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CASE REPORT

Maxillofacial infections in post covid-19 era: A series of 2 cases

[1]Pranil Jaiswal, [2]Satish Karandikar, [3]Mamta Singh, [4]Shubham Gupta, [5]Aayushi Verma, [6]Mahendra Mohan Katiyar

[1,4,5,6]Resident, [2,3]Professor, Index Institute of Dental Sciences, Indore, Madhya Pradesh, India

ABSTRACT:
Everybody in the world including the health care sector has witnessed the devastating effects of COVID- 19 infection. It is an enigma to say whether COVID -19 has gone for good or not, but has definitely presented as a challenge in itself for dental professionals. Complications have escalated especially at the end of the 2nd wave, probably due to various immunosuppressant drugs that have been used for it's aggressive treatment. These cases highlights osteomyelitis of maxilla and surrounding structures in patients due raised levels of blood sugar and also due to steroidal therapy. Recent reports that have been published, show a rate of approximately 80.76% of such cases in maxilla, out of which 61.53% patients were found to be diabetic before diagnosis. These cases presents post COVID-19 osteomyelitis which is believed to be triggered by highly raised blood sugar levels in a patient who was not a known case of diabetes mellitus.
Key words: Covid-19, Immunosuppresion, Steroid Therapy, Diabetes Mellitus, Osteomyelitis.

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Corresponding author: Pranil Jaiswal, Resident, Index Institute of Dental Sciences, Indore, Madhya Pradesh, India

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INTRODUCTION

"Osteomyelitis" refers to an inflammation ("itis") of the bone marrow ("osteomyel") only but means an inflammation of the entire bone including the periosteum, the cortical, and cancellous bone as well as the bone marrow.[1] Most common predisposing factor for the cause of osteomyelitis is infection of odontogenic origin and tooth root densely placed to the medullary cavity of bone, other sources of infection are also reported. Apart from virulence of microorganisms, host resistance and vascularity alteration also play a vital role. This condition was originally described by Rees in 1947.[2] Osteomyelitis is an inflammatory response of bone to the extended infections arising from apical region of tooth (root canal), periodontal ligaments or extraction sites, fractured segments of bone, unhealed soft tissue wounds and surgical or unapproximated sutured sites. Most frequently occurring site for osteomyelitis in head and neck region is mandible, incidence is less in maxilla due to its high vascularity. Thin cortical plate and a relatively rare paucity of medullary tissue in the maxilla preclude confinement of infection within bone and permit the dissipation of edema and pus into the soft tissue and paranasal sinuses.[3] Maxillary necrosis can occur due to bacterial infections such as osteomyelitis, viral infections or fungal infections such as mucormycosis, aspergillosis etc.[4] There are many different classifications that are either based on the etiology, pathogenesis, pathologic or anatomic differences, the clinical course of the disease, or radiologic patterns. The Zürich classification differs between three different kinds of osteomyelitis, the acute osteomyelitis, the secondary chronic osteomyelitis, and the primary chronic osteomyelitis. The secondary chronic osteomyelitis results from the acute osteomyelitis and therefore is the same disease at a different time stage. Once the osteomyelitis persists for more than 4 weeks, it is defined as chronic.[1,5] At the global level, one of the major causes of morbidity is Diabetes mellitus (DM), becoming one of the risk factors for certain infectious diseases owing to the development of an immunocompromised state, the main culprit being hyperglycemia, affecting overall defence mechanisms of the body via various pathways.[6] Osteomyelitis is one of the major complication caused due to diabetes mellitus. Excessive usage of immunosuppressant drugs (steroidal therapy) as a treatment protocol of Covid 19 leading to the immunocompromised state igniting the

spark of already complicated scenario of uncontrolled diabetic patients ending in deadly situation of post covid osteomyelitis. In established suppurative osteomyelitis, symptoms include deep pain, malaise, fever and anorexia. Within 10-14 days after onset, teeth in the involved area begin to loosen and become sensitive to percussion. Pus exudes around the gingival sulcus or through mucosal and cutaneous fistulae. Firm cellulitis of the cheek, enlargement of the dimensions of the bone from increased periosteal activity, abscess formation with localized warmth, erythema and tenderness to palpation may be noted. Suppurative osteomyelitis can involve all three components of bone: periosteum, cortex and marrow. Osteomyelitis of the jaws usually requires both medical and surgical treatment.[7]

CASE REPORT

Current case series presents with 2 atypical cases of post covid19 osteomyelitis of maxilla reported in our department with common history of uncontrolled type 2 diabetes mellitus and history of long-term usage of immune-suppresent drugs as a treatment protocol for covid 19.

CASE 1

Female patient of age 58 year came with the chief complaints of pain and swelling with pus discharge in her upper left back teeth region in the last 20 days. 4 months back patient had a history of covid19 for which patient took treatment and was also on immunosuppresent drug for the same, patient recovered within 20 days. Patient was a known case of type 2 diabetes mellitus and was on oral hypoglycemics for the same in the last 20 years. Also had a history of multiple extractions 20 days back with 22,23,24,25,26,27,28 within 3 days gap every 2 teeth were extracted, last extracted teeth was 27,28. Patient was apparently alright 20 days back, then she had undergone an extraction of multiple teeth in her upper left back teeth region after that she had pain in the same extracted site which was dull, continuous, which gradually increased in intensity, it was aggravated on food intake, relieved on medication. Pain was associated with swelling in same region after 2 days, swelling was soft in consistency, diffused and tender, overlying tissue was slightly red in color. Socket was unhealed even after a week then she observed, yellow colored discharge from the socket which was salty and sour in taste with foul odor and by now it is more painful causing more difficulty in eating. She also had mild episodic fever since 10 days. Then she went to primary health center where they medicated her and referred to higher center. Then patient came to our department. On extra-oral examination, a diffuse swelling of approximately 5cm x 5cm over left middle third of face, no signs of proptosis or ptosis, vision of both the eyes were normal. On palpation pain and tenderness over left zygomatic buttress and cheek region, mouth opening was normal. On intra-oral examination denude necrotic alveolar bone with erythematous and irregular borders from left canine region to tuberosity of left side of maxilla, crossing mid line about 1cm and posteriorly extending to the junction of hard and soft palate. Segmental mobility with pus discharge was apparent from left first premolar to third molar region. The patient then was advised for CBCT. Various sections of CBCT revels diffuse bone loss with thinning of outer cortical bone of both buccal and palatal bone in left maxillary alveolus. Chronic osteolytic lesions are evident in left side of maxilla. Destruction is evident in left side of maxilla including left zygomatic process of maxilla. Impressions made by CBCT were Osteomyelitis infection in left maxilla and maxillary sinus. Biopsy was performed cytological smear and PAS stains showed aseptate fungal hyphae and conidia showing irregular branching suggestive of mucormycotic fungal growth.

Fig 1 – Pre operative image showing unhealed extraction socket with pus discharge

Fig 2 – Pre operative OPG showing degenerative changes in left side of maxilla unhealed sockets with irregular bony margins

Fig 3 – CBCT imaging revelling Osteolytic changes in left maxilla and maxillary sinus

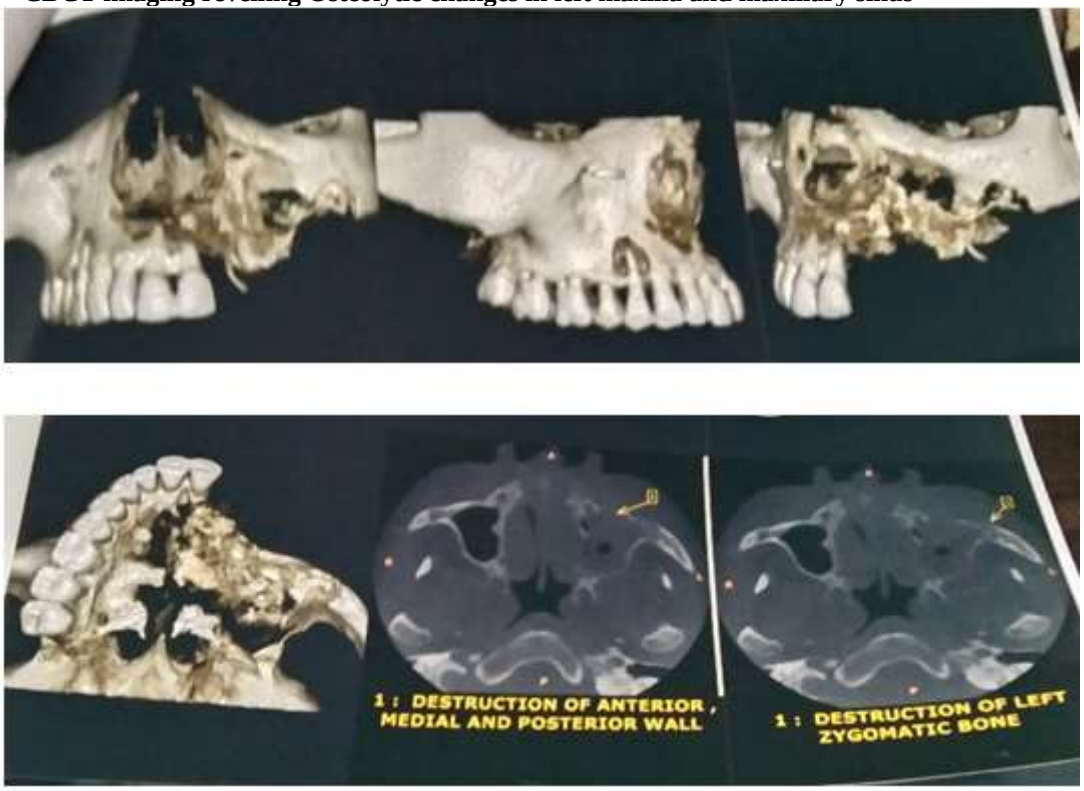


Fig 4 – Biopsy done under LA

Primary impression was made and cast was poured and mock surgery was performed to make interim stent with cold cure to close the defect until epithelisation of soft tissue occurs. After all investigations, pre anaesthetic evaluation was done. Under all septic conditions patient was taken to operation theatre followed by nasal intubation for giving general anaesthesia, after achieving anaesthesia

patient was painted and draped local anaesthesia delivered in the site of interest, intra-orally. Incision was marked from central incisor to tuberosity on left side of maxilla, enveloped periosteal flap raised exposing the necrotized bone. Sequestrectomy and curettage was done saving healthy peripheral bone. Closure was done in layers. Interim stent placed. Since it was a suppurative lesion the patient was kept on antibiotic coverage for 2 weeks, which drastically improved the condition Regular follow ups was done post operatively till day 7th, suture removal done on day 10th, then left for healing for 15 days provided by primary stent. After 1 month stent was relined with soft liner according to healing tissue and shape of defect and left for another 1 month to heal. After 2 months post operatively patient was provided with an obturator to cover the defect and also providing functional occlusion. Antifungal medication which were prescribed- Posaconazole 300 mg tablets twice daily (bid) for 15 days. Augmentin 625 mg tablets thrice daily (bid) for 15 days. Dynapar tablets twice daily (bid) for 7 days. Hydrogen peroxide mouthwash 3 times a day for 15 days. A to Z (multivitamin) capsule for 15 days

Fig 5 – Intraoperative image showing necrotized bone which is to be resected

Fig 6 – Intraoperative image showing site left after necrotized bone is resected.

Fig 7 – Intraoperative image showing sutured site after the procedure

Fig 8 – Extracted 21,11 and 14 teeth with resected necrotized bone and adjacent soft tissue.

Fig 9 – Post operative OPG showing remaining healthy bony tissue on left side on maxilla

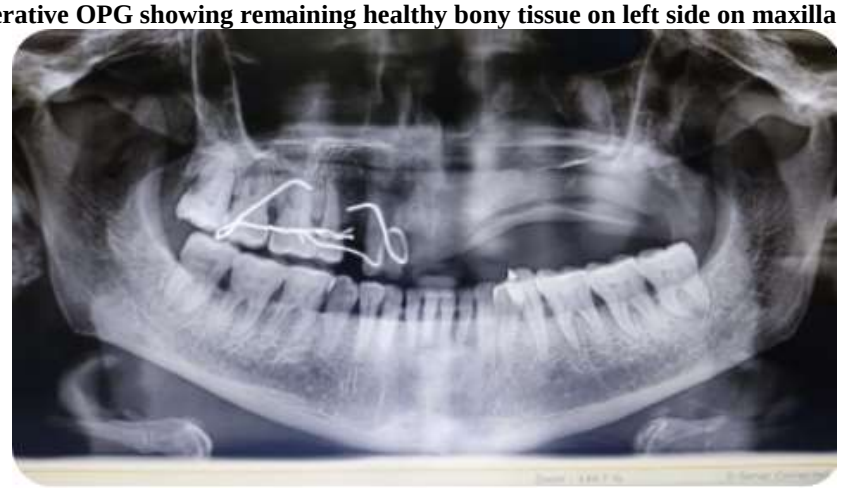


Fig 10 – Interim splint provided for healing of tissue

Fig 11 – 1-month post-operative follow up showing defect with its smooth margins

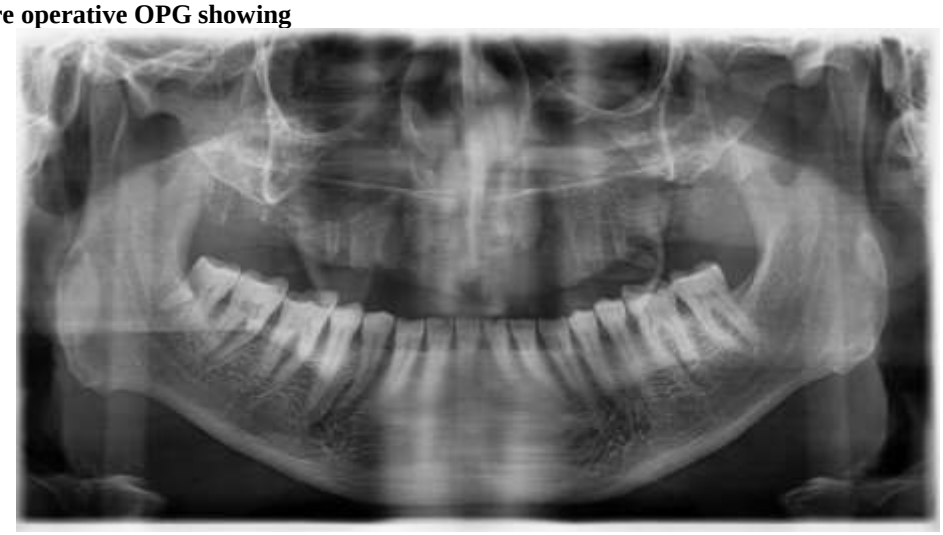
Case 2

A case of 60-year-old male patient came with the chief complaint of pain and pus discharge in his upper front and back teeth region in both left and right side in the last 1 month. Patient had a history of covid19, 3 months back for which patient was hospitalized for 15 days and was on immunosupressant drugs. It took 15 days to fully recover from covid19 and patient was also a known case of diabetes mellitus in the last 20 years and was on hypoglycemic drugs since then. Patient also had a history of multiple extractions with unhealed extraction sockets. Patient was apparently alright 1 month back then he went to dentist for extraction of all the remaining teeth in his upper jaw as the teeth left in his upper jaw was carious and was of no use. He wanted to replace them with denture. Extraction was done under local anaesthesia and was uneventful. Patient is provided with classical regimen of medication for 5 days and was left for healing. Since, the day after extraction patient had severe pain which was dull aching, continuous, gradually increased in intensity as the day passes. Pain gets aggravated on food intake and relieved on taking medication. Pain was associated with mild swelling by day 3 post extraction which was localized in upper jaw. After 4th day patient observed a yellow-coloured discharge coming out of unhealed socket of extracted site. Discharge was foul smelling. Patient took primary treatment and medication from primary health care centre and was not relieved.

Fig 12 – Pre operative image showing necrotizing bone

On extra-oral examination, bilateral symmetry of face was appreciable, slight horizontal linear swelling bilaterally over upper lip extending on middle third of cheek. On palpation pain and tenderness over upper lip and middle third of cheek region, mouth opening was adequate. On intra-oral examination denuded necrotised bone can be appreciated covering whole maxillary alveolus, soft tissue being recessed and inflamed obliterating the buccal vestibule foul smelling with food lodgement in the unhealed extracted sockets extended palatally about 1 cm from periphery to centre. Whole segment of necrotizing bone was mobile.

Fig 13 – Pre operative OPG showing



The excision biopsy was performed report confirmed the lesion to be chronic suppurative osteomyelitis of maxilla. Sequestrectomy and curettage of denuded necrotizing bone was planned and performed under general anaesthesia. After all investigations, pre anaesthetic evaluation was done. Under all septic conditions patient was taken to operation theatre followed by nasal intubation for giving general anaesthesia, after achieving anaesthesia patient was painted and draped local anaesthesia delivered in the site of interest, Sequestrectomy and curettage was done, thorough irrigation was done followed by collagen sheet placement over healthy tissue and then closure was achieved, classical regimen of antibiotics given for 2 weeks due to its suppurative nature. Suture removal done on 10^{th} day, regular follow ups were done till 6 months. Healing was uneventful.

Fig 14 – Intra-operative image showing selective maxillary osteotomy

Fig 15 – Resected segment of maxilla

Fig 16 – follow up after 6 months.

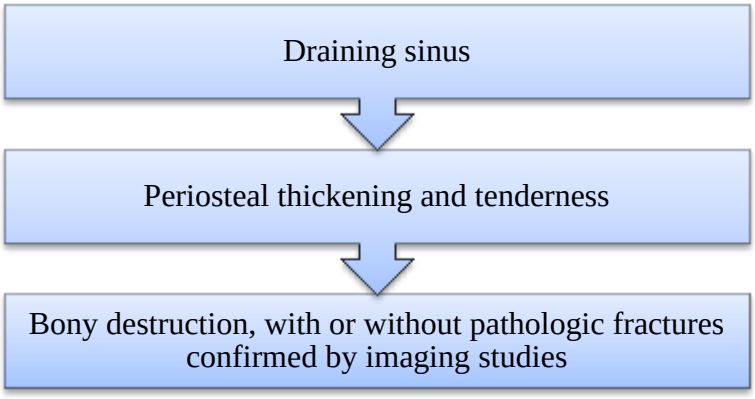
Fig 17 – Post operative OPG showing remaining peripheral healthy bone

DISCUSSION

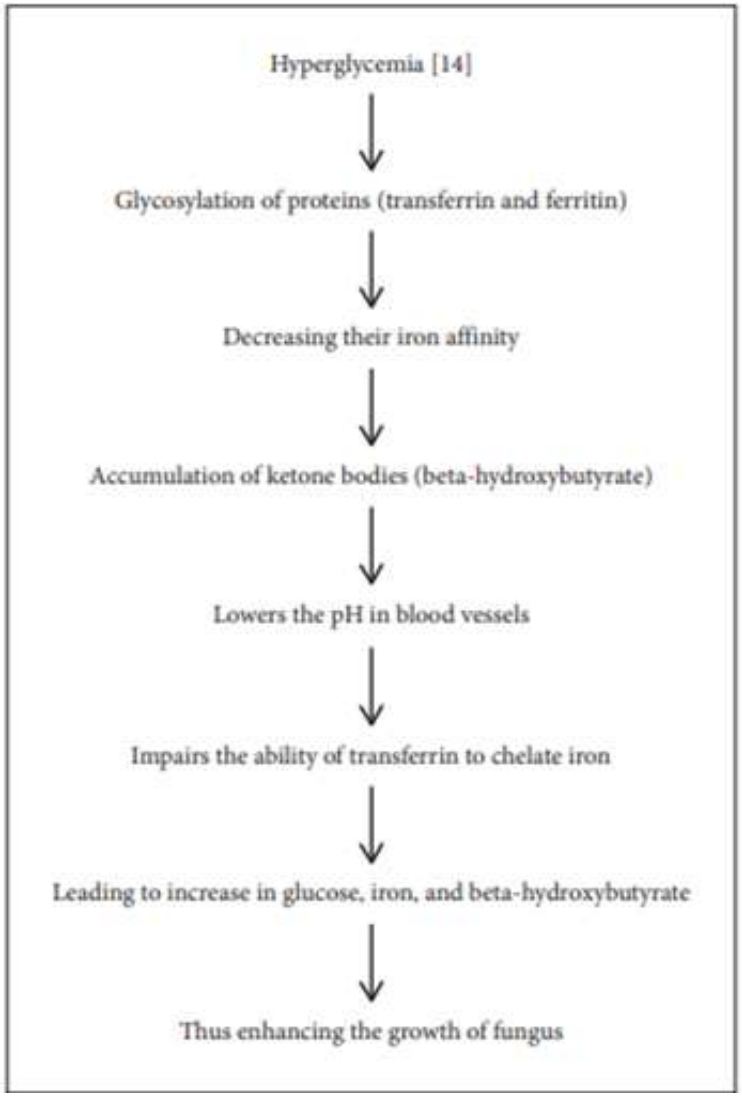
Etiological factors, such as traumatic injuries, radiation, and certain chemical substances, among others, may also produce inflammation of the medullary space, the term "osteomyelitis" is mostly used in the medical literature to describe a true infection of the bone induced by pyogenic microorganisms (Marx 1991).Osteomyelitis is heterogeneous in its pathophysiology, clinical presentation, and management. It is estimated to be one of the most difficult-to-treat infectious diseases. Hallmarks of osteomyelitis are progressive bony destruction and the formation of sequestra. Osteomyelitis can result from hematogenous seeding, contiguous spread of infection, or direct inoculation of microorganisms into intact bone.[8]

Anatomically, In osteomyelitis of the skull, the bones involved are the mandible, maxilla, nasal bone, frontal bone, temporal bone, and skull base bones. Although the diagnosis is rapidly made clinically, when the diagnosis is uncertain or to help gauge the severity of infection and extent of involvement, radiographic imaging is commonly used for early detection and confirmation of the disease.

CLINICAL SEQUEL OF OSTEOMYELITIS INCLUDE



Consequences of such an infection can be as minor as a draining tract up to malignant transformation to carcinoma at the infected site.[9] Coronavirus disease 2019 (COVID-19) infection may be associated with a wide range of bacterial and fungal co-infections. There are specific pathophysiologic qualities of COVID-19 that may initiate secondary or opportunistic infections, including a tendency to cause extensive pulmonary disease and the subsequent alveolointerstitial pathology that may enhance the risk of opportunistic infections. Subsequently, the immune deregulations associated with COVID-19, with reduced numbers of T lymphocytes, CD4+T, and CD8+T cells, may alter innate immunity.[10] Drugs which could be a route to osteomyelitis as a complication on eternal use are steroids, Bisphosphonates and chemotherapuetic agents. On analysing the existing literature, Candida and Aspergillosis were the most common causative agents of fungal infections.[11] Urs et al., in their prospective study which was commenced from 2011 to 2013 December, discovered only five cases which showed the characteristics of fungal osteomyelitis. All those five cases were primarily intraosseous and have shown the radiographic changes in bone. Out of these five cases, maxilla was involved in three cases and out of these three cases two patients were presented with a history of uncontrolled diabetes.[12] Niranjan et al., in their ten-year study (from January 2005 to December 2015) which was conducted to evaluate the prevalence of fungal osteomyelitis of the jaws associated with diabetes mellitus, reported that 52% of all the osteomyelitis cases were of fungal osteomyelitis, whereas 48% belonged to the non-fungal category. In the same study, they also stated that fungal osteomyelitis was frequently found in the individuals above 40 years of age and is more common in males when compared to females. Maxilla is the most common jaw bone being affected by fungal osteomyelitis and is more commonly associated with diabetes mellitus.[13]



Siddanagouda Biradar et al. In 2016, reported a case of mucormycosis in a diabetic patient. Patients, urine analysis revealed 1.5% glucose & ketone bodies and albumin of more than 2%.[14] In maxillary osteomyelitis, diabetes mellitus is usually a proliferating factor. The presence of ketone bodies favours the suitable environment for the growth of fungus in diabetic patients. Ketoreductase is the

enzyme produced by the fungus that acts on the ketone bodies.[11] Infection in maxilla can turn out to be in serious complications to the patient such as infection of cranial cavity and brain. Thus, it is crucial that any maxillary osteomyelitis should be treated aggressively by the surgeons to avoid consequent terrifying consequences. In our cases, the patients with maxillary osteomyelitis were under medication for diabetes in the last 20 years and also gone through the therapy of immunosuppressant drugs for different period of time. Osteomyelitis usually occurs due to polymicrobial odontogenic bacteria such as bacteroides, peptostreptococcus, and microaerophilic streptococcus along with the opportunistic pathogens in tooth bearing area, as shown in our case 2. Osteomyelitis due to fungal organisms is rare, but it is seen in immunocompromised patients.[15] Microscopic examination shows aseptate fungal hyphae and conidia showing irregular branching in case 1. Fungal growth is quite fast and extensive in nature proliferates every single tissue of its reach, in this case growth and its extension is assessed.

CONCLUSION

The pandemic COVID-19 has directed to the rise of the previously less dominant opportunistic fungal infection that is mucormycosis. It has become the centre of attention as being a super infection in immunocompromised and weakened patients, who have either recovered or are still suffering from COVID-19 infection. Osteomyelitis is one of the oldest diseases existing in literature. However, fungal osteomyelitis is a rare variant of it, usually seen in patients with diabetes and those who are on immunosuppressant drugs. Care must be taken in precise diagnosis through appropriate investigations in every way such as histological and radiological assessment. These investigations confirm whether the osteomyelitis is of fungal origin or due to some other cause. However, identification of fungal species can be done only through the culture. Treatment of osteomyelitis includes combined therapy of surgical debridement and antibiotics. The present case of osteomyelitis with fungal infections has been treated by Excisional biopsy followed with bony curettage along with Beta-lactam antibiotics for two weeks. Accurate antifungal treatment is necessary for the fungal osteomyelitis. Complications can vary from just a draining sinus to extensive bony destruction.

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