

SINO NASAL MUCORMYCOSIS (WITH INVOLVEMENT OF HARD PALATE) - A CASE STUDY**Dr. Noorush Shifa Nizami^{*1} and Dr. Shaik Mohammed Sumeer²**^{2,1*} Doctor of Pharmacy (PHARM-D) Intern, St. Paul's College of Pharmacy, Nagarjuna Sagar Road, Turkayamjal, Hyderabad, T.S – 501510.***Corresponding Author: Dr. Noorush Shifa Nizami**

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ABSTRACT

We report a case of post COVID-19 Sino-orbital Mucormycosis infection and its management. The patient was diagnosed with COVID-19 and was treated according to the persisting protocols with the recovery on the 16th day. A diagnosis of mucormycosis was established after Biopsy within 16 hours of admission surgical debridement was performed and then followed by conservative management with intravenous (IV) Amphotericin B was done and along with this post operatively antibiotics, antipyretic, antiemetic and supportive treatment was given. Mucormycosis generally will develop secondary to immunosuppression or any debilitating diseases. In Head and Neck cases, the fungus usually gains entry through the respiratory tract which basically involves the nose and sinuses, and further progresses into the orbital and intracranial structures. Therefore, an early diagnosis and along with that inter-vention is required for a good prognosis in order to decrease the morbidity and to increase the quality of life of patient. This can be accomplished on the basis of clinical picture and the direct smears. However, Research needs to be carried out for COVID-19 patients in order to get better prevention and management of this type of opportunistic infection in order to reduce its morbidity and incidence, and also the Prophylactic treatment protocols should be established, along with the rational use of corticosteroids.

KEYWORDS: Mucormycosis, Amphoterecin B, Covid-19, case study, fungal infection.**INTRODUCTION**

The covid-19 outbreak has spread rapidly on a global scale.^[1] In spite of great efforts, there is no particular definitive treatment of this disease, so however, prevention and symptomatic management are the only best options. The super infections and the coinfections in covid 19 pneumonia are still under exploration.^[2,3] mucormycosis infection is not new however; a spike in such cases has been reported during this covid 19 era and hence the rise in cases of mucormycosis is basically due to covid 19 and that remain associated with impaired immune system of the infected patient.^[4] The Central Research Institution throughout the world including - CDC emphasizes the increase in mucormycosis cases after covid 19 infection. The poor as well as the impaired immune functioning is the major cause of rise in mucormycosis cases further confirmed.

The cell mediated immunity known as Th1 and IFN- γ are mainly involved in offering the protection during viral infections. The novel coronavirus/ SARS-CoV-2 infection remains associated with impaired functioning of the cellular and humoral immunity and this may effectively trigger the higher risk of these fungal infections. Therefore, not only novel SARS-CoV-2 infection but also the treatment that is associated with the

administration of the immunosuppressive drugs and anti-inflammatory drugs further increases the risk of fungal infections. The decline in the selective methods for fungal infections culture, diagnosis and treatment results in necrotic and inflammatory outcome of mucormycosis.

Basically, secondary infections are reportedly more common in severely ill covid-19 patients, hospitalized, encompassing between 10 and 30% of cases, fungal being 10 times more common.^[3] The nature of the disease is not completely unveiled and it can't be confirmed whether it is the complication of a disease or its management. Corticosteroids such as Methylprednisolone and Dexamethasone are believed to be the main risk factors which modulate inflammation mediated lung injury and thereby reduce the progression of respiratory failure^[3,4] in covid-19, adverse effects usually include immune modulation, increased secondary infection, manifestation of latent diabetes mellitus, weight gain, dizziness, mood changes, muscle weakness and insomnia.^[5] Mucormycosis is amongst the most severe form of Zygomycosis which is caused by Mucorales species of phylum Zygomycota^[5,6] described as the potentially lethal infection that occurs mostly in patients who are immunocompromised, particularly and mostly in those with diabetes mellitus, lymphoma and

leukemia.^[7] The incidence rate- of mucormycosis varies around from 0.005 to 1.7/million population.^[8] However, in Indian population the prevalence is 0.14 per 1000, that is about 80 times higher than the developed countries^[9] and also the fatality rate of mucormycosis is 46 percent globally.^[10] Moreover, the factors like intracranial or irreversible immune suppression, orbital involvement increases fatality to 50% to 80%.^[10,11] The highest suspicion for this disease must be greatly considered in such patients who are immunocompromised. Tissue necrosis known as a hallmark of mucormycosis is often/sometimes a late sign. Mucormycosis Is greatly difficult in orderto diagnosis which affects outcome and results in poor prognosis, hence Early diagnosis is important and treatment is essential. Delay of about a week may often double the 30 day mortality rate from 35% to 66%. However, early aggressive combined therapies i.e. surgical and medical therapy, mucormycosis has a very poor prognosis.^[12]

Review of literature

1. Globally COVID-19 crisis is leading challenge across the world, to fight against SARS-COV-2 it is mandatory to attain and maintain good nutritional status. Body has its own natural defense mechanism. Because of certain risk factors such as, serious heart diseases, asthma, obesity kidney and lung diseases, diabetes, smoking, drinking alcohol, and sleep disturbances the natural defense mechanism fails to produce its effect against infectious diseases. The healthy diet can boost up the immune system and body will have more stamina to fight against COVID-19 or other chronic infectious diseases. A healthy balanced diet will automatically give rise to a strong immune system that can help withstand any assault by the virus. healthy dietary habits can help to maintain the physical as well as mental health of the individual because strong immunity can be a major weapon to fight against COVID-19 and also so many other diseases and infections (Noorush Shifa Nizami et al).
2. Drugs such as Corticosteroids i.e., "Methylprednisolone and Dexamethasone" are believed to modulate inflammation mediated the lung injury and it is thereby reducing the progression of the respiratory failure in covid-19, the side effects include increase in secondary infections, dizziness, weight gain, immune modulation, manifestation of latent diabetes mellitus, mood changes, insomnia and muscle weakness (Aastha Maini et al).
3. Mucormycosis is known as "angioinvasive disease" which is caused by fungi (and the order is Mucorales like Mucor, Rhizopus, Rhizomucor, Absidia and Cunninghamella). The prevalence rate of mucormycosis in India is nearly about 0.14 cases per 1000 population, nearly about 80 times the prevalence in the developed countries, covid-19 infection is associated with the fungal infections. However, Mucormycosis is more often reported in immunocompromised individuals, and the risk

factors of orbital and cerebral involvement are likely in the diabetic ketoacidosis patients and with concomitant use of steroids but, the most common risk factor that is associated with mucormycosis is diabetes mellitus in India. In background of COVID-19 pandemic, only the limited number of cases of mucormycosis infection have been reported, however, there are no documented cases of sudden onset of visual loss with the incidental covid-19 infection in the newly detected young non-ketotic diabetic (Shweta Mallikarjun Revannavar et al).

PRESENTATION OF CASE

A 55 year male was admitted to the hospital, a tertiary care center on 31st may 2021. Patient was presented with complaint of left cheek swelling and pain since 10 days and with history of covid – 19 infection 1 month back. Admission glucose was 378 mg/dL, upon *physical examination*, Nose-b/l MM clear, Palate- left upper alveolar region swelling with pus discharge. Patient had history of diabetes and hypertension. On admission the derranged investigations were: *Renal function test*: Blood urea- 51.0mg/dl (17.0-43.0), creatinine- 1.35mg/dl (0.67-1.17), GFR- 58.32 ml/min (>=60), sodium- 134.6 mmol/l (136.0-145.0), potassium- 3.3 mmol/l (3.5-5.1), chloride- 98.2mmol/l (98.0-107.0), magnesium- 1.4 mg/dl (1.8-2.6). *Biopsy medium specimen*: gross appearance- container 1 (maxillary sinus) received multiple (4) grey brown hemorrhagic soft tissue bits altogether measuring 2×1.0×0.5 cms (4 squash smears prepared), container 2 (maxillectomy) further received bone measuring 7×4×2.5 cms. External surface shows grey brown friable soft tissue mass. Microscopic appearance was showing the sections fro maxillary sinus tissue with necrotic sino nasal mucosal fragments with necropurulent exudate, giant cell reaction, along with fungal organism displaying broad aseptate hyphae, wide angled branching. There is also an evidence of tissue invasion and vascular invasion. Sections from the maxillectomy specimen show degenerated bone and necrotic soft tissue covered with purulent exudate and infiltrated by fungal organisms and bone invasion. Squash diagnosis was found to be positive for fungal organism favouring mucormycosis.

MANAGEMENT AND FOLLOW UP

On the day of admission patient underwent surgery (ESS with debridement with left maxillectomy under GA, patient was intubated, -B/L MMA, B/L anterior and posterior ethmoidectomy and sphenoid sinus opened, B/L inferior turbinectomy was done, fungal debri removed from B/L maxillary and ethmoid sinuses, B/L MM packed with Velez, B/L nasal cavity packed with merocele pack) procedure was uneventful. He was monitored in the hospital for 16 days and also was started on inj. Cefoperzone+sulbactam 1.5gm twice in a day intravenously, inj. Metronidazole 500mg thrice in a day intravenously, inj. Pantoprazole 40mg once a day intravenously, inj paracetamol 1gm thrice in a day intravenously, inj. Tramadol 100mg twice in a day

intravenously, inj ondansetron 8mg twice in a day intravenously as post operative medications. Patient was also started with Inj. Amphotericin B 250mg once daily intravenously, nasoclear nasal gel thrice in a day, (E/T), Betadine mouth gargle thrice a day p/o. for diabetes patient was on diabetic diet, inj actrapid subcutaneously 12 Units before breakfast, 12 Units before lunch, Inj. Human mixtard 14 Units before dinner was administered. Swelling and pus discharge was slightly reduced and healthy wound was seen after 10 days of treatment.

Total hospitalization of patient was 16 days on discharge isotonic nasal spray solspre2 puffs in each nostril four times daily, mometasone aqueous nasal spray Nasonex 2 puffs once daily for 5 days, tab. Posaconazole 300mg once daily for 2 weeks, betadine mouth gargle 3 times daily was prescribed. For diabetes- diabetic diet, inj actrapid subcutaneously 12 Units before breakfast, 12 Units before lunch, Inj. Human mixtard 14 Units before dinner, along with this regular home glucose monitoring. Therefore the patient was satisfied with treatment and outcome.

DISCUSSION

Mucormycosis is by anatomic site localization and not by mycologic classification. At the head and neck region, they are classified into the following types isolated nasal, rhino-orbital or rhino orbital cerebral Mucormycosis and the other accepted forms are disseminated, pulmonary, cutaneous, gastrointestinal and miscellaneous.^[12,13] Fungi of the genus "Rhizopus" account for most of the clinical isolates. Mucoraceae are known to be the ubiquitous saprophytic fungi and they are most common inhabitants of the decaying matter which are found in soil, bread, hospital ward rooms, air and dust.^[13,15] However, Seasonal variance theoretically is related to the use of air conditioners. These organisms are known to be potent in temperate climates. Risk factors includes, diabetes mellitus, immunosuppressive therapy, neutropenias, leukemias.^[7] However, patients with, hematopoietic stem cell transplantation, neutrophil dysfunction, iron-overload, HIV/AIDS and diabetic ketoacidosis are some of the identifiable risk factors which have been reported. This mold will usually enter into the host through the respiratory tract and it also exhibits the remarkable affinity for arteries and starts to grow along the internal elastic lamina which in turn causes thrombosis and infarction.^[16] The progression of mucormycosis is from nose and sinuses is through vascular occlusion or direct. Therefore, the Intracranial involvement will also occur by the invasion through superior orbital fissure, ophthalmic vessels, cribriform plate, carotid artery / perineural route.^[17]

Diagnosis depends on the clinical features, imaging and pathological findings plays an important role in defining the extent of involvement.^[18] Early diagnosis and also prompt surgical intervention aids in order to control the extent of the infection and severity of the disease.^[19] The

primary guideline for treatment of the disease is to find out and then correct the underlying cause, but it cannot be found in patients those who are dependent on high dose steroid therapy, such as in covid-19 infection.^[20]

There are the two mainstays used for treatment are

1. Medical treatment with Amphotericin B.
2. Surgical debridement.

Local treatment with Amphotericin B and Hyperbaric oxygen therapy are adjunctive modalities. Amphotericin B (a fungistatic agent rather than fungicidal), which leads to a longer treatment duration.^[11,21] However, the prognosis depends on multiple factors and also early initiation of treatment would be an important element. Once the diagnosis is confirmed then conservative management can be initiated for the patient.^[22] Orbital exenteration is the toughest decision in rhino-orbital cases, because of concerns about disfigurement and disability. However, exenteration is the last resource but it can be life-saving at the price of mutilating procedure.

CONCLUSION

It is known that, Mucormycosis infection is not new but a spike in the cases has been reported during covid-19 era and hence the rise in cases of mucormycosis is due to covid 19 and especially the management of covid 19 and that remain associated with impaired immune system of the infected patient. However, the question still prevails about the cause and the origin of prevalence in post covid-19 patients. Research is still needed, for the better prevention and the management of these kind of opportunistic infections in covid-19 patients and the use of the "prophylactic treatment protocols" for the same thing has to be assessed and the guidelines need to be established for the reduction in morbidity and the use of Immunosuppressants should be more judicious along with the continuous monitoring.

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