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Narrative Literature Review of Mucormycosis in Post-COVID-19 Patients: Etiology, diagnosis, & Treatments Available.

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Introduction

Corona virus syndrome 2019 (COVID-19) is a recent infection created via a positive strand RNA novel corona virus (SARS-CoV-2) that cause disease to human, and household and pet animals. First acknowledged in China's Wuhan city of Hubei Province on December 31 of 2019 and subsequently caused a worldwide pandemic. (1) COVID-19's predominant action causes diffuse alveolar injury with significant inflammatory exudation. Immune suppressants, as well as a decline in CD4+ and CD8+ T cells, are a frequent finding. (2) Critically ill patients, particularly those hospitalized to the intensive care unit (ICU) and requiring mechanical breathing, as well as those who had protracted hospital stays, often as long as 50 days, were indeed immune suppression susceptible. These patients are more prone were for development of fungal co-infections. (3)

Co-infections with respiratory viruses (other than SARS-CoV-2), bacteria and fungi have been reported in COVID-19 patients were reported in recent literature and in COVID-19 cases, opportunistic infectious diseases were found to be one of the predictors of fatality. In India, COVID-19 infected patients in post-COVID-19 stage were found susceptible to Opportunistic Invasive Fungal Disease among them "Mucormycosis" was the most rampant. In India, 40,845 cases of mucormycosis were reported till 28th june 2021 in COVID-19 infected patients during post-COVID-19 stage. A significant proportion of

which invaded the rhinocerebral and paranasal sinuses of covid-19 patients. Out of the 40,845 cases, 31,344 are rhinocerebral in nature. The number of people who have died as a result of the infections is 3, 129. (4) The aim of the literature review is to reveal development of opportunistic fungal infections during recovery phase of covid-19 patients, disease progression, prognosis, treatment options and preventive measures.

Method

To investigate the known instances of mucormycosis following Covid-19, a literature search was conducted using PubMed and Google Scholar. This article includes articles with crucial data depending on their abstracts and/or full text. Cases of Mucormycosis other than pandemic was excluded. Prior to the pandemic, reports of patients with other fungal ailments were omitted from the research.

Results

This narrative review discusses the relevant literature; reveal development of opportunistic fungal infections during recovery phase of covid-19 patients, disease progression, prognosis, treatment options and preventive measures. The search of review literature on the subject of opportunistic invasive fungal disease, mucormycosis, covid-19 done since December 2019 up to the current date. Upon conducting a literature survey utilizing ProQuest, MEDLINE, and PUBMED, Google Scholar search engines have been used. COVID-19, Corona virus, mucormycosis, “opportunistic infection”, “invasive fungal disease”, and “infection monitoring and control” were the keyword phrases selected. After reading the article titles and abstracts, full text. Occurrences of mucormycosis with ocular compartment syndrome, rhino ocular mucormycosis, gastro - intestinal mucormycosis, pneumonia, and a middle cerebral artery infarction were among the findings. 24 articles were included based on the quality of the studies.

Kazem Ahmadikia, Seyed Jamal Hashemi et.al, a 44-year-old woman with poorly controlled diabetes with a history of fever since 5 days, malaise, myalgia, dry cough, and partial dyspnea was documented. A physical assessment showed that the patient had slight shortness of breath with nasal flaring. Upper airway swab samples positively identified for influenza but inconclusive for COVID-19 using RT-PCR. Bilateral multifocal patchy ground-glass opacities were seen on computed tomography (CT) of thorax. As a consequence of the poorly controlled DM, an acute pneumonia condition had been diagnosed. Patient was treated using intravenous dexamethasone therapy & discharged after 4 days after her symptoms subsided.

The patient had toothache and headache three weeks following her discharge, accompanied by earache, nasal congestion, and unilateral facial edema. She went to the dentist and underwent symptomatic therapy but her situation did not improve, raising speculations of mucormycosis. The patient was given intravenous liposomal amphotericin B, and functional endoscopic sinus surgery (FESS) demonstrated sinusitis with incomplete necrosis in the right maxillary sinus. A CT scan of the paranasal sinuses revealed indications of mucosal enlargement in the right maxillary sinus. Both direct and histopathologic tests revealed non-septate, ribbon-like, broad hyphae with right-angle branching, indicating mucormycosis. Liposomal amphotericin B was continued for 2 weeks & discharged after 18 days from the hospital. (7)

Amanda Werthman-Ehrenreich has documented symptoms of left-sided ptosis and proptosis with altered sensory conditions on a 33-year-old woman who has a proven history of hypertension and asthma. The patient started with vomiting, cough and shortness of breath

symptoms 2 days earlier to the examination. Facial computed tomography (CT) indicated considerable bilateral maxillary sinus thickening of the mucosal sinus and ethmoid sinus thickening of the ostiomeatal units. Staphylococcus aureus was found in the sinuses, as well as extensive fungal components such as hyphae and yeast, indicating mucormycosis. For mucormycosis, the patient was given IV Vancomycin and piperacillin-tazobactam, followed by liposomal amphotericin B. The patient passed away on the 26th day of her stay. Timely detection of fungal co-infections, according to the researcher, could considerably minimize morbidity and mortality. (6)

A 60-year-old male patient with an established record of diabetes appeared with symptoms of acute breathlessness, fever, tachypnea, and widespread malaise for three days before the hospitalization, according to Salil Mehta and Abha Pandey. On physical assessment, bilateral crepts at the lung bases were discovered. On his right foot, he had a non-healing ulceration, which was compatible with diabetic peripheral vascular disease. Nasopharyngeal swab was positive & later confirmed by CT scan thorax. Numerous patchy ground-glass opacities in both lungs, affecting the upper lobes, the right middle lobe, and the lingual, were discovered on computed tomography (CT) thorax, indicating aggressive fungal infection, most likely mucormycosis. Intravenous antifungal therapy was initiated, but the condition deteriorated over time, necessitating non-invasive ventilation to preserve his oxygen saturation. Prognosis becomes poor and expired on day 6 of his hospitalization. (7)

The 56-year old male patient with a known history of end-stage renal illness, was documented by Anubhav Kanwar, Alex Jordan. A nasopharyngeal swab was positive for COVID-19 by RT–PCR. He was hospitalized after complaints of fatigue and shortness of breath. The treatment started with methyl prednisone therapy for five-days and a single dose of tocilizumab, and one unit of convalescent plasma transfusion was done. He was then discharged after negative blood culture. He was re-hospitalized after worsening of pulmonary status. He was started on empiric intravenous (IV) vancomycin and piperacillin-tazobactam. Sputum culture showed fungal hyphae growth. Sputum and pleural fluid culture were repeated showed Rhizopus azygosporus growth. Antibacterial medications were later replaced by Anti fungal therapy using liposomal amphotericin B (5mg/kg) was started. However the status of the patient worsened as time progresses repeated blood culture showed Enterococcus spp. and Bacteroides fragilis which were found resistant to vancomycin. piperacillin-tazobactam were re instated after blood culture reports. On the very next day i.e. 17th day after hospitalization, the patient developed cardiac arrest and died. (8)

The 32-year- old female patient with known history of uncontrolled diabetes since last 6 months, has been documented by Marina Saldanha, Rashmitha Reddy and Mark Jittu Vincent. Rapid antigen test was performed for COVID-19 showed positive status. Case history examination revealed complete ptosis left eye along with facial pain on since 5 days. A nasal endoscopic examination was recommended, which indicated pus development and a deviated nasal septum in the left middle meatal region. The left ethmoid, maxillary, and frontal sinuses were nearly completely opacified on computed tomography (CT) of the nose and paranasal sinuses, indicating sinusitis caused by a fungal infection. A brain MRI was recommended, which demonstrated a peripherally enhancing subperiosteal lesion in the superomedial extraconal part of the left orbit, indicating a subperiosteal abscess with optic neuritis owing to sinusitis. On an emergency basis, the patient's treatment approach comprises endoscopic surgery with or without

debridement. Samples acquired during endoscopic surgery were used for histological analysis and KOH mount, resulting in a final diagnosis of mucormycosis. The patient received Anti Fungal treatment using liposomal Amphotericin B, the treatment was discontinued because of financial constraint. 2 month follow up was done which revealed resolution in facial pain & ptosis but no improvement in vision. (9)

The 46 year-old male subject with a documented record of diabetes mellitus was recorded by Mrittika Sen, Sumeet Lahane, Tatyarao P Lahane. A nasopharyngeal swab was positive for COVID-19 by RT–PCR. He was hospitalized after complaints of fatigue and shortness of breath additionally he complained initial symptoms of pain, redness, and periocular swelling. Later on drooping of eyelids, limitation of ocular movements, pain and loss of vision. MRI of Brain advised and revealed involvement right cavernous sinus & frontoparietal lobe. The treatment plan for the patient includes fiber endoscopic sinus surgery with sinus debridement on emergency basis. Samples obtained during endoscopic surgery were later sent for histopathological assessment suggestive of Mucormycosis & aspergillus as the infective fungus on microbiology culture was found. The patient was given antifungal therapy with oral posaconazole at first, and then IV liposomal amphotericin B with voriconazole subsequently.One week of intraorbital irrigation using amphotericin B were performed. Postoperatively patient developed a sino-cutaneous fistula through the exenteration wound. Patient was alive and stable upon with regular follow up but loss of vision was present. (10)

Discussion

Acute respiratory distress syndrome is a complication of severe viral pneumonias such as influenza, SARS-COV, COVID-19, and others. To prevent major airway inflammation, this condition necessitates critical care, including ventilator support, corticosteroids, and other adjuvant medications. Secondary bacterial and aggressive fungal infections (IFIs) believed to be the downsides of steroid therapies for the management of viral pneumonia, affecting patient morbidity and mortality. (FIG.1) (5)

Mucormycosis is an infrequent opportunistic fungal infection exemplified by host tissue infarction and necrosis produced due to vascular invasion by the fungal hyphae. Mucormycosis is a fungal infection with a high proclivity for contiguous spread and a potentially fatal consequence if not detected and managed early. (5, 11)

Mucormycoses intruding into the sinuses are a type of aggressive sinusitis hazardous to life, usually affecting immunocompromised people with a deteriorated neutrophilic defense. Patients with uncontrolled diabetes, acquired immunodeficiency syndrome, neutropenia, especially with kidney disease, iatrogenic and haematological immunosuppression and organ transplant, can include patients with extremes of age, broad-spectrum antibiotics, iron overload, skin trauma, intravenous drug abuse, prophylactic voriconazole for aspergillosis and malnutrition. (12, 13)

In India, 40,845 cases of mucormycosis were reported till 28th june 2021 in COVID-19 infected patients during post-COVID-19 stage. A significant proportion of which invaded the rhinocerebral and paranasal sinuses of covid-19 patients. Out of the 40,845 cases, 31,344 are rhinocerebral in nature. The number of people who have died as a result of the infections is 3, 129. Of the total numbers, 34,940 patients had COVID (85.5%), 26,187 (about 64.11%) were co-morbid for diabetes while 21,523 (52.69%) of those infected were on steroids. 13,083 patients were in the age group 18-45 (32%), 17,464 were in the age group 45-60 (42%) while 10,082 (24%) patients were 60+ years of age.(4)

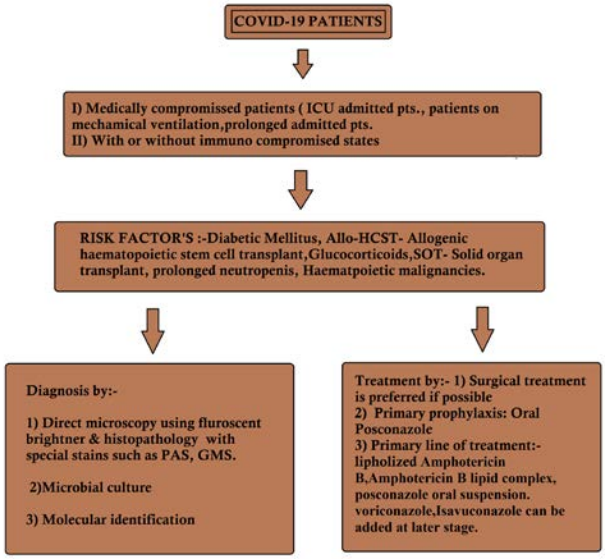

Figure 1: Guidelines on Mucormycosis diagnosis and therapy in COVID-19 patients. (14)

Invasive Mucormycosis

Paltauf a pathologist from Germany gave the first scientific description of Mucormycosis in 1885 and termed as Mycosis Mucorina. Cases of Mucormycosis were increased during 1980s and 1990s among individual with immuno compromised status as per the observations. (14) The incidence of Mucormycosis varies from 0.005 to 1.7 per 100,000 populations and the global case fatality rate is as high as 46%. Mucormycosis has a ratio of 0.01 to 0.2 per 100,000 people in Europe and the United States of America. The reported prevalence of mucormycosis in France has been documented to be increasing at a rate of 7.4 percent each year. In India Prevalence rate of mucormycosis reported was14 per 100,000 populations. Variation in the prevalence rate of mucormycosis can be possible due to seasonal occurrences throughout the world. Mucormycosis shows varied etiology throughout the world in developed countries, it was mostly seen in patients suffering from hematological malignancies (HM), whereas in developing countries like India, it was commonly seen in patients with uncontrolled diabetes mellitus (DM) or trauma.(15,16)

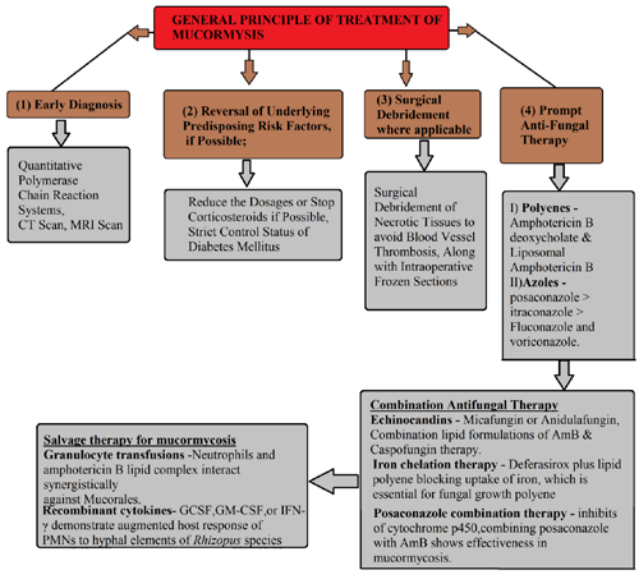

Figure 2: General Principle of Treatment of Mucormycosis.(16)

In immunocompromised patients, the main route of Mucormycosis infection seems to be due to inhalation of sporangiospores brings about pulmonary infection. Acute sinusitis, nasal congestion, purulent nasal discharge, and headache are common symptoms of mucormycosis infection. Even though some people may be asymptomatic, the significant proportion of patients has a persistent fever. Clinical symptoms originate from sinus involvement with concomitant spread to surrounding regions including the palate, orbit, and brain. (FIg.3, 4) Obtundation occurs when it spreads from the ethmoid sinus to the frontal lobe. (17, 18)

Cutaneous and soft tissue mucormycosis is among the most prevalent forms of Mucormycosis in immunocompromised individuals. The lungs, are the second most frequently affected manifestation (58%) with a mortality rate up to 80% owing to its violent clinical course. (18, 19) The most common manifestation of mucormycosis is the rhino-orbital cerebral infection where the infection of the fungus from the paranasal sinus

(FIG.5) into orbit and invades into brain. Rhino-orbito-cerebral mucormycosis typically advances in individuals with uncontrolled diabetes (about 70%), and as a result, these patients rarely get lung infection. At the time of presentation, the majority of them had diabetic ketoacidosis. In a recent pan Indian multi-center case study on Mucormycosis revealed 57% of patients had uncontrolled diabetes mellitus (FIG.6) and 18% had diabetic ketoacidosis. Mucormycosis may take a invasive course of disease.

It may develop into a rare manifestation known as Orbital apex syndrome. The condition of orbital apex syndrome is typically fatal, progressing to total ophthalmoplegia with progressive vision loss, including the II, III, IV, V, and VI cranial nerves. (20, 21, 23)

Rhino-cerebral disease or Rhino-orbital- cerebral infection has a survival rate of approximately 75% in patients without any systemic diseases; with other diseases survival rate becomes approximately 50%.; and in cases with pulmonary disease it is believed to be fatal and life threatening. Symptoms of rhino-orbital mucormycosis may arise as late as 30–42 days after the diagnosis of COVID-19. Delays of even six days in commencing treatment double the 30-day mortality from 35% to 66%. (10, 22)

Orbital compartment syndrome (OCS) is caused by the initiation of an expansile process within the orbit's closed segment, resulting in elevated orbital pressure. This can lead to ischemia and visual loss. To decompress the orbit, emergency operations such as lateral canthotomy and inferior cantholysis are required. Stalling therapy can lead to permanent blindness. Retrobulbar hemorrhage, cellulitis, orbital malignancy, or previous orbital surgery can all be causes of orbital compartment syndrome. (24)

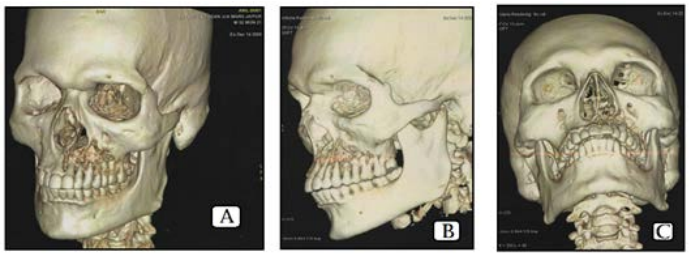

Figure 3: 3D CT scan of face showing osteolytic activity on left anterior maxillary region due to mucormycosis.

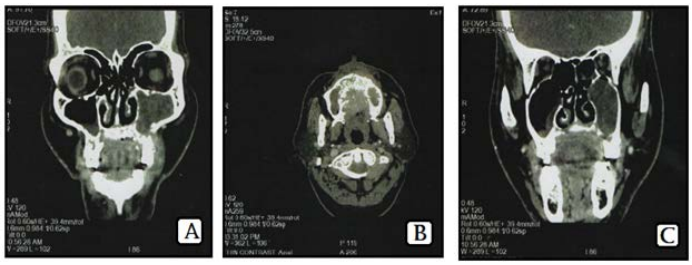

Figure 4: MRI of the face showing radio-opacity with thickened sinus lining involving left maxillary sinus & osteolytic activity on left anterior maxillary region in a patient diagnosed with mucormycosis.

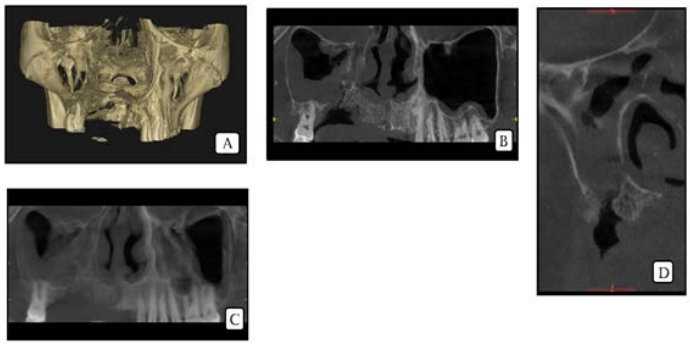

Figure 5: 3D CT scan & MRI of face showing destruction of alveolar & anterolateral wall of maxillary bone, nasal floor in right maxilla. MRI also shows radio-opacity involving right maxillary sinus with thickening sinus lining. Perforation of the lateral wall near nasal floor is present.

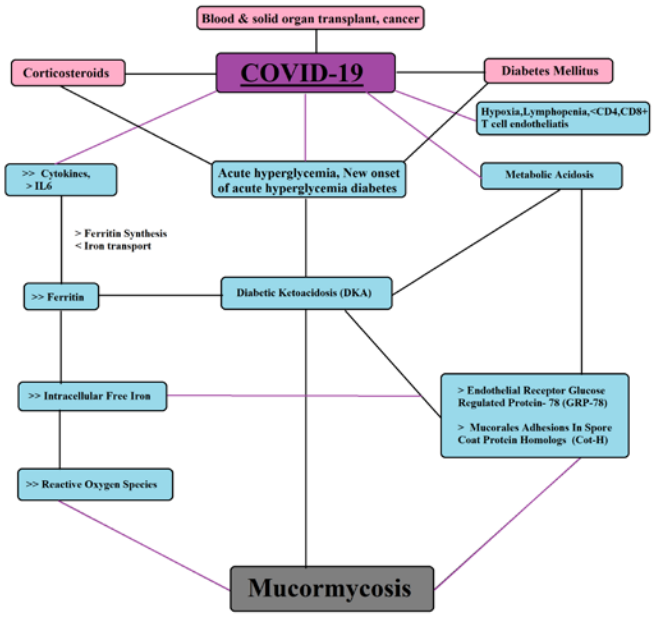

Figure 6: Hypothesizing relations of diabetes, corticosteroid, blood & organ transplant, cancer and COVID-19 with mucormycosis.

Treatment

Rapid accurate diagnosis, administration of drugs, accessory application of hyperbaric oxygen, recombinant cytokines or administration of granulocyte, surgical debridement, and prosthetic rehabilitation using obturator are the techniques implicated in triumphant management for mucormycosis.(FIG.2)

Echinocandins are the first-line treatment for invasive infections, while fluconazole, liposomal amphotericin B, voriconazole, posaconazole, and isavuconazole are the second-line therapeutic options. The management of invasive pulmonary mucormycosis involves use of voriconazole as the first-line treatment. The second medicine of choice and main alternative choices for IPA treatment in the ICU are isavuconazole and liposomal amphotericin B. Itraconazole could be an alternate anti fungal drug for treatment of COVID-19-related invasive pulmonary mucormycosis. (25-28)

Polyene Antibiotics

Their heavily double-bonded structure gives them the term polyene. Amphotericin B (AMB) is an antifungal antibiotic with a broad spectrum of activity. It is effective against Cryptococcus, Coccidioides, Candida, Aspergillus, Blastomyces, Histoplasma, Sporothrix, fungi causing mucormycosis, etc. Polyenes have a strong affinity for ergosterol, which is found in the fungal cell membrane, and they bind with it. The polyenes are delivered into the membrane, and multiple molecules arrange themselves in such a way that they generate a 'micro pore,' allowing intracellular components to disperse and the fungi to die (fungicidal). (27, 29-30)

For the treatment of mucormycosis, Amphotericin B deoxycholate (AmB) remains the solitary approved antifungal agent. It is also available in lipid formulations (LFABs). Liposomal amphotericin B effectively cured mucormycosis with various organ involvement patterns as per several case series, present in the review literature. The daily dosage varied from 1 mg/kg to 10 mg/kg each day. Rising doses to the recipients found to have higher response rates. The recommended dose for liposomal amphotericin B (AmB) is 5 mg/kg/day in the absence of CNS involvement.

The most serious complication of Amphotericin B deoxycholate is nephrotoxicity (AmB). It manifests as azotaemia, diminished GFR, acidosis, hypokalaemia, and failure to concentrate urine in a dose-dependent manner. Liposomal amphotericin B (LFABs) hence are more preferred as, It is much less nephrotoxic than AmB and can be given at bigger doses for longer periods of time without harming the kidneys. Patients who have had a kidney transplant Amphotericin B lipid compound can be unharmed dispensed at the rate of 10 mg/kg per day. (27, 31-33)

Azoles

Azole antifungals are largely separated into imidazoles and triazoles. They interfere with the fungal cytochrome P450 enzyme lanosterol 14-demethylase, causing ergosterol production to be disrupted, leading to a cascading of fungus membrane abnormalities. Because fluconazole and voriconazole do not show persistent antifungal activity against mucormycosis agents, Isavuconazole is recommended as a first-line treatment for mucormycosis. Isavuconazole IV @ 3 200 mg for 1–2 days, then 1 200 mg per day from day 3 forward. Isavuconazole is utilized in salvage therapy because it is effective in clinical settings, refractory disease, and intolerance or toxicity. In Europe, isavuconazole has exclusively been approved for the treatment of mucormycosis as a last resort. Posaconazole oral suspension, as well as posaconazole delayed release tablets and infusions, are suggested as first-line treatments. Posaconazole has 90 percent minimum inhibitory concentrations (MIC90) of 1 to 4μg/mL, indicating that it has improved Mucorales in vitro activity. The activity of itraconazole is mostly restricted to Absidia species. Posaconazole should be taken twice daily at a dose of 400 mg. Posaconazole IV @ 2 300 mg on the opening day then 1 300 mg on the second day. Since it is statistically less effective than Amphotericin B deoxycholate, posaconazole monotherapy cannot be recommended as a primary measure for mucormycosis. Individuals with mucormycosis who've been non - compliant or intolerant of polyenes should consider posaconazole as a substitute. (34-36)

Echinocandins

Caspofungin Acetate is a semi synthetic antifungal agent successful against **C**andida and Aspergillus when the patient is not responding to or intolerant to other antifungal agents. Echinocandins work by causing immune stimulation and fungi death in mucormycosis by causing extended / increased exposure of β-glucan on the fungal surface.

Mono therapy or placebo therapy using **C**aspofungin **A**cetate semi synthetic antifungal agent is not better therapy for mucormycosis. In neutropenic and DKA mice with disseminated mucormycosis, combination therapy with caspofungin plus Liposomal amphotericin B complex (ABLC) significantly enhanced survival when compared to combination therapy with LAmB plus either micafungin or anidulafungin. Caspofungin is prescribed at a dosage of up to 3 mg/kg each day. (37-40)

Iron Chelation Therapy

deferoxamine improves the release of iron to Mucorales which in turn cause growth of the fungi in mucormycosis thus, in vivo animal experiments, creatures infested with R. oryzae who are given iron or deferoxamine have a significantly lower survival rate / prognosis. Deferoxamine iron chelation therapy predisposes to mucormycosis.

Deferasirox is an oral iron chelator that has been licensed by the FDA and is commercially available. It is used to treat iron overload in patients with transfusion-dependent anemia. Deferasirox has been shown to be fungicidal in an in vitro research in mucormycosis, with a MIC90 of 6.25 μg/mL. Deferasirox is prescribed at a dose of 20 mg/kg/day for 14 days.

The most common side effects of deferasirox medication are gastrointestinal discomfort (e.g., nausea and diarrhea). The major toxicity of significance, meanwhile, is renal. Creatinine elevations occurred in up to one-third of patients in deferasirox clinical studies, but they were minor and reversible after the drug was stopped. (40-43)

Adjunctive Therapies

Although its involvement in the primary treatment of mucormycosis is unknown, pro-inflammatory cytokines

improve granulocytes' potential to destroy mucormycosis agents. Recombinant interferon-γ, recombinant granulocyte colony-stimulating factor, with granulocyte macrophage colony-stimulating factor are examples of pro-inflammatory cytokines. Several case reports and research show that adjuvant immune therapy, in addition to LFAB, is effective in treating mucormycosis.

Adjunctive immune therapy such as despite data is sparse, granulocyte colony-stimulating factor–mobilized granulocyte transfusions have been increasingly employed for refractory mycoses, including mucormycosis, preferably in neutropenic individuals with mucormycosis as a lifesaver intervention. Hyperbaric oxygen therapy can be utilized as an adjunct therapy in health care centers that have the necessary technical skills and infrastructure in order to establish a better oxygen-enriched cell state while also introducing cytokines concurrently with antifungal therapy. The usefulness of hyperbaric oxygen therapy in mucormycosis & other fungal infections is based upon limited data available from review literature. (44-47)

Surgical Management

Throughout the course of mucormycosis blood vessel thrombosis develops, resulting in tissue necrosis and preventing antifungal medicines from reaching the infection site. As a result, surgical treatment with necrotic tissue debridement is critical for complete eradication of mucormycosis. Surgical treatment considered in case of soft tissues, cerebral disseminated, localized pulmonary lesion and rhino-orbital-types and should be very aggressive. Due to the massive spread capability of Mucorales hyphae into the neighboring environment excision must not only encompass necrotic tissues but also neighboring contaminated healthy-looking tissues. Surgery is possible in cases of a single isolated pulmonary lesion, but it appears to be impossible in cases of widespread mucormycosis or when the infection has spread to inaccessible places (brain, lung parenchyma near major vessels). In circumstances where reconstructive surgery is effective, it will be used to restore deformed bodily portions.

Surgical debridement using orbital exenteration is decided by the treating physician when there is loss of vision & course of the disease is restricted to the orbit without or least extension to the cavernous sinus. Orbital exenteration becomes an imperative treatment modality particularly in patients with extensive involvement along with necrotic orbital tissue. Surgical debridement (FESS and/or orbital exenteration) not only diminish the disease burden, permit better penetration of intravenous drugs, and restricts further spread of the disease but also allows intra operative diagnosis with distinguishing necrotic tissue and supply sample for histopathological and microbiological authentication. Surgery was found to be an influential variable in a logistic regression model for improving outcomes in patients with mucormycosis. Furthermore, in many case series, individuals who did not get surgical debridement of mucormycosis had a far greater mortality rate than those who did. These findings support the notion that surgical debridement is required to improve recovery rates. (48-52)

Conclusion

Alteration in innate immunity, substantial use of steroids, monoclonal antibodies, and broad-spectrum antibiotics, as well as uncontrolled hyperglycemia with COVID19 disease, all contribute to the emergence of opportunistic fungal infections of the airways, particularly the sinuses and lungs.COVID-19 causes alteration in the innate immunity by means of immune deregulations differentiated by diminished T cells; consist of CD4 and CD8 cells. Doctors should be vigilant with the likelihood of opportunistic secondary fungal infections in patients

with COVID-19 infection, especially those with pre-existing risk factors.

Hematological malignancies (HM), uncontrolled diabetes mellitus (DM) or trauma, renal failure mandating hemodialysis, abdominal surgery, triple lumen catheters, parenteral nutrition, delivery of multiple antibiotics, length of ICU stay >7 days, and previous abdominal infections are all possible causes for aggressive fungal infections. Rapid accurate diagnosis, administration of drugs, accessory application of hyperbaric oxygen, recombinant cytokines or administration of granulocyte, surgical debridement, and prosthetic rehabilitation using obturator are the techniques implicated in triumphant management of opportunistic fungal infections. All efforts should be made to preserve optimal hyperglycemia and only sensible evidence-based utilization of corticosteroids in patients with COVID-19 is suggested in order to diminish the burden of fatal mucormycosis, candidiasis, aspergillosis & other fungal infections.

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