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CASE SERIES: MUCORMYCOSIS IN COVID-19 RECOVERED PATIENTS

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ABSTRCT

Background: Mucormycosis is a rare fungal infection mostly affecting in patients with recently recovered from Covid-19, diabetes Mellitus and immune-suppressed state. **Methodology:** The cases for current study were collected retrospectively which had confirmed diagnosis of mucormycosis in a single tertiary care hospital. The patient records were used for the clinical presentations. **Case Presentation:** In current study, five covid-19 recovered patients with mucormycosis were presented. The etiologic agents of mucormycosis swelling around eyes, pain in the eye, drooping of eyelids. **Conclusion:** Surgery, anti-fungal drugs and proper treatment of co-morbidities can improve outcome and survival if it's diagnosed early and treated since mucormycosis is a rare and opportunistic fungal infection.

KEYWORDS: Mucormycosis, Covid-19 recovered, fungal infection.

INTRODUCTION

Mucormycosis is a rare fungal infection but currently it is increasing in patients who have recovered from covid-19. Mucormycosis comes from the Mucorales order of filamentous fungi and family Mucoraceae. Mucormycosis is a less common opportunistic fungal infection

compared to Aspergillus species and Candida.[1] The disease can be displayed as of different syndromes, with pulmonary infections and rhino cerebral being the most commonly reported.[2] The most five commonly reported forms of mucormycosis include cutaneous, gastrointestinal, rhino cerebral, pulmonary, and disseminated.[3] Recently recovered from Covid-19, diabetes mellitus, hematologic malignancies, stem cell transplant, systemic corticosteroid therapy, neutropenia, and immune-compromised state are the predisposing situations for Mucormycosis.[3,4] In the United States of America, the annual incidence of Mucormycosis ranges from 1.7 cases per 1,000,000 inhabitants to 140 cases per 1,000,000 in India.[5] Comprehensive prolonged antifungal therapy, surgical debridement, and tight control of underlying co-morbidities are essential but before this early diagnosis and recognition are important.[6]

We present a case series of five patients diagnosed and treated for Mucormycosis at a single tertiary care hospital.

METHODOLGY

Since the pandemic of coronavirus in India, our hospital has cared for thousands of patients. Of these patients, only 5 patients developed Mucormycosis. For current case series, the relevant data were collected retrospectively. The inclusion criterion includes the patient with the confirmed diagnosis of Mucormycosis and Co-Morbidity (If any present).

RESULT

CASE REPORTS

Case 1

A 49-year-old man was admitted to the emergency department of our hospital, who had persistent headache and pain over left lower back teeth region for last 4 to 5 days, no loss of consciousness. He had recently recovered from COVID-19. Complete Blood Count (Hb-11.5g/dl, WBC- 10710cells/cmm, platelet- 290,000mcL), C-Reactive Protein (56.6mg/L), Serum Creatinine (1.26mg/dL), Sodium (138mEq/L), Potassium (4.2mEq/L), PCT (3.08ng/mL) analysis provided the information. The patient was admitted for that and on examination; there was a blister of size 2x2 cm over the left hard palate which shows the sign of Mucormycosis changes.

Para Nasal Sinuses (PNS) CT Scan was performed. There was evidence of Mild to moderate mucosal thickening involving bilateral maxillary sinuses associated irregular lytic erosion of

anterior, lateral, and remnant portion of medial wall of the left maxillary sinus, left Medial and lateral pterygoid plates, the floor of left maxillary sinus / maxillary alveolar process (at the level of left upper 1st premolar tooth), bilateral frontal, ethmoidal and sphenoidal sinusitis associated blockage of bilateral fronto-ethmoidal and spheno-ethmoidal recesses. Brain Magnetic Resonance Imaging (MRI) showed sinusitis with infective etiology. Histopathological and fungal smear culture-confirmed our diagnosis.

Fess surgery for mucormycosis was performed after 3 days and the nasal pack was removed on 4th day. inj liposomal amphotericin (50mg in 500ml DNS) was prescribed for 6 days, tab. posaconazole 300mg bd followed by od and tab. voriconazole 200mg bd was prescribed along with isotonic nasal spray 2-3 times/days. After 10 days the patient was discharged. We followed up with the patient and fortunately, there was no recurrence of infections.

Case 2

A 54 year old male patient with comorbidity of type 2 diabetes, and hypertension with a history of COVID-19 lower respiratory tract infection (turned negative) with complaints of pain in the right eye, drooping of eyelids for since last 4-5 days was admitted at our hospital for further management. The patient's HbA1c was (14.55%) and mean glucose was (361.41mg/dL) which was showing uncontrolled blood sugar level, platelet count (2, 24,000mcL). On 2nd day, the patient had complaints of right eye proptosis and pain. On examination, signs include - vision intact, edema, erythema, chemosis, congestion, total ophthalmoplegia (right Ethmoid / frontal / Sphenoid) eye involvement for which extensive debridement of sinuses (RT) and CT of Para Nasal Sinuses (PNS) was done which showed signs of left side deviation of the nasal septum with a small bony spur on left side mucosal thickening involving bilateral maxillary, frontal, right anterior and right sphenoid sinuses with obliteration of bilateral OM units. Frontal recesses and right Spheno-Ethmoidal recesses by mucosal thickening. The MRI of the orbit showed the inflammation and edematous extra-ocular muscles, soft tissue thickening in pre septal periorbital and prenasal region with edema of eyelids and mild proptosis of eyeball represent orbital and periorbital cellulitis. Aerobic culture shows the result of specimen (swab from sphenoid sinus) signs of fungus morphologically resembling Mucor isolated. So on nasal structures, the procedure of Retrobulbar transcandular was performed on the 4th day. inj liposomal amphotericin was started on 1st day for 10 days, tab. tenglyn-m, tab .glimy-m2, and exocin ointment were also started; tab. posaconazole was started on the 6th day and was continued. On the 10th day,

fess surgery plus RT sphenoidecyomy with intraorbital injection were performed. The whole eyeball excised and Jelonet packing was done. On the 11th day, re-exploration of right eye exenteration was performed. After this, the patient was shifted to ICU; gradually shifted to general ward as his condition was stable, afterwards he was discharged. We followed up with the patient and fortunately, there was no recurrence of infections.

Case 3

56 year-old male patient a k/c/o of Hypertension, Diabetes Mellitus and recently recovered from Covid-19 was admitted to our hospital with complaints of pain in right eye with swelling around right orbit since 1 day, Fever, cough and generalized weakness for 1 week. On arrival patient was conscious and stable. The laboratory investigations showed as Complete Blood Count (Hb- 12.4gm/dL, RBC- 4.16 million/mm3, WBC- 14,700cells/cmm, Neutrophils- 83%, Lymphocytes- 10%, Platelet- 570,000mcL), NB-Pro(BNP)- <700pg/mL, HbA1c - 11.73%, Sodium- 140mEq/L, Potassium- 4.1mEq/L, D-Dimer- 1580mcg/dL, CRP-60.0mg/dL, Interleukin 6- 39.3IU.

CECT PNS and orbit which showed signs of minimal mucosal thickening in right sphenoid and MRI showed signs of RT pansinusitis and left sided Maxillary and ethmoid sinusitis with bony erosions was done on 4th day. Smears from zygomatic buttress and palatal mucosa sent for KOH mount which turned out to be negative. inj amphotericin b for 12 days, inj caspofungin for 7 days, tab posoconazole, inj human atrapid, tab metolar-xt were prescribed. Bone biopsy was done from maxilla and zygomatic bone on 8th day. Patient gradually improved and was discharged after 3 days.

Case 4

A 68 year old male patient with co-morbidity of diabetes mellitus type 2, lower respiratory tract infection and recently recovered from COVID-19 was admitted in emergency department of hospital. The patient came with complaints of pain and swelling around eyes in left side, general weakness, backache, bilateral leg pain and fever since 3-4 days. The laboratory investigation was done HB (7.4g/dL), RBC (2.11millions/mm3), WBC (6880cells/cmm), platelet count (70,000mcL), Urea(89.3mg/dL), BUN(41.73mg/dL), CRP(167.2mg/L), serum creatinine (1.11mg/dL), Na(147mEq/L), Potassium(2.8mEq/L). On examination there was blister over left hard nard palate which shows sign of Mucormycosis changes.

CT scan of the Para nasal sinuses (PNS) was performed. There was evidence of Mild mucosal thickening involving bilateral maxillary sinuses associated irregular lytic erosion of anterior, lateral and remnant portion of medial wall of left maxillary sinus, left Medial and lateral pterygoid plates, floor of left maxillary sinus / maxillary alveolar process, bilateral frontal, ethmoidal and sphenoidal sinusitis associated blockage of bilateral fronto-ethmoidal and spheno-ethmoidal recesses. Aerobic culture shows the result of specimen (swab from sphenoid sinus) signs of fungus morphologically resembling to Mucor isolated. Fees surgery was done on 5th day. inj cefepime + inj tazobactum and liposomal amphotericin-b continue for 10 Days. But All sudden patient developed episode of fever , breathlessness and severe electrolyte imbalance on 10th day. Lab investigation were done serum creatinine (1.45mg/dL), Na (149mEq/L), potassium (3.3mEq/L) then after USG abdomen was done which shows the s/o complex hepatic cyst, bilateral renal cortical cyst, bilateral raised cortical echogenicity with maintained cortical-medullary differentiation. Possibility of renal parenchymal diseases. inj levofloxacin, inj aztreonam for 5 days, tab.picoconasol was continued for 7 days. Patient gradually improved and was discharged after 3 days. We followed up the patient and fortunately there was no recurrence of infections.

Case 5

A 62 year-old female with co-morbidity of hypertension and recently recovered from Covid-19 with complaints of swelling along with pain around the eyes, redness of eye, weakness and Fever was admitted to the critical Care department of our hospital. On examination patient had increased blood pressure so tab aldectone 25mg and inj lasix stat was given. The laboratory parameters like Sodium (145mEq/L), Potassium (3.4mEq/L), Serum Creatinine (0.84mg/dL), Urea (49.10mg/dL), CRP (54.5mg/L), Interleukin 6-(52.79IU), WBC (17200cells/cmm), Neutrophils (90%), Lymphocytes (80%) Platelets (185,000mcL), Lactate Dehydrogenase (1602U/L), D-Dimer (2250mcg/mL), HbA1c (8.85%).

CT scan and MRI suggest signs of minimally enhancing soft tissue noted in supero-medial extraconal compartment of right orbit adjacent to lamina papyracea, extending into the intraconal compartment surrounding the optic nerve with associated orbital fat inflammation, edematous extra-ocular muscles, soft tissue thickening in pre septal peri orbital and pre nasal region with edema of eyelids and mild proptosis of eyeball represent orbital and peri-orbital cellulitis. Therefore plan for FEES surgery was suggested.

Urine culture showed signs of Candida Tropicalis, fungal smear showed presence of fungal

elements and was treated with antifungal and antibiotics according like inj meropenem 1gm, inj voriconazole 400mg, inj caspofungin 50mg, tab finofibrate 160mg. The patient's ammonia levels were increased and was not able to maintain SpO2 level and eventually the condition worsened up and patient got unconscious thus endotrachial incubation was done along with mechanical ventilation support. After sometime the patient was continuously detoriating and all sudden went into cardiac arrest. Patient was given CPR according to protocol but could not revive and declared dead on 5th day of hospitalization.

DISCUSSION

Mucormycosis is a rare invasive fungal infection. The fungus of the patients was of the Mucorales order belonging to the class called Zygomycete. Mucorales spread can occur via inhalation or ingestion of spores, or more importantly in immune-compromised hosts, via direct inoculation.[7] These ubiquitous organisms exist in the environment, compost piles, animal excreta, soil, air and food, and play an important role in the cycle of decomposition in the natural world. Although the majority of fungi require oxygen, these pathogens are capable of growth in microaerophilic and anaerobic conditions.[8] The nomenclature of the fungi is suggested by anatomic site localization. Nasal, rhino-orbital, or rhino-orbital-cerebral Mucormycosis is classified under the head and neck region. Other forms of mucormycosis are gastrointestinal pulmonary, disseminated, cutaneous, and miscellaneous. The majority of clinical isolates are from the fungi of the genus Rhizopus.[9] The initial medical approach to Mucormycosis is to treat any underlying predisposing disorder. Surgical management can also be optioned as a first line therapy against the disease. This should involve debridement of the tissues that are infected, which was done in our cases. The same treatment was suggested by many peer professionals, who stated that early intervention by antifungals and surgical treatment has good prognosis for early stages; however for patients with cerebral involvement, chances of survival are slim even after surgical debridement and treating with antifungals. There was a poor prognosis in the second case because of cerebral involvement. Radical resection may be required in some cases. The use of Amphotericin B in patients with mucormycosis has been widely published, with a survival rate of up to 72%. Combination therapy of amphotericin B and surgery has a survival rate of 80% and 70% of those who do survive will encounter some type of functional deficit. In present cases, liposomal Amphotericin B was used for the treatment which is the antifungal drug of choice for the treatment of mucormycosis. Itraconazole and Posaconazole are antifungal drugs that act by inhibiting ergosterol synthesis. Hyperbaric oxygen helps by reducing tissue hypoxia and

acidosis caused by vascular invasion of the fungus.[10] Mucormycosis of the oral cavity can be of two origins, one is from direct wound contamination and the other is from disseminated infection where the gateway of entry is through the nose as a common complication. When it's from the PNS and nose, the infection causes palatal inflammation which leads to necrosis and the affected area turns black in the preponderance of the case.[11]

Clinical presentation can be vivid. The most common signs in the literature are blood-stained nasal discharge, facial swelling; the most frequently reported ophthalmological signs are ophthalmoplegia, proptosis, loss of vision, and chemosis, palatal ulceration, or necrosis, black necrotic eschar in the nasal cavities.[12,13,14]

All cases of this study had one or two clinical presentations and were in consequence of good management of infection. In this study, five cases of Mucormycosis with having co-morbidities of patient's condition such as hypertension, uncontrolled Diabetes mellitus, and Post COVID-19 infection. The use of amphotericin B to treat mucormycosis may not be desirable due to the nephrotoxicity effects of the drug.[15]

Fortunately due to availability inj. liposomal amphotericin B, all patients have treated with it along with other drugs like inj. Voriconazole, and Posaconazole to treat mucormycosis. Most of the patients had successful FESS (functional endoscopic sinus surgery) surgery and were discharged but one person in this case series had died before the surgery could be done.

CONCLUSION

Mucormycosis, a fungal disease that is acute, invasive, and often fatal, mostly affects patients with underlying conditions such as Diabetes Mellitus, patients having suppressed immune system and recently recovered from Covid-19 patients. Diagnosis relies on histo-pathological analysis, CT imaging and MRI performed to assess the extent of the disease. Surgical procedures, vigilant treatment with anti-fungals, and appropriate treatment for the underlying conditions can improve the prognosis of the patients, ultimately increasing the chances of survival if the condition is diagnosed early and treated diligently.

REFERENCES

1. B. Spellberg and J. Maertens, "Mucormycosis," in Principles and Practice of Transplant Infectious Diseases, A. Safdar, Ed., Springer, New York, NY, 2019.
2. Kauffman CA, Malani AN: Zygomycosis: an emerging fungal infection with new options

for management .Current Infect Dis Rep, 2007; 9: 435. 10.1007/s11908-007-0066-4.

3. Mekki SO, Hassan AA, Falemban A, Alkotani N, Alsharif SM, Haron A, et al. Pulmonary Mucormycosis: A Case Report of a Rare Infection with Potential Diagnostic Problems. Case Reports in Pathology, 2020; 2020: 1–4.
4. Serris, F. Danion, and F. Lanternier, "Disease entities in mucormycosis," Journal of Fungi, 2019; 5(1): 23.
5. Balai E, Mummadi S, Jolly K, et al. (November 29, 2020) Rhinocerebral Mucormycosis: A Ten-Year Single Centre Case Series. Cureus 12(11): e11776. DOI 10.7759/cureus.11776.
6. Onyango JF, Kayima JK, Owen WO: Rhinocerebral mucormycosis: case report. East Afr Med J, 2002; 79: 390- 393. 10.4314/eamj.v79i7.8845.
7. Arul E. Suthananthan, Sharnice A. Koek, Kishore Sieunarine, Cutaneous mucormycosis in an immunocompromised patient: a case report, Journal of Surgical Case Reports, 2017; 3, March 2017, rjx056, https://doi.org/10.1093/jscr/rjx056
8. Mignogna MD, Fortuna G, Leuci S, Adamo D, Ruoppo E, Siano M, et al. Mucormycosis in immunocompetent patients: a case-series of patients with maxillary sinus involvement and a critical review of the literature. International Journal of Infectious Diseases, 2011; 15(8).
9. Aastha Maini, Gaurav Tomar, Deepak Khanna, Yogesh Kini, Hardik Mehta, V. Bhagyasree, Sino-orbital mucormycosis in a COVID-19 patient: A case report, International Journal of Surgery Case Reports, 2021; 82: 105957, ISSN 2210-2612,https://doi.org/10.1016/j.ijscr.2021.105957.
10. Nallapu V, Vuppalapati HB, Sambhana S, Balasankulu B. Rhinocerebral mucormycosis: A report of two cases. J Indian Acad Oral Med Radiol, 2015; 27: 147-51.
11. Afroze, Syeda Neelam et al. "Mucormycosis in a Diabetic Patient: A Case Report with an Insight into Its Pathophysiology." Contemporary clinical dentistry, 2017; 8,4: 662- 666. doi:10.4103/ccd.ccd_558_17.
12. Kolekar JS: Rhinocerebral mucormycosis: a retrospective study. Indian J Otolaryngol Head Neck Surg, 2015; 67: 93-96. 10.1007/s12070-014-0804-5.
13. Nezafati S, Kazemi A, Asgari K, et al.: Rhinocerebral mucormycosis, risk factors and the type of oral manifestations in patients referred to a University Hospital in Tabriz, Iran 2007-2017. Mycoses, 2018; 61: 764-769. 10.1111/myc.12802.
14. Bhansali A, Bhadada S, Sharma A, et al.: Presentation and outcome rhino-orbital-cerebral mucormycosis in patients with diabetes. Postgrad Med J, 2004; 80: 670-674.

15. Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis: A review of the clinical manifestations, diagnosis and treatment. Clin Microbiol Infect, 2004; 10: 31-47.