron than can *A. fumigatus* or *C. albicans*. Finally, the chief threat element to the occurrence of mucositis during transplantation is a basal myelodysplastic syndrome, which is caused by ferrous overburden due to frequent plasma exchange, which makes patients more susceptible to the disease. Fungi can extract iron from hosts using high sympathy ferrous permeases or less molecular weight iron chelators. High-affinity iron permease has existed inside mold comprised reduction system that contains an excess of surface reductase that reduces ferrous toward a greater solvable structure of iron. Reduced iron produced by surface reductase is, in turn, captured by a protein complex consisting of multicopper oxidase and iron permease. Another method besides thus mold gains ferrous through an entertainer using heme.[13]

Risk Factors in Patients with Mucormycosis

Just backdated education was accessible till recently to determine threat components for mucositis patients. Prolonged neutropenia, underlying leukemia, retard starting about polyene treatment, and utilization about fungicidal treatment other than lipoid preparations about amphotericin were all connected alongside prominent chance about the end in those trials. The results of the first randomized, controlled trial on mucormycosis patients were recently published. The results of the experiment revealed that patients who were given deferasirox had a significant death rate.[2]

Crucial Threat Elements for Zygomycosis

- Tumors of the hematopoietic and lymphoid tissues
- Blood cancer
- Carcinoma
- Myelomatosis
- Thrombocytopenia
- Epidemiological immunocompromisation
- Anticancer radiotherapy
- Adrenal cortical steroid treatment
- Antirejection treatment
- Solid organ transfer
- Desferal treatment
- Blaze
- Injury
- Malnourishment inside the youngster
- Endovenous medicine usage

Diagnosis

Nuclear magnetic resonance imaging of the sphenoid depression and cerebral contrast study is the radiological study used for diagnosis of rhino-orbital-cerebral mucormycosis, and simple computerized tomography about the chest is used to recognize pneumonic mucositis. In histopathological diagnosis, the biopsy appropriate to damaged stuff is important to identify mucormycosis. Microscopic examination is important for the initial recognition of mucormycosis. This is carried out using a stain containing eosin and a blue dye.[14]

Clinical Diagnosis

Mucositis can be attributed to gangrene by cause of vascular lesions and thrombosis, but the absence of a necrotic slope refuses to eliminate identification. Necrotic skin wounds inside immunosuppressed sufferers perhaps occur due to onychomycosis, but distinctive recognition comprises further microorganisms such as *Aspergillus*, *Fusarium*, *Pseudallescheria*, and *Scedosporium*. Sick persons having type 1 diabetes and sinus infection have been carefully evaluated for the possibility of mucositis. Recognition and cure of rhinocerebral mucormycosis in juvenile diabetes tolerant are proposed. Their symptoms include double vision, sinus pain, bulging eye, periorbital edema, apex syndrome, or palate ulcers. If these signs are found, additional tests are immediately needed, comprising plasma trial, picturing, eye and/or sinus surgery, endoscopic correction, and beginning regarding fungicidal therapy. It should be noted that diabetes with or without ketoacidosis is the main disease of non-cerebral mucormycosis, yet this is to happen inside patients with malignant neoplasms, HSCT or SOT recipients, and other immunocompromised patients. Another imaging technique that is not widely used is positive electron excretion imaging using [18F]-fluorodeoxyglucose (FDG).[15]

Routine Laboratory Diagnosis

Laboratory diagnosis of mucormycosis in clinical practice includes histopathology, direct examination, and wet culture.

Histopathology

It can be the most chief symptomatic instrument because this is essential to determine the presence of fungi as pathogens in cultured samples of contaminants and to determine vascular invasion. It may also indicate a concomitant infection with other forms. The genus Mucorales is usually not pigmented (5–20 μm) and forms thin-walled hyphae, usually not pigmented, unlike *Aspergillus* species or other forms of the vitreous, and vertically branched with or without septa, 3 ~ 5 m wide, split, and from sharp branches. Spots that can help highlight the fungal wall include methenamine silver Grocott (GMS) and periodic acid–Schiff (PAS), although PAS makes surrounding tissue more visible than GMS.

Direct Microscopy

A straight microscope with a KOH absorber shelf can be used to quickly diagnose suspected mucormycosis. For materials sent to clinical laboratories, it is preferable to use fluorescent brighteners such as Blankophor and Calcofluor white with KOH, which visualize the properties of fungal hyphae when fluorescence microscopy is required. Direct microscopy about new substances is a cheap but very valuable method during early identification and definitive determination of the surgical site of intraoperative invasive fungal infections, which is actively utilized by the batch of experts (ECMM/MSG ERC) with histopathologists.[16]

Culture

Specimen culture is essential to recognize onychomycosis as it determines the genus and species levels and ultimately allows fungal susceptibility testing. Most medically important mucous membranes are heat resistant and can grow rapidly at 37°C. They grow on almost all carbohydrate substrates, colonies usually appear within 24–48 h, and identification is based on colony morphology, microscopy, and growth temperature. The detection of MALDI-TOF in cultured mucous membranes is a promising method in well-equipped laboratories. Positive cultures from sterile sites confirm the diagnosis, while useful cultures through barren sites may be associated with contamination. Therefore, false-positive results must be recycled by caution, especially if cellular pathology is never accessible. Correct sampling and handling of samples before testing are prerequisites for optimal results. Therefore, in case of doubt, good communication and near compliance with the physician and the microbiological laboratory are essential to make certain that total stages of the diagnostic procedure were executed suitably.[17]

Description of Superbugs

Black Fungus or Mucormycosis

Mucormycosis exist as a probably lethal fungal disease caused by Mucorella and Zygomycota fungi. The American pathologist RD Baker coined the name myxedema, also known as zygomycosis. Mucositis is linked by the breakdown of organic matter such as animal droppings and occurs primarily in the soil. Ear auricularia is a very commonly eaten mushroom in the world. Polysaccharides, melanin, polyphenols, and flavonoids should be a few beneficial nutrients they contain. Hence, onychomycosis is considered one of the nutrient-rich and pharmacologically active fungi with immune stimulating, anti-inflammatory, antiviral, anticoagulant, and cancer suppressing effects as lead constituents about herbal medicine.[18-20]

White Fungus

Candidiasis, often known as white mold, is a dangerous fungal infection. White mold, so-called incursive moniliasis, can damage the blood, heart, vagina, brain, ocular, and osteo etcetera organs in the body. Candidiasis is a fungal contamination coming from *Candida fungus*. *Candida* is established on the skin, as well as on the body, including the intestines, mouth, vagina, and throat, beyond creating anyone complication. *Candida* causes an infection, and if it continues to develop, the infection becomes unmanageable. This is called an *Aspergillus* flavus infection. Infectious Disease Expert Sanjay Pujari, a member of the National COIVD-19 Working Group, argues that the use of the white mold to treat candidiasis or other diseases associated with candidiasis is a total misconception. Fungal infections caused by *Candida* are easily treated with inexpensive oral antifungal drugs.[21,22]

Yellow Fungus

"The secondary ripple about COVID-19 has finally slowed down thanks to daily cases in India." However, new fungal diseases have emerged, the latest of which is an outbreak of deadly yellow mold. *Mucor septicus* is another name for yellow mold (Figure 2). It is a fungus that, according to experts, infects "reptiles like lizards" without affecting humans. If not treated immediately, this fungus will attack the body and vital organs. This causes organ failure and acute necrosis. A yellow yeast infection can damage vital organs in the body. Compared to other fungal infections, yellow mold affects the inner parts of the body. "These properties of yellow mold often help delay diagnosis," said Doctor According to ANI Thiaghi. The characteristics of this yellow mold can be hard to conduct as early detection is essential in such situations. Yellow mold, like the other two, is caused by dirty environments, steroids, and other medications.[23,24]

Green Fungus

Green mold, often known as aspergillosis, is a mycosis that occurs due to the common indoor fungus, *Aspergillus niger*. Aspergillosis is transmitted to the environment by inhalation of small *Aspergillus* spores. People with weakened immune systems or lung disease are more likely to suffer from *Aspergillus*. Doctors say that additional experiments are required to determine if the type of green fungus infection in patients recovering from COVID is different from other patients. However, experts disagree on the color code of *Aspergillus* mold. "According to Dr. P. V. Pandey (MGM Medical Sector Director), no color coding. The only difference is that they occur due to *Aspergillus* as well as cause mucormycosis." According to Dr. Ravi Dozi, Sri Aurobindo Institute of Medical Sciences Respiratory System (according to HOD data), fungal infections do not affect body tone. Anita Muta (HOD Microbiology Department, MGM) gets its name from the flowers that appear when grown and tested in the laboratory. There are green, yellow, black, and porcini mushrooms, but there are all kinds of mucositis, Cinderella, and *Aspergillus*. He also said that Mushroom produces black flowers, Cinderella produces white flowers, and *Aspergillus* produces various types of green and yellow flowers.[25-27]

Symptoms

Since green mold is a rare disease, there are fewer infections, but several symptoms may explain this infection. Symptoms of a green fungal infection include nosebleeds, severe fever, insufficiency, and excessive weight loss.

Treatment

Antifungal Treatment

The only *in vitro* mucosal antifungal agents are amphotericin B (Amb) and its lipid constituents, as well as Posaconazole. Recently, a new antifungal drug isavuconazole has been added to our arsenal. Liposomal Amb (L-Amb) is the preferred antifungal agent after oral or intravenous administration.[28]

Immunostimulating Drugs

According to a case study, an immunocompetent patient with severe abdominal mucositis resistant to conventional therapy was recently treated with checkpoint inhibitors nivolumab and interferon-Y. Another additive is hyperbaric oxygen. CT scans (of the lungs/sinuses) can be viewed and performed.

Treatment of White Fungus

The white fungus, often known as *Candida*, is usually easy to treat. Unless the immune system does not work properly or *Candida* has migrated to your bloodstream, you do not need to be hospitalized. The following is a classification of antifungal agents used to treat *Candidiasis*.[29]

Systemic Antifungal Agents

1. Amphotericin B
2. Pyrimidine Analog: Flucytosine.
3. Triazoles: Flocazole, itraconazole, voriconazole, posaconazole, and ketoconazole.
4. Echinocandins are caspofungin, anidulafungin, and micafungin.

Topical Antifungal Agents

1. Topical azoles: Terconazole, butaconazole, miconazole, clotrimazole, tioconazole, sulconazole, oxiconazole, and econazole.
2. Topical allylamines: Terbinafine and naftifine. One of the selection criteria for the antifungal agents is *Candida* species susceptibility.[30]

Treatment of Yellow Fungus

Because yellow fungus is a relatively novel fungal ailment, little information is currently accessible. Infection with a fungus individual with compromised and pre-existing conditions thrives. Diabetes patients should maintain a healthy blood sugar level. They must guarantee that they are surrounded by hygienic conditions. Make certain that all surfaces have been disinfected. Remove any old food or stale if possible. If you're on oxygen, ensure your oxygen is filtered properly and your water filter is clean and changed regularly. Medication and steroid use should be maintained to a minimum. Because this ailment is new in India, more information regarding yellow fungus therapy is unavailable at this time. Patients are currently recommending the use of various common medications. These medications should only be used if medical practitioners prescribe them. Amphotericin B injection, a broad-spectrum antifungal medication, is currently being employed by charitable doctors in contemporary therapies. Only take amphotericin B injections if your doctor recommends it.[31]

Treatment of Green Fungus

If you have any green fungus on your body, then please set up an appointment with your doctor as soon as available. Be cautious and seek medical advice if necessary. The first patient with green fungus is being treated in Mumbai, and then, the treatment details for green fungus will be revealed.[32]

Conclusion

Thus, mucormycosis is becoming progressively usual contamination within immunodeficient patients. This disease is causing alarming mortality. The true etiology varies around the world, and diagnosis of the disease remains a challenge for clinicians. Thus, the most severe form of mucositis and its subsequent course largely depends on the effectiveness of the host's immune system.

Conflicts of Interest

The authors declare no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

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References

1. Kwon-Chung KJ. Taxonomy of fungi causing mucormycosis and entomophthoramycosis (zygomycosis) and nomenclature of the disease: molecular mycologic perspectives. Clin Infect Dis 2012;54:8-15.
2. 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. Clin Infect Dis 2005;41:634-53.
3. Spellberg B, Edwards J, Ibrahim A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. Clin Microbiol Rev 2005;18:556-69.
4. Szalai G, Fellegi V, Szabo Z, Vitez LC. Mucormycosis mimics sinusitis in a diabetic adult. Ann N Y Acad Sci 2006;1084:520-30.
5. Gamaletsou MN, Sipsas NV, Roilides E, Walsh TJ. Rhino-orbital-cerebral mucormycosis. Curr Infect Dis Rep 2012;14:423-34.
6. Lin E, Moua T, Limper AH. Pulmonary mucormycosis: Clinical features and outcomes. Infection 2017;45:443-8.
7. Ericsson M, Anniko M, Gustafsson H, Hjalt CA, stenling R, Tarnvik A. A case of chronic progressive rhino-cerebral mucormycosis treated with liposomal amphotericin B and surgery. Clin Infect Dis 1993;16:585-6.
8. Harrill WC, Stewart MG, Lee AG, Cernoch P. Chronic rhino-cerebral mucormycosis. Laryngoscope 1996;106:1292-7.
9. Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino-orbital-cerebral mucormycosis. Surv Ophthalmol 1994;39:3-22.
10. Ferry AP, Abedi S. Diagnosis and management of rhino-orbit-cerebral mucormycosis (phycomycosis). A report of 16 personally observed cases. Ophthalmology 1983;90:1096-104.
11. Blitzer A, Lawson W, Meyers BR, Biller HF. Patient survival factors in paranasal sinus mucormycosis. Laryngoscope 1980;90:635-48.
12. Ruoppi P, Dietz A, Nikanne E, Seppa J, Markkanen H, Nuutinen J. Paranasal sinus mucormycosis: A report of two cases. Acta Otolaryngol 2001;121:948-52.
13. Raj P, Vella EJ, Bickerton RC. Successful treatment of rhino-cerebral mucormycosis by a combination of aggressive surgical debridement and the use of systemic liposomal amphotericin B and local therapy with a nebulized amphotericin-a case report. J Laryngol Otol 1998;112:367-70.
14. Oliveira-Neto MP, Da silva M, Monterio PC, Laser M, Rodrigo DA, Novellino AB, *et al*. Cutaneous mucormycosis in a young, immunocompetent girl. Med Mycol 2006;44:567-70.
15. Hampson FG, Ridgway EJ, Feeley K, Reilly JT. A fatal case of disseminated mucormycosis associated with the use of blood glucose

self-monitoring equipment. J Infect 2005;51:269-72.
16. Lalayanni C, Baliakas P, Xochelli A, Apostolouc C, Arabatzis M, Velegraki A. An outbreak of cutaneous Zygomycosis associated with the use of adhesive tape in hematology patients. J Hosp Infect 2012;81:213-5.
17. Johnson JB, Affolter KE, Samadder NJ. A rare cause of Hematochezia: Colon mucormycosis. Clin Gastroenterol Hepatol 2012;11:A22.
18. Wajszczuk CP, Dummer JS, Van Thiel TE, Iwatsuki S, Shaw B. Fungal infections in liver transplant recipients. Transplantation 1985;40:347-53.
19. Adriaenssens K, Jorens PG, Meuleman L, Jeuris W, Lambert J. A black necrotic skin lesion in an immunocompromised patient. Diagnosis: Cutaneous mucormycosis. Arch Dermatol 2000;136:1165-70.
20. Barbara J, Munoz P, de Quiros JC, Bouza E. Cutaneous mucormycosis in a heart transplant patient associated with a peripheral catheter. Eur J Clin Microbiol Infect Dis 1995;14:813-5.
21. Carpenter CF, Subramanian AK. Images in clinical medicine. Cutaneous zygomycosis (mucormycosis). N Engl J Med 1999;341:1891.
22. Chakrabarti A, Kumar P, Padhye AA, Chatha L, Singh SK, Das A, *et al*. Primary cutaneous zygomycosis due to Takenaka vasiform and apophysomyces elegans. Clin Infect Dis 1997;24:580-3.
23. Vainrub B, Macareno A, Mandel S, Musher DM. Wound zygomycosis (mucormycosis) in otherwise healthy adults. Am J Med 1988;84:546-8.
24. Adam RD, Hunter G, Ditomasso J, Comerci G Jr. Mucormycosis: Emerging prominence of cutaneous infections. Clin Infect Dis 1994;19:67-76.
25. Kobayashi M, Hiruma M, Matsushita A, Kawai M, Ogawa H, Udagawa S. Cutaneous zygomycosis: A case report and review of Japanese reports. Mycoses 2001;44:311-5.
26. Hata TR, Johnson RA, Barnhill R, Dover JS. Ecthyma-like lesions on the leg of an immunocompromised patient. Primary cutaneous mucormycosis. Arch Dermatol 1995;131:833-4.
27. Cocanour CS, Miller-Crotchet P, Reed RL, Johnson PC, Fischer RP. Mucormycosis in trauma patients. J Trauma 1992;32:12-5.
28. Gartenberg G, Bottone EJ, Keusch GT, Weitzman I. Hospital-acquired mucormycosis (*Rhizopus rhizopodiformis*) of skin and subcutaneous tissue: Epidemiology, mycology, and treatment. N Engl J Med 1978;299:1115-8.
29. Lee FY, Mossad SB, Adal KA. Pulmonary mucormycosis: The last 30 years. Arch Intern Med 1999;159:1301-9.
30. Glazer M, Nusair S, Breuer R, Lafair J, Sherman Y, Berkman N. The role of BAL in the diagnosis of pulmonary mucormycosis. Chest 2000;117:279-82.
31. Wanishsawad C, Kimbrough RC, Chinratanalab S, Nugent K. Mucormycotic osteolytic rib lesion presenting as subacute pleural effusion. Clin Infect Dis 1996;22:715-6.
32. Chawla N, Reddy SJ, Agrawal M. Ileocolic mucormycosis causing intestinal obstruction. Indian J Med Microbial 2012;30:373-4.