

Post-Covid-19 Rhino-Cerebral Mucormycosis: an Observational Study During the Second Wave

Anandkumar SAJJAN^a, Anand V. NIMBAL^a, Roopa SHAHAPUR^a, Ishwar. B. BAGOJI^b, Vinutha. A. CHINIWAR^a, Sreedevi K. CHILLALASHETTI^a

^aDepartment of Dentistry, BLDEDU, Vijayapura Karnataka, India

^bDepartment of Anatomy, BLDEDU, Vijayapura Karnataka, India

ABSTRACT

Mucormycosis is one of the most lethal and rapidly spreading fungal infection which is caused by fungus of the order Mucorales. The swiftness of spreading and high mortality rate that characterize mucormycosis cases added more burden to the enormous challenge brought by the Covid-19 pandemic globally. The aim of this article is to identify and discuss mucormycosis and review the literature related to its diagnosis and management. A total of 15 mucormycosis cases with a history of Covid-19 infection were identified in the Department of Dentistry of Shri B M Patil Medical College Hospital and Research Centre BLDE (Deemed to be University), Vijayapura, India. The duration of the study was between April 1st and mid-September 2021. Nasal swab and tissue samples from oral and maxillofacial region were collected. Blood investigations, RT-PCR and HbA_{1c} tests and radiography revealed changes in the trabecular pattern and bone loss associated with periodontal inflammation. Mucormycosis is a life-threatening infection. Hence, dental and other clinical professionals must be aware of this possible fatal complication, so as to avoid an unfavorable outcome in clinical practice.

Keywords: Covid- 19 infection, mucormycosis, maxillectomy.

INTRODUCTION

Coronavirus disease is caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2), which can progress to severe health problems, including pneumonia, acute

respiratory distress syndrome (ARDS), and multi-organ dysfunction (1-4). It is globally accepted that systemic glucocorticoids will help in improving the condition in moderate to severe Covid-19 patients, but if used in excess, it will lead to a serious risk of developing secondary bacterial or fungal infection. Whereas the risk of fungal infection with

Address for correspondence:
Dr Roopa Shahapur, Associate professor
Department of Dentistry, BLDEDU, Vijayapura, Karnataka, India
Email: roopa.shahapur@bldedu.ac.in

Article received on the 14th of December 2021 and accepted for publication on the 28th of March 2022

Candida, *Aspergillus* and *Pneumocystis jiroveci* in Covid-19 settings is well recognized, the unexpected surge in reporting of infection with mucor in these subtypes of cases is a new emerging challenge. The swiftness of spreading and high mortality rate that characterize mucormycosis cases added more burden to the enormous challenge brought by the Covid-19 pandemic globally (5, 6). Mucormycosis is one of the most fatal fungal infections, which is caused by a fungus of the order *Mucorales*, and also it is the third most common fungal infection apart from candidiasis and aspergillosis (7). These infections facilitate the entry of organisms into the body through the exposed part such as dental extraction site. The nose is the most common entry site and even organisms gain entry by perforation through the skin and mucus membrane (8). Commonly, mucormycosis presents as an acute pulmonary, rhinocerebral or gastrointestinal infection or it can spread through the skin. The diagnosis of mucormycosis is difficult and in most of the cases it is a contributing factor in death or even its cause (9).

This unusual but deadly fungal infection initially occurs in the nasal cavity and paranasal air sinuses, presenting with similar features to those of acute sinusitis but has propensity for rapid spread to orbital and intra cranial sites in an immunosuppressed host, with a subsequent worsening clinical result (3, 4). So, a high index of doubt that would lead to early diagnosis and aggressive management is of uppermost importance in these patients for a successful treatment result (10). We report our experience in the management of mucormycosis in Covid-19 patients admitted to our tertiary care hospital. □

MATERIAL AND METHODS

A total of 15 mucormycosis cases with a history of Covid-19 infection were identified in the Department of Dentistry of Shri B M Patil Medical College Hospital and Research Centre BLDE (Deemed to be University), Vijayapura, India. The duration of the study was between April 1st to mid-September 2021. A proper institutional protocol was mentioned in the management of these cases. Nasal swab and tissue samples were collected with all aseptic precaution measures from medial meatal and then sent for tests with potassium hydroxide (KOH) staining for microscopic exam using special stains – periodic acid Schiff

and Grocott (or Gomori) methenamine silver – and fluorescent brightener. All samples were subjected to fungal culture, bacteriological culture, Gram stain, and all other required blood and biochemical investigations were done. After admission of Covid-19 cases with mucormycosis, all essential investigations such as RT-PCR, HbA_{1c} were done along with computed tomography (CT). □

RESULTS

Fifteen mucormycosis cases (total maxillectomy done in nine cases and subtotal maxillectomy done in six cases) of the maxilla were operated in our clinic during a routine check-up for dental infections. Later on, we correlated these patients with Covid-19 infection. There was a history of Covid-19 infection, supported by routine systemic and radiological findings, and also clinical findings such as extrapulmonary manifestations of Covid-19, characterized by necrosis of maxilla with the underlying systemic condition, which may be a post-Covid-19 complication.

Clinical symptoms manifested as toothache of non-odontogenic cause with radiating pain with altered sensation. Radiologically (CT scan) there was an unexplained erosion of the alveolar process (Figures 1 and 3). In some cases, an erosion of the inferior wall of the orbital bone (Figure 2) and an erosion of the anterior and lateral wall and floor of both maxillary sinuses were noted (Figure 4). The biopsy report helped in diagnosing these cases and mucormycosis. In all mucormycosis cases, maxillectomy was planned with debri-



FIGURE 1. Computed tomography scan showing erosion of the maxilla



FIGURE 2.
Erosion of the inferior wall of the orbital bone

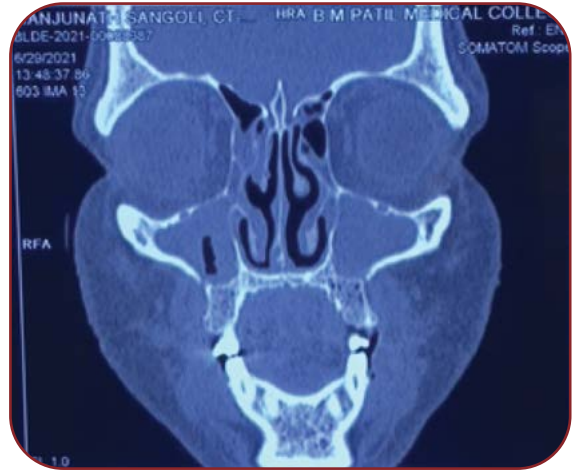


FIGURE 3. Erosion of the alveolar process of the maxilla

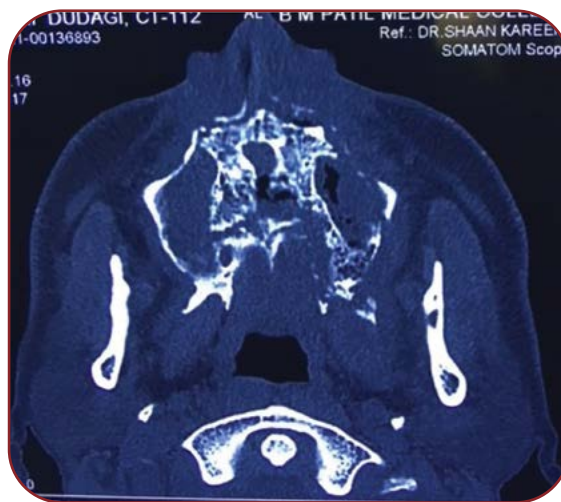


FIGURE 4.
Erosion of the anterior and lateral wall and floor of both maxillary sinuses

dement and curettage with possible tissue preservation. □

DISCUSSION

Mucormycosis is caused by fungi pertaining to the order *Mucorales*. *Rhizopus oryzae* is a typical organism seen in infected patients and is accountable for the majority of mucormycosis cases (around 70 to 80% of patients) (11). Uncontrolled diabetes mellitus in ketoacidosis, other types of metabolic acidosis, management of patients with corticosteroids, neutropenia, malignant hematologic disorders and also patients who are receiving deferoxamine therapy and undergoing hemodialysis are at high risk of getting

mucormycosis. Usually, in Covid-19 positive cases diabetes mellitus, prolonged hospitalization and use of immunosuppressive medication will lead to more risk in such cases (12). This disease generally spreads mainly through inhalation of spores from one person to another through environment (13).

The main symptoms of Covid-19 create perfect homeostasis for the growth and development of *Mucorales* inside the human body (14). Hosts susceptible to mucormycosis include persons with diabetes, those on systemic corticosteroid treatment, patients with neutropenia and hematologic malignancies, stem cell transplant patients and immunocompromised individuals. According to the current literature, diabetic patients are more prone to acquire Covid-19 accompanied by mucormycosis infection (15). For the detection of mucormycosis, CT is the generally selected initial imaging method. However, CT finding scan be non-specific in the early stages of disease; even if a patient has an invasive mucormycosis, he/she can present a normal sinus on a CT scan. Bone erosion and extra sinus spread are distinct features of mucormycosis and therefore comprise strong evidence for its diagnosis (16). Tissue necrosis is the distinguished feature of mucormycosis and is seen due to angioinvasion and successive vascular thrombosis. Clinically, bone exposure and necrosis are seen in the oral and maxillofacial region, and for diagnostic confirmation histopathological investigation are done. The feature is quite similar to osteomyelitis, trauma and iatrogenic infections. The main feature of pathogenesis and also a peculiarity of this disease is the substantial angioinvasion leading to vessel thrombosis and tissue ne-

crisis (17). This angioinvasion is incorporated with the capability of the organism to spread through the blood stream from the primary site of infection to cause sepsis (18). Curiously, even *Rhizopus oryzae* is destroyed by antifungal treatment but interestingly, these dead *Rhizopus* will cause substantial damage to endothelial cells. This is the likely reason for which solely antifungal treatment will not be helpful in controlling this disease, so further systematic debridement is required to clean the dead fungi or tissue to prevent further tissue destruction leading to necrosis. Amongst all these types, rhinocerebral mucormycosis is a very common disease which accounts for 1/3 –1/2 of all reported cases (19, 20). Usually, rhino-orbital-cerebral and rhinomaxillary mucormycosis (21) are used similarly in the literature, but we feel they are different from each other, even though the phrase used for them are mutual in published studies. Given the closeness to the base of the skull, there are often more chances of cerebral involvement, and thus, rhino-orbital mucormycosis needs to be considered more fatal than others. □

CONCLUSION

Mucormycosis is a fine drawn, destructive infection of fungal origin. It is a very difficult and crucial task to recognize or detect this infection in an early stage. In patients with mucormycosis, dentists and/or maxillofacial surgeons play a vital role due to the appearance of oral manifestations at the very early stage mainly in immunocompromised cases. For a clear and better diagnosis, histopathologic studies will be very useful. Intermodal remedies, which include both medical and surgical procedures, are of great use in bringing down patients' morbidity and death rates. Mucormycosis is challenging to detect, diagnose, and treat by clinicians who are not so familiar with its clinical findings. It is considered as life-threatening disease associated with poor prognosis. Therefore, proper diagnosis of this infection in a very early stage is essential to reduce death rates among infected patients. □

Conflicts of interest: none declared.

Financial support: none declared.

REFERENCES

- Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. *Nat Rev Microbiol* 2019;17:181-192.
- Cauchemez S, Van-Kerkhove MD, Riley S, Donnelly CA, et al. Transmission scenarios for Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and how to tell them apart. *Euro Surveill* 2013;18:18.
- Cascella M, Rajnik M, Cuomo A, et al. Features, evaluation and treatment coronavirus (COVID-19). *StatPearls* 2020 [Internet].
- Habibzadeh P, Stoneman EK. The novel coronavirus: A bird's eye view. *Int J Occup Environ Med* 2020;11:65-71.
- Chakrabarti A. The recent mucormycosis storm over Indian sky. *Indian J Med Microbiol* 2021. PMID:34175143.
- Jose A, Singh S, Roychoudhury A, et al. Current Understanding in the Pathophysiology of SARS-CoV-2-Associated Rhino-Orbital-Cerebral Mucormycosis: A Comprehensive Review. *J Maxillofac Oral Surg* 2021. PMID:34155426.
- Priyanka Choudhary, Deepak Bhargava, Vidyadevi Chandavarka, Ritika Sharma. Mucormycosis of maxilla. *Indian J Dent Adv* 2014;6:1503-1506.
- Bakathir AA. Mucormycosis of the jaw after dental extractions: two case reports. *Sultan Qaboos University Medical Journal* 2006;6:77-82.
- Castrejón-Pérez AD, Welsh EC, Miranda I, et al. Cutaneous mucormycosis, *Anais Brasileiros de Dermatologia* 2017;92:304-311.
- DelGaudio JM, Swain RE Jr, Kingdom TT, et al. Computed tomographic findings in patients with invasive fungal sinusitis. *Arch Otolaryngol Head Neck Surg* 2003;129:236-240.
- Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. *Clin Microbiol Rev* 2000;13:236-301.
- Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: a systematic review of cases reported worldwide and in India. *Diabetes Metab Syndr Clin Res Rev* 2021;15:102146.
- Mahalaxmi I, Jayaramayya K, Venkatesan D, et al. Mucormycosis: An opportunistic pathogen during COVID-19. *Environ Res* 2021;201:111643.
- Binder U, Maurer E, Lass-Flörl C. Mucormycosis—from the pathogens to the disease. *Clin Microbiol Infect* 2014;20:60-66.
- Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. *Cureus* 2020;12:e1072.
- Spellberg B, Edwards J Jr, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation, and management. *Clin Microbiol Rev* 2005;18:556-569.
- Selvamani M, Donoghue M, Bharani S, Madhushankari GS. Mucormycosis causing maxillary osteomyelitis. *J Nat Sci Biol Med* 2015;6:456-459.
- Ibrahim AS, Spellberg B, Walsh TJ, Kontoyiannis DP. Pathogenesis of mucormycosis. *Clin Infect Dis* 2012;54(Suppl 1):S16-S22.
- Janjua OS, Shaikh MS, Fareed MA, et al. Dental and Oral Manifestations of COVID-19 Related Mucormycosis: Diagnoses, Management Strategies and Outcomes. *J Fungi* 2022;8:44.
- Bhardwaj R, Sharma A, Parasher A, et al. Rhino-Orbital-Cerebral Mucormycosis During the Second Wave of Covid-19: The Indian Scenario. *Indian J Otolaryngol Head Neck Surg* (2021). <https://doi.org/10.1007/s12070-021-02978-y>
- Koc Z, Koc F, Yerdelen D, Ozdogu H. Rhino-orbital-cerebral mucormycosis with different cerebral involvements: infarct, hemorrhage, and ophthalmoplegia. *Int J Neurosci* 2007;117:1677-1690.