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Case Report

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Are the Long-Term Complications of COVID Still Haunting the Immunity?- A Rare Case Report on Isolated Mandibular Mucormycosis

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Abstract

The COVID-19 pandemic has left an indelible mark on global health, with far-reaching consequences that extend beyond the initial infection. One of the deadliest, rapidly spreading, and profound fungal diseases in humans is mucormycosis, often known as black fungus. Mucormycosis is an opportunistic fungal infection commonly seen in patients with immunocompromised states. There had been a drastic surge in cases of mucormycosis worldwide and especially in India after the SARS CoV-2 outbreak in 2021. Among the different types of mucormycosis, Rhino-orbital-cerebral involvement has mainly been observed in the recent surge of cases. Mucormycosis of the mandible is a rare fungal infection, and worldwide only few cases had been reported till date. We present a unique case with the radiographic features of what appears to be an extensive osteomyelitis of mandible but came out as mucormycosis. A rare phenomenon affecting isolated mandible.

Keywords: Mucormycosis, Osteomyelitis, COVID, Cone Beam CT.

INTRODUCTION

The COVID-19 pandemic has left an indelible mark on global health, with far-reaching consequences that extend beyond the initial infection. As the world continues to grapple with the aftermath of the pandemic, a growing body of evidence suggests that COVID-19 can have a profound impact on the immune system, leaving individuals vulnerable to a range of diseases long after recovery. One of the most alarming examples of this is the emergence of mucormycosis, a rare and deadly fungal infection that has been increasingly reported in COVID-19 survivors, even years after initial infection. This phenomenon raises critical questions about the long-term effects of COVID-19 on immune function and the potential for increased susceptibility to opportunistic infections.

Mucormycoses is the third most common opportunistic fungal infection after candidiasis and aspergillosis. It is a deep fungal infection caused by a saprophytic fungus that is a member of the Phycomycetes phylum [1].

There are six accepted clinical types of mucormycosis namely, Rhino Cerebral, Pulmonary, Gastrointestinal, Cutaneous, Renal, Disseminated [2]. In recent times, this opportunistic infection was predominant to occur in patients recovering from COVID-19 infection. This post-COVID mucormycosis has been reported globally; however, in 2021, it reached alarming proportions in India [3]. This angio-invasive disease was found to occur in individuals with various immunosuppressive conditions like uncontrolled diabetes mellitus, corticosteroid therapy, etc. But in a Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) patient, the interaction of several factors like immune system deregulation, steroid therapy, and exacerbation of pre-existing diabetes may allow the mucoralean fungi to invade the host easily [4].

The Rhino cerebral form of mucormycosis is the most common type, because nasal cavity and oral cavity gets frequently exposed to the contaminants. The jawbones are predisposed to infections because of a

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primary contaminated environment of the oral cavity, periodontal pockets that harbour multitudes of anaerobic bacteria, a thin mucosal lining that adheres to the periosteum. Mandibular mucormycosis, in particular, is a rare variant, with only 23 cases reported till 2023 worldwide [5].

One of the complications of mucormycosis is Osteomyelitis, it is a severe infection of the bone and bone marrow, leading to devastating consequences if left untreated. Here we present a rare case of isolated mandibular mucormycosis with osteomyelitis in a patient who recovered from COVID-19. This life-threatening condition was diagnosed long after COVID-19 recovery, highlighting the challenges in diagnosis and the importance of early detection and interdisciplinary treatment.

CASE REPORT

A 37-year-old male patient reported to the department of Oral Medicine & Radiology with the chief complaint of intermittent dull pain, bleeding, pus discharge from lower right back jaw region and numbness over right side of mandible. Patient was known diabetic for 3 years and had a history of SARS-CoV-2 infection in April 2021. Extraorally, there was a gross asymmetry with diffuse bulging on right side of mandible. Intraorally there was loss of gingival soft tissue in lower right molar teeth region from crest of alveolar ridge till sulcus region. A segment of dead denuded bone was seen in that region measuring approximately 1.5 x 3 cm in relation to teeth 46, 47, 48. The bone segment was yellowish grey in colour and was slightly mobile along with teeth 46,47,48. There was evident pus discharge from the lower right back sulcus region [Figure 1]. The right submandibular lymph nodes were firm and tender on palpation, while there was numbness over right side of mandible from corner of mouth till angle of mandible.

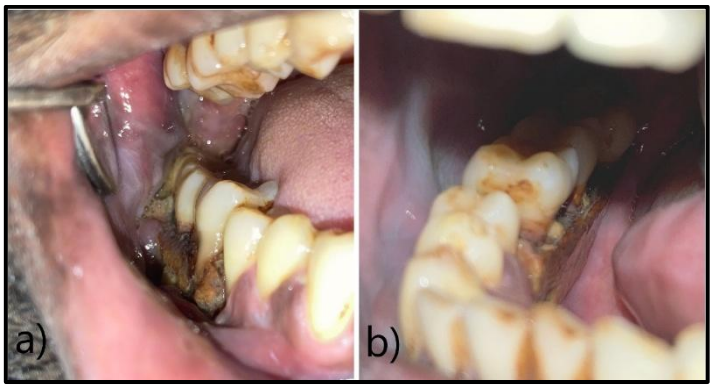

Figure 1: Denuded bone, **a)** Buccal aspect; **b)** Lingual aspect

A provisional diagnosis of chronic osteomyelitis was given based on history and clinical presentation of lesion. Deep fungal infection and malignancy were given as differential diagnosis. OPG, CBCT and Incisional biopsy was done, in which OPG revealed ill-defined irregular periapical radiolucency extending from distal surface of root of 43 to retromolar area approx. 1cm into ascending ramus region.

The CBCT scan showed reduced bone density of alveolar region from 43 to 48 and extending posteriorly in the ascending ramus with a moth-eaten radiolucent region below it. The right lower border of mandible showed hyperdense bone extending from mesial of 43 till the neck of condyle posteriorly. There was loss of buccal and lingual cortical plates. Lesion was measuring approx. 40.11 mm antero-posteriorly and 12.96 mm bucco-lingually. There were radiopaque bony masses surrounded by radiolucent area which was suggestive of sequestrum formation. The lesion caused displacement of inferior alveolar nerve canal inferiorly and lingually with some compressed areas in between the course of nerve. Expansion of jaw bone seen bucco-lingually on right side in ramus area. After radiographic examination patient underwent incisional biopsy, and the biopsy specimen then sent for histopathological investigation [Figure 2].

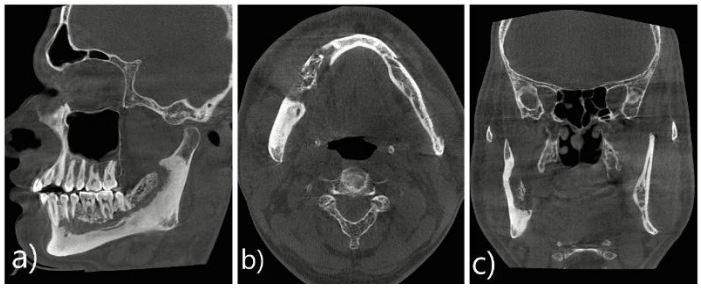

Figure 2: CBCT images **a)** Moth-eaten radiolucency apical to posterior teeth and hyperdense bone extending till neck of condyle; **b)** Sequestrum; **c)** Hyperdense bone, Moth-eaten radiolucency and sequestrum on mandibular right side

Histopathological examination showed decalcified bone with multiple resorbing bony trabeculae with multiple abscess. Fungal spore and hyphae were evident within the abscesses. Special stain to demonstrate fungal apparatus was then performed. Grocott-Gomori's Methenamine Silver (GMS) stain showed numerous spores and non-septate hyphae of mucoromycetes [Figure 3].

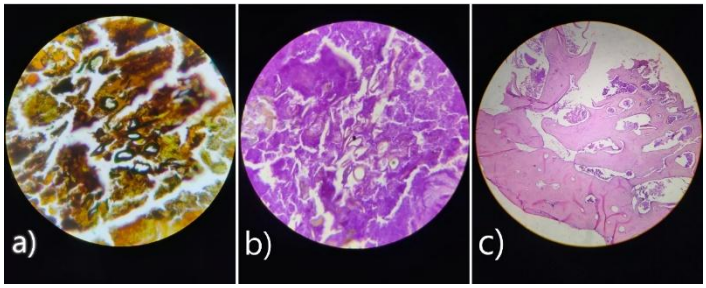

Figure 3: a) 40x, GMS showing spores and non-septate hyphae; **b)** 40x, H&E, showing spores and nonseptate hyphae; **c)** 10x, H&E, decalcified bone showing resorbing trabeculae with multiple abscesses

Final diagnosis of Osteomyelitis with Mucormycosis of Isolated Mandible was made, based on the clinical, radiographic and microscopic features. Treatment involved right Hemi-mandibulectomy followed by reconstruction plate. Satisfactory healing was seen on 6 months follow-up [Figure 4].

Figure 4 Six month follow up OPG of patient showing reconstruction plate on right side

DISCUSSION

Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) quickly swept through the world and became a pandemic only months after its first isolation and identification. Worldwide, mucormycosis incidence ranges from 0.005 to 1.7 cases per million people. According to estimates, the prevalence of mucormycosis in India is 140 cases per million people, around 80 times greater than in affluent nations.

389/851 (46%) patients had reported deaths in a systemic review and meta-analysis of 851 case reports published in 2018. Patients with disseminated mucormycosis had the highest fatality rate (68%) while patients with cutaneous disease had the lowest fatality rate (31%) [4].

With the advent of the SARS-CoV-2 pandemic, fungal infections have increased tenfold worldwide, with rhino-cerebral and pulmonary mucormycosis being the most prevalent type. For COVID patients, corticosteroids such as methylprednisolone and dexamethasone are frequently recommended. In order to slow the progression of respiratory infections, corticosteroids control inflammation-mediated lung damage [5].

The side effects of Corticosteroid, like secondary infections and latent hyperglycemia, resulted as the primary causes of mucormycosis. Since 70% of instances of mucormycosis resulted from the indiscriminate use of steroids after COVID, diabetes was identified as the primary predisposing risk factor, either predominantly or secondary. An acidic environment is created by hyperglycemia, particularly in ketoacidosis, which is conducive to the growth and spread of fungi [6].

The most prominent character of mucormycosis is arterial invasion and formation of emboli, with resulting necrosis of involved tissue. In the rhino-cerebral form, mucormycosis usually begins in the nose, spreads to involve the paranasal sinuses and palate, and spreads fast to involve the orbit and central nervous system, sometimes causing death [4]. Fungal osteomyelitis is a life-threatening and seldom seen opportunistic infection. It is commonly an affectation of the nose and paranasal sinuses within the orofacial region, making its occurrence rare in mandible. It is an aggressive infection that needs to be addressed promptly to prevent fatal consequences [3].

Early diagnosis and treatment are crucial to improve outcomes, but the disease often presents with non-specific symptoms, delaying diagnosis. The fungus is frequently difficult to culture; instead, a biopsy for culture and direct examination should be performed [7]. The histopathology shows necrosis and non-septate hyphae, which are best demonstrated by a periodic acid– Schiff stain or the methenamine silver stain. Necrosis and occlusion of vessels are also frequently present. Newer techniques of identification include the use of PCR; however, this is not generally commercially available [8].

Surgical debridement, antifungal therapy, and management of underlying conditions is the first line of treatment. The effectiveness of antifungals like amphotericin B varies, it still considered the drug of choice. Azoles like Posaconazole showed promising results with lesser side effects compared to Amphotericin B [9].

According to published literature, the recurrence rate is high, ranging from 20-50%, and the mortality rate is significant, ranging from 25-60% depending on the site of infection and underlying predisposing factors. The newer approaches for treatment include the lipid formulations of amphotericin B along with that, the combination therapy between polyenes and echinocandins proved to be synergistic [9]. Adjuvant to the antifungals, post-surgical hyperbaric oxygen (HBO) therapy showed promising results with up to 86% survival rate in life threatening fungal infections [10].

This case report emphasizes the need for increased awareness and education among healthcare professionals about this rare and life-threatening condition. The mucormycosis itself is a rare phenomenon and when it occurs in mandible in the isolated form, it becomes more unique presentation. Early recognition, prompt intervention, and multidisciplinary management are crucial for improving outcomes and reducing the recurrence and mortality rates associated with mucormycosis.

The complex interplay between COVID, immune dysfunction, and the rising incidence of diseases like mucormycosis, highlighting the need for ongoing research and vigilance in the face of this evolving global health crisis.

CONCLUSION

This case report emphasizes the need for increased awareness and education among healthcare professionals about this rare and life-threatening condition. The mucormycosis itself is a rare phenomenon and when it occurs in the mandible in isolated form, it becomes a more unique presentation. Early recognition, prompt intervention, and multidisciplinary management are crucial for improving outcomes and reducing the recurrence and mortality rates associated with mucormycosis.

Patient Perspective

The patient expressed satisfaction with the treatment received and reported significant relief from the spontaneous pain and sensitivity that initially brought him to the clinic. He noted that the procedure was comfortable and that the dental team kept him well informed at every stage of the treatment. The patient appreciated the explanation provided about the unusual root canal anatomy and was reassured by the careful approach taken to ensure all canals were treated. He reported no post-operative complications and expressed confidence in the outcome, mentioning that he would recommend similar care to others if needed.

Conflicts of Interest

The author reports no conflicts of interest.

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