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COVID-19 Related Osteonecrosis of Jaw (CRONJ) challenge ahead: A Case Report

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Abstract:
Various oral manifestations have been reported in patients with COVID-19. However, there is still a question about whether these lesions are due to coronavirus infection or secondary manifestations resulting from the patient's systemic condition. Oral conditions in a patient diagnosed with COVID-19.COVID-19 has emerged as a challenge to the clinicians worldwide. Since the outbreak in December 2019, COVID-19 has affected > 08,00,00,000 world wide till December 2020. The most common symptoms are fever and dry cough and in few cases shortness of breath, dysosmia, and dysgeusia. Present understanding among researchers shows that coronavirus invades human cells via the receptor angiotensin-converting enzyme 2 (ACE2) through scRNA-seq data analyses. The prevalence of clinical manifestations is still unknown, the range of COVID-19 manifestations on the oral cavity has been considered of broad. The current case series aims to report a rare finding of bone and soft tissue defect in maxilla as a possible sequelae of C0VID-19 infection.

Key Words: *COVID-19, Sars-CoV2, Oral Manifestation, Osteomyelitis, Osteonecrosis*

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I. Introduction:

COVID-19 has emerged as a challenge to the clinicians worldwide. Since the outbreak in December 2019, COVID-19 has affected >08.00.00.000 people (World Health Organization 2020b). (1) The most common symptoms are fever and dry cough and in few cases shortness of breath, dysosmia, and dysgeusia (2,3). Most human cases of COVID-19 are mild (80%), while 20% of patients presented with severe disease, and 5% may become critical and develop severe pneumonia or acute respiratory distress syndrome, which requires mechanical ventilation and intensive care unit hospitalization (4). Present understanding among researchers shows that coronavirus invades human cells via the receptor angiotensin-converting enzyme 2 (ACE2) through scRNA-seq data analyses. The study identified the organs that are at risk and are vulnerable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (5). Therefore, cells with ACE2 receptor distribution may become host cells for the virus and cause inflammatory response in related organs and tissues, such as the tongue mucosa and salivary glands (6,7). SARS-CoV-2 interaction with ACE2 receptors may also impair taste bud sensitivity, which could induce dysfunctional gustatory responses (8). Available evidence has not yet established an efficient and safe pharmacologic therapy against COVID-19, and the potential ones are related to several adverse reactions (9). Therefore, COVID-19 acute infection, with associated therapeutic measures, could contribute to adverse outcomes concerning oral health. The oral signs and symptoms related to COVID- 19 are taste disorders, unspecific oral ulcerations, desquamative gingivitis, petechiae, and coinfections such as candidiasis (4). However, it is still uncertain whether these manifestations could be a typically clinical pattern resulting from the direct SARS-CoV-2 infection or a systemic consequence, given the possibility of coinfections, impaired immune system, and adverse reactions of medical treatment (10,11) Since the prevalence of clinical manifestations is still unknown, the range of COVID-19 manifestations on the oral cavity has been considered broad. The current case aims to report a rare finding of bone and soft tissue defect in maxilla as a possible sequelae of C0VID-19 infection.

II. Case History:

A 38-year-old male reported to my clinic with a chief complaint of inability to chew food from right upper back tooth region and atypical facial pain since 15 days. He developed this complaint over a period of one month. The patient gave a history of COVID-19 infection a month back admitted for the same and discharged after 14 days. The hospital stay was uneventful and medications were given as per COVID-19 Government of

India standard guidelines. Patient is having Type 2 Diabetes Mellitus since last 4 years and is on Oral Hypoglycemic Agents. On Intra Oral Examination overall oral health was satisfactory however multiple small pus filled vesicles were observed in relation to the right upper front and back tooth region confined to attached gingiva. On further investigation, pus discharge was observed from swellings. On hard tissue examination, 11,12,13,14,15,16,17 teeth had grade II mobility and there was intermittent tenderness on percussion. The patient was advised for all routine blood investigations radiological investigations to rule out all plausible causes. Blood workup shows Total Leukocyte Count(TLC), Bleeding time (BT), Clotting Time (CT) with no significance. However, his Glycosylated Haemoglobin was 9.0 suggestive of severe glycemic derangement in the last couple of months. Computed tomography revealed Left maxillary sinus showing hyperdense area involving full sinus area Suggestive of pathological changes of sinus lining and inflammation of the mucosal lining of the sinus. The palatal cortical plate with the tuberosity and the alveolar bone around the 26,27,28 shows mild trabecular thinning and sinus floor periapical to the 27 shows resorption and thinned out floor with loss of cortical plate. The palatal cortical plate shows irregular resorptive changes irt 26,27 region particularly. The trabecular pattern of the 24-25 area also shows mild thinning and reduced density with likely resorptive changes. The right alveolar bone with the tuberosity area does not show any changes. CT angiogram was also done to ruleout any thrombosis in vasculature in oro-facial region due to COVID-19. CT Angiogram shows no evidence of thrombus in oro-facial region. Extraction of mobile teeth along with curettage of involved region was planned under aggressive antibiotic and antifungal agents.

III. Discussion:

The aim of this case report is to aware clinicians and researchers about possible post COVID oral more specifically dental complications and to better understand the relationship between SARS-CoV-2 and oral manifestations after the hospitalization. Several clinicians have observed many extrapulmonary manifestations of COVID-19. In fact, the recent literature suggests that the hematologic, cardiovascular, renal, gastrointestinal and hepatobiliary, endocrinologic, neurologic, ophthalmologic, and dermatologic systems can all be implicated [12,13]. On the other hand, numerous studies have drawn attention to the oral cavity as the main route of infection [14]. Although recent evidence suggests a relevant role of the oral cavity and its mucosae in the transmission and in the pathogenicity of SARS-CoV-2, as the entrance to the body of the virus, its protective or aggravating element for the infection and progression of the virus is still controversial [14]. In present case it is still an enigma regarding etiopathogenesis of bone and soft tissue defect in the maxilla. As in COVID-19 there is high prevalence of thrombocytosis followed by thrombus formation its not clear whether macrovascular thrombus can cause these type of bone necrosis as maxilla already have rich vascular supply and even after thrombus formations collateral supply forms rapidly. Other plausible reason we hypothesize is Medication related osteonecrosis of the Jaw (MRONJ) as patient received high dose steroid therapy during hospitalization with cumulative dose of 600-800 mg. Glucocorticoid induced osteocytes apoptosis with the resultant disruption of bone vascularity and diminution of bone hydraulic support could be the mechanisms behind the osteonecrosis and greater decline in bone strength than in loss of bone mass that occurs with glucocorticoid excess. The direct adverse effects of administered glucocorticoids on bone cells are evident from a series of experiments in transgenic mice overexpressing the inactivating enzyme 11β-HSD2 in osteoblasts and osteocytes. It may also occur due to immunomodulation and immunosuppression due to aggressive drug therapies used during COVID-19 treatment causing dysbiosis and sudden change on periodontopathic bacteria's causing rapid destruction of tissues.[15,16,17,18] It has been demonstrated that there is an association between periodontitis and a higher risk of increased gravity of COVID-19 in periodontopathic patients [19]. In fact, it has been shown that xerostomia can also be induced by different drug therapies such as: antidepressants, antipsychotics, anticholinergics, antihypertensives, antihistamines, and sedatives [20]. Furthermore, there is strong evidence that xerostomia is very common in diabetic patients and may be present in >50% of cases, and recently it was reported that the use of artificial saliva spray was shown to be effective in the treatment of xerostomia in type 1 and type 2 diabetes [21,22]. However, in our study, only 15% of patients were affected by diabetes (not specified if type 1 or type 2). Focusing on the patient's systemic conditions, it appears significant that most of the patients hospitalized for COVID-19 had previous systemic conditions such as hypertension, heart disease, oncological pathologies, pathologies affecting the thyroid gland, diabetes, and pathologies affecting the respiratory system. In addition, it should be noted that, in a recent study on 5700 patients, the most common comorbidities were hypertension in 56.6% of cases, obesity in 41.7%, and diabetes in 33.8% of patients with diagnosis of COVID-19 [23].

IV. Conclusion:

COVID-19 an ongoing pandemic is a challenge which has been tackled till now with limited knowledge available about it in literature. CRONJ may lead to a reduced quality of life due to jawbone infections, chronic pain, tooth loss and compromised function. Although notable progress has been made, there

remain a number of controversial aspects on CRONJ, especially regarding pathogenesis, diagnosis and treatment. It posses a risk of systemic complications including oral complications. We need to prepare our practices in near future to face these kind of complications as well to build protocols for their management in favour of our patients, clinicians and humanity.

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Legends:
Fig 1:Labial View
Fig 2: Multiple Pus filled vesciles in Buccofacial region
Fig 3: CT Angiogram
Fig 4: CT- 3D Reconstruction