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Case Report

Mucormycosis of Maxilla, as a Post Covid Complication in a Diabetic Patient, A Case Report

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Abstract

The current pandemic for coronavirus disease (COVID-19) has caused great concern around the world, as it is capable of causing severe lung disease, and even death, in many patients. The people who develop more severe complications when infected by this disease are people with comorbidities such as Diabetes Mellitus (D.M.). The current medication used to manage the symptoms of COVID-19 includes systemic glucocorticoids, which suppress the immune system. Moreover, poorly controlled D.M. also predisposes to the development of infections by opportunistic germs. That is why people with COVID-19 and D.M. are more prone to develop opportunistic infections than others. In this case, a clinical case is reported about a diabetic patient diagnosed with COVID-19 who received corticosteroids in the treatment, later developing mucormycosis of the maxilla.

Keywords: Mucormycosis; COVID-19; COVID complications; Diabetes mellitus; Mucorale; SARS-CoV-2.

Clinical case report

In January 2021, a 58-year-old male patient reported to the Department of Oral Medicine, G.P.R Dental College, and Hospital, Kurnool, Andhra Pradesh, India with a chief complaint of swelling in the right side of the face associated with a teeth loss in the right upper jaw, which started approximately one month before. Among his personal medical history, he was diagnosed with Diabetes Mellitus fifteen years ago, under medication. Likewise, highlighted the fact that he was COVID-19 positive three months before consulting with a C.T. scan of the chest reporting as Small nodular density in the apical segment of the right lower lobe- Granuloma. Few small faint ground-glass opacities in bilateral lower lobes and left upper lobe suspicious for COVID-19 (CO-RAD-4)-C.T. severity score 4. He required hospitalization, and, among others, he received corticosteroids.

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During the physical examination, a diffuse swelling on the right side of the face was detected extending from the lateral wall of the nose to the pre-auricular region. The skin over the swelling area was shiny, but no ulcers or other lesions were detected. An oval-shaped swelling in the oral cavity measuring approximately 1.1cm in the right upper vestibule and posterior palatal region was noticed with a pus discharge with a foul smell in the premolar and molar region (Figures 1 and 2).

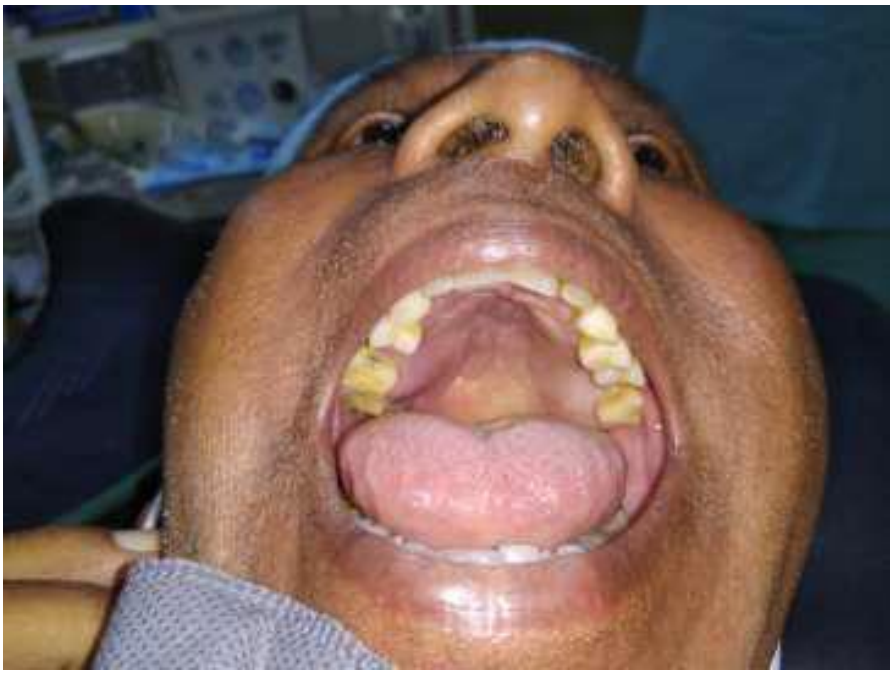

Figure 1: Oval-shaped swelling in the extral oral region on the right mid facial region.

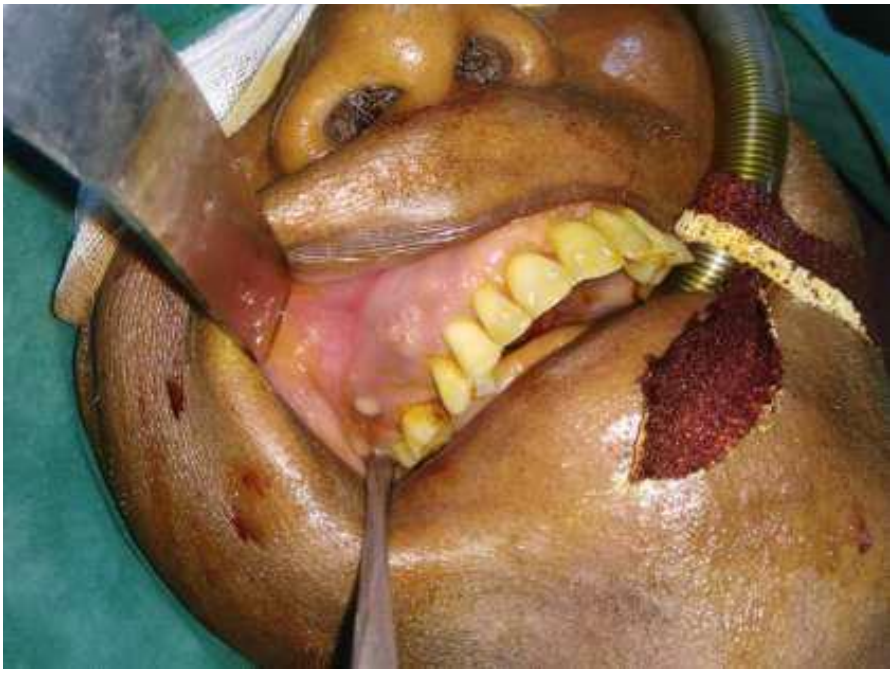

Figure 2: Oval-shaped swelling in the oral cavity in the right upper vestibule and posterior palatal region was noticed with a pus discharge with a foul smell.

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A head C.T. scan revealed haziness in the maxilla, extending into the sinus and posterior palatal region (Figure 3). To obtain the definitive diagnosis, an incisional biopsy was performed initially which revealed a fungal mucormycosis.

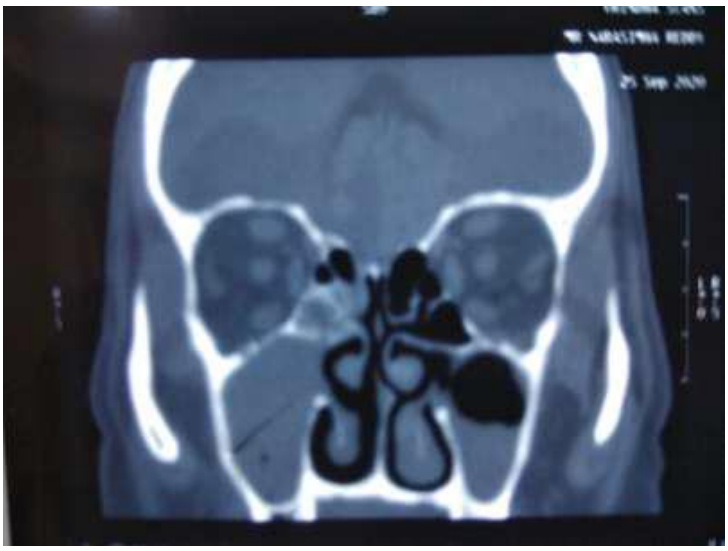

Figure 3: CT scan of head showing opacification of right maxillary sinus.

The patient was surgically treated by Hemi-maxillectomy using the Weber Ferguson's incision. A complete curettage and debridement of the area was performed to remove the necrotized tissue (Figure 4,5). General anesthesia was used during the procedure. The maxillectomy specimen was sent for histopathological examination. Sections examined show keratinized stratified squamous epithelium. Sub epithelium shows fibro collagen tissue with infected granulation tissue consists of sheets of neutrophils, lymphocytes, and plasma cells admixed with scattered multinucleated foreign body types of giant cells with capillaries (Figure 6).

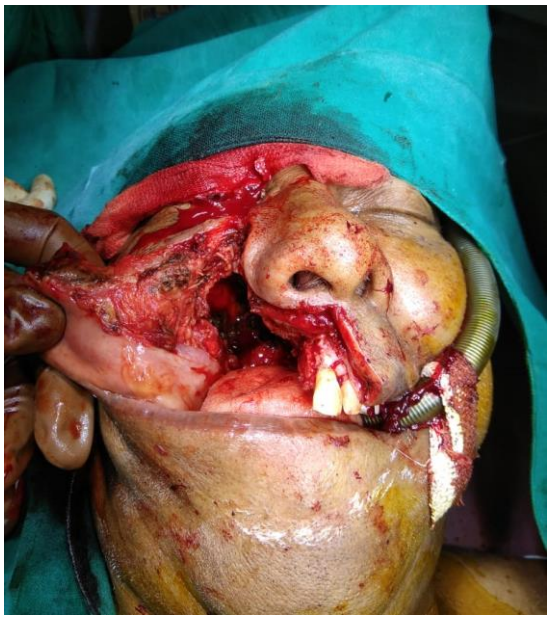

Figure 4: Intra operative specimen.

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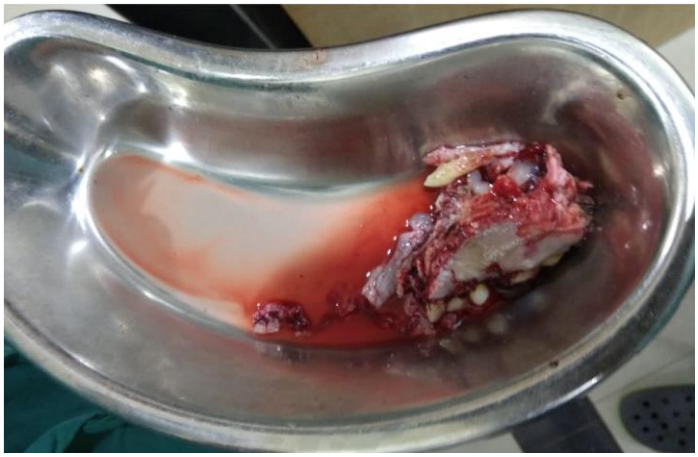

Figure 5: Intra operative specimen.

HISTOPATHOLOGY REPORT (LARGE BIOPSY)

Biopsy No. 3523 / H-20 / 7218

Clinical Diagnosis : Not provided

Nature of specimen : Maxillectomy specimen for HPE.

Gross :

Received maxillectomy specimen measuring 6.5 x 2 x 2 cm with 6 attached teeth (granulation seen over maxilla).
Few areas show grey white discoloration. *(Partly embedded). (Grossed by : Dr. S. Ravindranath Reddy).*

Sections for histology : A,B,C,D,E - Soft tissue around maxillectomy. F,G - Bony bits.

Microscopic Examination :

Sections examined show keratinised stratified squamous epithelium. Sub epithelium shows fibrocollagen tissue with infected granulation tissue consist of sheets of neutrophils, lymphocytes and plasma cells admixed with scattered multinucleated foreign body type of giant cells with capillaries.
Sections from mucosal lining show pseudo stratified ciliated columnar type of epithelium. Sub epithelium shows infected granulation tissue with few epithelioid cell granulomas consist of foreign body type of giant cells.
DC Bits - Sections from bone bits show presence of fungi, mucor with bits of necrotic bone. Trabeculae of bone shows increased osteoclastic activity with resorption of bone.

Impression : **Maxillectomy specimen - Features suggestive of Mucor mycosis of maxilla with increased osteoclast activity with resorption of bone. Please exclude hyper para thyroidism.**

** Correlate clinically.*

Figure 6: Histopathology report.

Sections from the mucosal lining show the pseudostratified ciliated columnar type of epithelium. Sub epithelium shows infected granulation tissue with few epithelioid cell granulomas consists of foreign body types of giant cells. DC Bits-Sections from bone bits show the presence of fungi, mucor with bits of necrotic bone. Trabeculae of the bone show increased osteoclastic activity with resorption of bone. Features suggestive of Mucormycosis of maxilla with increased osteoclast activity with resorption of bone. Under the microscopic examination: Necrotized tissue with no features of dysplasia. A post-operative obturator was placed, and the specimen containing both hard and soft tissue was sent for histopathological examination. A post-operatively anti-fungal treatment, amphotericin B injection of 50mg, administered through an IV line for one to two weeks. The patient is advised to have a

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soft diet and thorough chlorhexidine mouth rinses during the post-operative time. Good post-operative recovery was noted (Figure 7).

Discussion

The current pandemic caused by the novel coronavirus disease 2019 (COVID-19) has infected more than 204 million people and has generated more than 4 million deaths worldwide since its outbreak [1]. The overall mortality rate of COVID-19 varies from one country to another. However, the elderly and people with underlying comorbidities such as hypertension, cardiovascular disease, and diabetes mellitus (D.M.) invariably develop severe illness and have a poor prognosis [2].

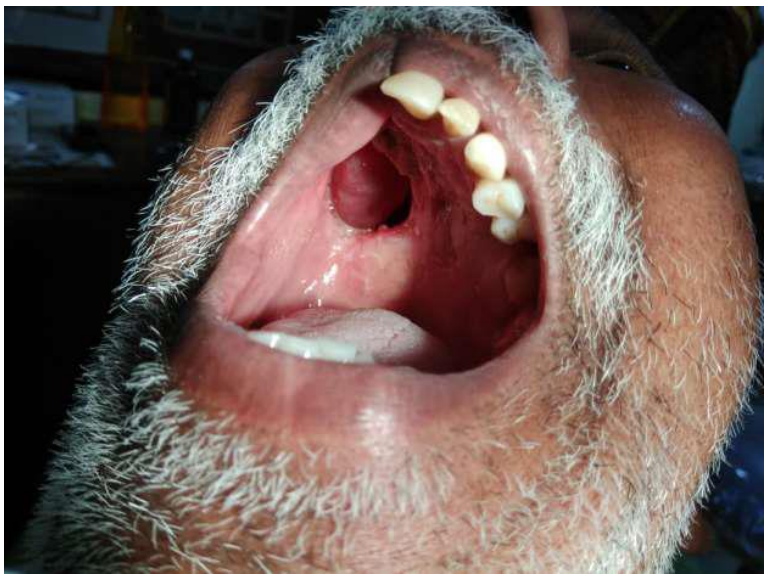

Figure 7: Post operative after 1 month.

COVID-19 wreaked havoc on the globe in ways no one could have foreseen, bringing with it a plethora of problems. In addition to producing pulmonary collapse and other systemic repercussions, SARS-COV2 causes a variety of metabolic processes in the body that lead to immunosuppression and an increased predisposition for opportunistic infections, including mucormycosis [3].

Mucormycosis is a serious fungal infection caused by mucormycetes, fungi of the order Mucorales. These fungi are generally found in the environment, but they usually cause illness in persons who have health problems or who use immune-suppressing medications. It also colonizes the sinuses and lungs more frequently after breathing fungal spores from the air [4]. Mucormycosis is a fungal infection that is angio-invasive and is associated with a high rate of morbidity and mortality. With the surge in prevalence, new causative agents, and a susceptible population, the epidemiology of mucormycosis has changed in recent years. The surge has been noticed all across the world, but it is especially noticeable on the Asian continent. In Asia, diabetes mellitus still outnumbers all other risk factors, but post-tuberculosis and chronic renal failure are emerging as new risk groups. Individuals with diabetes mellitus are more likely to develop rhino-cerebral mucormycosis, whereas patients with hematological malignancy and transplant recipients are more likely to develop pulmonary mucormycosis. Mucormycosis has diverse causal factors

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depending on where you live. Though Rhizopus arrhizus is the most commonly isolated agent worldwide, Apophysomyces variabilis and Lichtheimia species are more common in Asia and Europe, respectively. Rhizopus homothallicus, Mucor irregularis, and Thamnostylum lucknowense are three novel causal agents described from Asia [5].

Mucormycosis risk factors might vary a lot depending on where you live. Hematological malignancies have surpassed diabetes mellitus as a leading risk factor, according to studies from France, the United States, and Greece [6-9]. Trauma has also been identified as a key rising risk factor for mucormycosis in France [10]. Diabetes mellitus is the most common risk factor for mucormycosis, according to research from Iran, India, and Mexico [11-13]. Diabetes Mellitus was found to be a risk factor for Mucormycosis in patients who had previously been diagnosed with COVID-19 [14]. Disseminated mucormycosis was observed in one [10 percent] of ten individuals in post-mortem research from the United Kingdom on histopathological findings and viral tropism with severe lethal COVID-19 [15]. Rhino–orbito–cerebral mucormycosis (ROCM) is an uncommon and sometimes deadly disease invasive fungal infection that is a common occurrence in diabetics as well as in other immunocompromised patients. This infection is linked to a high prevalence of morbidity and mortality. For the patient's survival, prompt diagnosis, rigorous surgical debridement, and antimycotic medication are critical [16]. Although the link between pulmonary aspergillosis and COVID-19 is becoming more widely known, opportunistic fungal infections are a rare consequence in both COVID-19 and Diabetes Mellitus patients. Mucormycosis infection, on the other hand, is still sporadic [4].

Its incidence is difficult to measure, there are only a few population-based studies, but multiple studies have shown that it is increasing. Diagnosis of mucormycosis is still a challenge. Histopathology, direct examination, and culture are the essential tools, nevertheless, the molecular methods are improving to help with diagnosis [17]. Mucormycosis has high morbidity and mortality and a very poor prognosis. Nevertheless, aggressive medical and surgical management can result in survival rates of over 80% [18]. Several factors are responsible for the spike in the incidence of maxillary mucormycosis. Mucormycosis is well documented to be more common in people with uncontrolled diabetes and hyperglycemic conditions [19]. By using univariate analysis, it was observed that diabetic patients with mucormycosis who presented with ketoacidosis had a higher fatality rate [13]. It is essential to highlight that some drugs used to treat COVID-19 also worsen glucose control. For example, the corticosteroids used in our patients are known for leading to glycemic increases. In addition, they promote superinfection by inhibiting the immune system [20,21].

There is a two-way interaction between COVID-19 and D.M., in which COVID-19 disease leads to worse glycemic control in patients with D.M. and, in turn, this dysglycemia exacerbates the severity of COVID-19 [22]. That is why diabetes mellitus is recognized as comorbidity, which is related to developing severe varieties of the COVID-19 disease, including the apparition of acute respiratory distress syndrome (ARDS), superinfection, and increased mortality [23]. Prevention of hyperglycemia will be helpful to avoid

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complications in patients infected by SARS-CoV-2. Diabetes patients should closely adhere to basic preventive guidelines, such as monitoring glucose levels more regularly, engaging in physical activity, eating a healthy diet, and controlling other risk factors [24].

It has been suggested that mouthwashes should be used to reduce the viral load of SARS-CoV-2 in the oral cavity [25]. Unfortunately, there isn't much data on the effectiveness of mouthwashes against certain fungi. Chlorhexidine digluconate kills gram-positive and gram-negative bacteria (aerobes and anaerobes), as well as fungi like yeasts [26]. Essential oils present in many mouthwash formulations have antibacterial, antifungal, and even antiviral properties [27,28]. A mouthwash-based strategy could help prevent the rise of Mucormycosis and D.M. patients afflicted by COVID-19.

Conclusion

There is a well-established complex and damaging relationship between COVID-19 and D.M., in which there is a higher chance of developing seq uelae from this viral infection, including poor glycemic control, which predisposes superinfection by bacteria and fungi. Because of the widespread use of steroids, monoclonal antibodies, and broad-spectrum antibiotics to battle COVID-19, pre-existing fungal infections may develop or worsen. Rhino-orbital-cerebral mucormycosis is treated with intravenous antifungal treatment and surgical debridement (with or without palatal invasion). Therapeutic drug use should be closely monitored to provide the optimal therapeutic effect at the lowest possible dose and in the shortest amount of time.

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