



## Acute osteonecrosis of the jaw due to aggravation by the SARS-CoV-2 virus: a clinical case report

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### Abstract

Although many patients recover from COVID-19, it is important to keep in mind that there may be complications after recovery. One such complication in the maxillofacial region is Avascular Necrosis. Viral downregulation of ACE-2 receptors leads to endothelial dysfunction, which together with virus-induced hyperinflammation. Several complications have been observed in the maxillofacial area in people who have suffered from the infection, including osteonecrosis and osteomyelitis of the mandible and maxilla. Osteomyelitis is an inflammatory disease, which occurs in medullary spaces or on bone cortical surfaces, originating due to insufficient blood circulation in the affected region and also by bacteria, fungi, and micro bacteria. In the specific case that will be addressed, the patient suffered a severe worsening of the infection due to microthrombi formed by the SARS-CoV-2 virus and severe worsening also due to diabetes mellitus. The treatment is varied, but the most efficient one is the surgical removal of the contaminated bone sequestration, accompanied by broad-spectrum systemic medications. With the combination of clinical history and laboratory tests, the possible cause of maxillary osteonecrosis was the formation of microthrombi resulting from the SARSCoV-2 virus that obliterated the sphenopalatine and descending palatine arteries. The progression and potentization of the infection are favored due to systemic decompensation caused by uncontrolled diabetes.

**Keywords:** COVID-19. SARS-CoV-2. Osteonecrosis. Osteomyelitis. Jaw.

### Introduction

The World Health Organization (WHO) report reported the epidemiological data of the SARS-CoV-2 virus (COVID-19) pandemic, resulting in a cumulative total of 332,617,707 confirmed cases, including 5,551,314 deaths and 3,156,986 new cases reported in the world [1]. Although many patients recover from COVID-19, it is important to keep in mind that there may be complications after recovery. One of these complications in the maxillofacial region is avascular necrosis [2,3].

In this sense, the pathogenicity of viral infection begins with the virus targeting Angiotensin Converting Enzyme Two (ACE-2) receptors, which allow viral entry into cells [3,4]. Downregulation of ACE-2 and recognition of SARS-CoV-2 spike glycoproteins by Pattern Recognition Receptors on cell membranes lead to activation of the innate immune system and local inflammation at the viral entry point, which results in a hyperinflammatory cytokine storm [4,5].

Furthermore, viral downregulation of ACE-2 receptors leads to endothelial dysfunction, which, together with virus-induced hyperinflammation, promotes endothelial dysfunction and endothelium, with subsequent microvascular dysfunction not only at viral entry points but also in various organs, promoting a state of hypercoagulability through unique mechanisms

and interactions between thrombosis and inflammation [4,5].

In this scenario, it has been postulated that the direct vulnerability of the oral mucosa to SARS-CoV-2 infection leads to oral manifestations associated with COVID19. These manifestations are reported as a consequence of the high expression of ACE-2 in the epithelial cells of the oral mucosa [6,7]. Some complications have been seen in the maxillofacial area in people who have suffered from the infection, including osteonecrosis and osteomyelitis of the jaw, and may result from the pathogenetic mechanism of the disease or a response to the therapeutic modalities used to treat the underlying disease and the overuse of specific medications - glucocorticoids, antirheumatics, interleukin-6 inhibitors and antibiotics [8].

Because of this, the present study reported a rare case of acute osteonecrosis aggravated by the SARS-CoV-2 virus during the COVID-19 pandemic in a 61-year-old patient, treated with surgical intervention, antibiotic therapy, respiratory physiotherapy, and corticosteroid therapy.

## Methods

### Study Design

The present study was elaborated according to the rules of the CARE case report (<https://www.care-statement.org/>). To prepare this article, the patient's medical records, clinical history, laboratory reports, and radiographic and tomographic images were used. For literary review, scientific articles and academic books were used. A descriptive literature review was also carried out to provide sufficient scientific data for the theoretical basis of this study. The descriptors used were. The most relevant works to the proposed theme were selected, excluding those that did not contemplate the objective of this study. The research was carried out from January to April 2023 and developed based on Google Scholar, Scopus, PubMed, Scielo, and Cochrane Library.

### Ethical Approval

This study respected the human rights rules of the 1964 Declaration of Helsinki and obtained the Informed Consent Form according to CNS/CONEP Resolution 466/12 from Brazil. Data from the patient under study were obtained through the collection and analysis of information contained in the patient's medical record, duly authorized by the user signing the Informed Consent Form. This clinical case study is concerning the COVID-19 pandemic and contributes to the public understanding of worsening osteonecrosis of the jaw.

## Case Report

### Patient Information and Clinical Findings, Timeline, Diagnostic Assessment, Therapeutic Intervention, and Follow-up

Patient H.L.S 61 years old, male, with diabetes mellitus, recently recovered from contamination by SARS-CoV-2 during the pandemic period, was admitted to the Padre Albino Saúde hospital in the city of Catanduva with signs of necrotizing osteomyelitis in the maxilla in stage acute, which presented grade III mobility of the dental elements, fetid odor, purulent secretion, exposed bone tissue, tissue necrosis, and oroantral communication. The patient was referred to the oral and maxillofacial surgery and traumatology team, which performed anamnesis, physical examination, imaging tests, and analysis of the old medical record.

During the analysis of the medical records, it was identified that the patient underwent intensive corticosteroid therapy due to complications from the SARS-CoV-2 virus, which led to the decompensation of the preexisting disease (diabetes), thus giving the hypothesis of the worsening of the infection. With the set of information obtained, the diagnosis of acute necrotizing osteomyelitis was made.







The patient was hospitalized days before the surgery to begin the treatment of diabetic decompensation and antibiotic therapy. After control and systemic stabilization, the patient was taken to the operating room, which underwent general anesthesia. Debridement of all contaminated bone sequestration was performed with a safety margin and removal of dental elements located in the infected region (Figure 1). When the entire necrotic area was removed, bilateral buccosinus communication was noted, which was treated with the displacement of the adipose body of the cheek (Bichat's ball). After the surgery was completed, all the debrided material was sent for pathological examinations to confirm the damage caused by micro-thrombi resulting from SARS-CoV-2 contamination. The patient was kept hospitalized and discharged days later.

Upon returning to the outpatient clinic, bilateral bucco-sinus communications were clinically observed, requiring a second surgical approach to close the fistulas. At the outpatient clinic, recommendations were given for the treatment of visibly contaminated cavernous sinuses (antibiotic therapy, washing with a saline solution daily, and requesting a return visit every 30 days) (Figures 2 to 5).

On October 11, 2022, the patient was hospitalized for reconstructive surgery, which was performed the next day. Under general anesthesia, oroantral communications were approached. The right fistula was sutured with a thick pedicled flap and the left fistula

closed with grafting using a Bichat ball (Figure 6).

Figures 1 to 6 below show the procedures for the surgical approach to the right fistula closed with the Bichat Ball flap, respectively.

Figure 1. Surgical Approach.	Figure 2. Bone Sequestrums Removed.
	
Figure 3. Suture after removal of bone sequestrations.	Figure 4. Left Buccosinusual Communication/Recurrent after 1 Surgical Approach.
	
Figure 5. Right Buccosinusual Communication/Recurrent after 1 Surgical Approach.	Figure 6. Right Fistula Closed With Bichat Ball Flap.
	

## Discussion

The present study reported a clinical case of acute osteonecrosis aggravated by the SARS-CoV-2 virus during the COVID-19 pandemic in a 61-year-old patient, treated with surgical intervention, antibiotic therapy, respiratory physiotherapy, and corticosteroid therapy. In this regard, it was shown that there are many predictors with the potential to contribute to the induction and spread of osteonecrosis of the jaw related to post-COVID19 infection. The main factor is the virus itself, which causes downregulation of ACE-2 and subsequent hyperinflammatory state, with elevation of cytokines and immune dysregulation, in addition to microvascular thrombosis and hypercoagulability state [2,4,5].

Still, there are drugs used to manage hyperinflammatory syndrome and cytokine storm, which are corticosteroids and biological drugs [9,10]. Also, co-infections, which can be secondary bacterial or fungal

infections [11-13]. Added to this, are the associated comorbidities, mainly diabetes, which further impair the body's local and innate immunity [14,15]. All of these factors are directly linked to the development of osteonecrosis of the jaw.

In this context, a study presented a series of twelve cases that survived SARSCoV-2 infection with manifestations of maxillary osteonecrosis, which developed after the infectious course of the disease in different periods. None of the patients had a fungal infection, confirmed by a negative preoperative fungal swab, and negative histopathological reports, and the treatment consisted of surgical debridement and antibiotic therapy without any antifungal medication. The mean time to diagnosis of osteonecrosis was  $5.5 \pm 2.43$  weeks after recovery from SARS-CoV-2 infection [16]. This period is in line with Boymuradov et al., who reported a minimum period of 2 months after SARS-CoV-2 infection to develop symptoms of osteonecrosis and a maximum symptom-free period of 8 months [17].

Also, a study presented a rare and interesting case of a patient who presented avascular necrosis of the maxilla associated with COVID-19 infection. The patient is a 72-year-old male. The COVID-19 infection confers a state of hypercoagulability in patients, leading to various complications in the head and neck region. Thromboembolic prophylaxis is imperative in patients with COVID-19 due to the high rate of possible systemic complications [18].

## Final Considerations

With the combination of clinical history and laboratory tests, the possible cause of maxillary osteonecrosis was the formation of microthrombi resulting from the SARSCoV-2 virus that obliterated the sphenopalatine and descending palatine arteries. The progression and potentization of the infection are favored due to systemic decompensation caused by uncontrolled diabetes.

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### Informed consent

Not applicable.

### Data sharing statement

No additional data are available.

### Conflict of interest

The authors declare no conflict of interest.

### Similarity check

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