Medical and Research Publications
International Open Access

Case Report **Journal of MAR Case Reports (Volume 5 Issue 1)**

Maxillofacial Management of Maxillary Osteonecrosis as a Complicated Sequence of Mucormycosis in Medically Compromised Patients with Recent History of (COVID 19) 2 Cases Report from Egypt

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Received Date: April 30, 2022

Published Date: May 10, 2022

Abstract

Mucormycosis is acute, angio-invasive, rapidly progressing disease, usually caused by fungal infection of Mucoraceae family, specifically by Mucor or Rhizopus (1). It is a life- threatening infections, especially in immunocompromised individuals, like: uncontrolled diabetes mellitus (especially in keto-acidosis), hematological malignancies, hematopoietic stem cell or solid organ transplant settings, long term glucocorticoids therapy and persistent neutropenia (1-4).There are other risk factors such as : iron overload or chelation with deferoxamine therapy, prophylaxis with voriconazole or echinocandins, breach of skin or mucosa due to trauma, burns or surgical wounds(1-4). This is a case report of Maxillary osteomyelitis with fungal infection (Mucormycosis) in a 54 years old patient From Egypt with uncontrolled diabetes mellitus and history of COVID 19, with detailed diagnosis, investigations, management and surgical intervention.

Key words: *Osteomyelitis, Diabetes mellitus, Fungal infection*

Introduction

Mucormycosis (previously called "zygomycosis") is an invasive, opportunistic fungal infection caused by fungi in the subphylum Mucoromycotina. More specifically, species in the Mucor, Rhizopus, Absidia, and Cunninghamella genera. The disease is characterized by hyphae growing in and around blood vessels. It's a rare case, can be life-threatening in diabetic or severely immunocompromised individuals (5).

Mucormycosis usually infects the sinuses, brain, or lungs. The most common sites of infection are: the oral cavity (rarely affects the maxilla) or brain, however; the fungus can also infect other areas of the body such as the gastrointestinal tract, skin, and other organ systems (6).

The process of Mucormycosis starts with fungal invasion into the blood vessels which results in the formation of blood clots that leads to surrounding tissue death due to a loss of blood supply. If the brain is involved, the symptoms may include a one –sided headache behind the eyes, facial pain, fevers, nasal congestion that leads to black discharge, acute sinusitis along with eye swelling. Affected skin may appear normal during the earliest stages of infection, and then this skin quickly becomes reddened and swollen before eventually turning black due to tissue necrosis (7). Predisposing factors for mucormycosis include HIV, uncontrolled diabetes mellitus, cancers (such as lymphomas), kidney failure, organ transplant, long term corticosteroid and immunosuppressive therapy and deferoxamine therapy (1-4).

Diabetes Mellitus is a metabolic disease characterized by a persistent hyperglycemia. Diabetes is a risk factor for many conditions involving the orbital, nose, and oral cavity with immunologic implications (8).

In December 2019, A new Corona Virus (COVID 19) was reported in Wuhan, China, then the virus subsequently spread rapidly throughout the country and around the world. During the year of 2022, COVID 19 became a pandemic (9-10). Till today, many efforts are exerted to find an effective therapy for this virus. The usual management of patients with COVID-19 is supportive therapy including: fluid management, oxygen therapy, and mechanical ventilation (11). Corticosteroids are usually used to treat severe acute respiratory viral infections such as COVID 19 to prevent Cytokine storm and inflammation induced by the immunologic response to the virus that leads to the fatal pneumonia that may follow infection with human corona viruses (12-14), however; The World Health Organization has recommended against routine Administration of systemic corticosteroids to patients with COVID-19 (15).

Case 1 report

A 54 years old patient came to the clinic with chief complain of pus drainage in his mouth without pain.

Clinical examination: revealed mobility in anterior teeth with mobility of the surrounding premaxilla, no swelling, no pain on palpation.

Medical history:

The patient suffers from uncontrolled diabetes mellitus with recent history of COVID-19 that required Corticosteroid's administrations and oxygen therapy.

Management:

When the patient firstly came to the clinic and after clinical examination and precise medical history, the patient was requested to perform a Cone Beam CT. The patient delayed performing the Cone Beam CT and came again to the clinic after 3 months of his first visit.

Culture was made and sent to the lab for microbiological investigation. Oral hygiene measures and mouthwash were taken to improve the oral hygiene.

The decision of surgical intervention is made and following steps were taken to prepare for the surgery:

- Pre-operative assessment
- Serological test
- Radiographic evaluation

The surgical intervention was made, extensive bone and soft tissue removal, releasing incision and tight suturing.

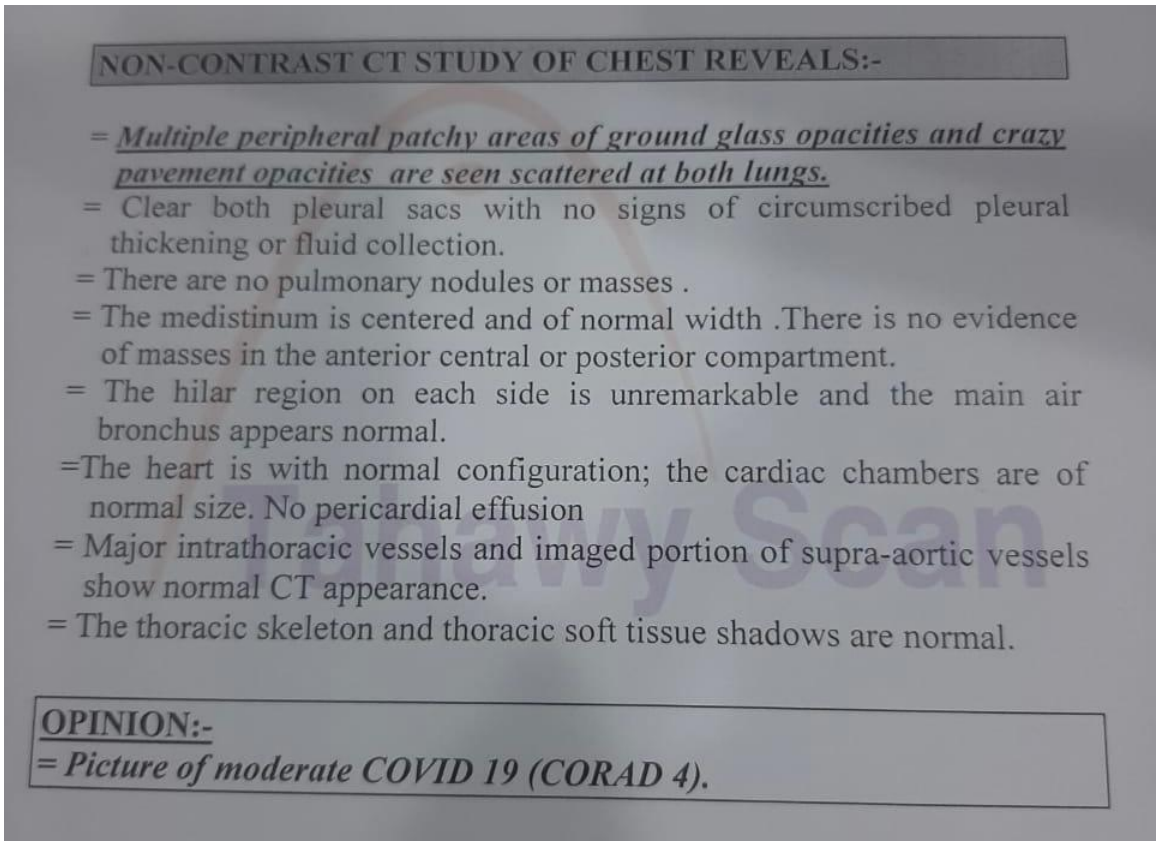
Post-operative antibiotic administration according to the culture results and antifungal therapy .

Close follow up 1,2 weeks then 1 and 2 months to assure healing and manage any complications or recurrence if happened.

Figure 1: The site of infection in the first visit

Figure 2: the second visit (after 3 months)

Figure 3: CBCT



NON-CONTRAST CT STUDY OF CHEST REVEALS:-

= *Multiple peripheral patchy areas of ground glass opacities and crazy pavement opacities are seen scattered at both lungs.*
= Clear both pleural sacs with no signs of circumscribed pleural thickening or fluid collection.
= There are no pulmonary nodules or masses .
= The medistinum is centered and of normal width .There is no evidence of masses in the anterior central or posterior compartment.
= The hilar region on each side is unremarkable and the main air bronchus appears normal.
=The heart is with normal configuration; the cardiac chambers are of normal size. No pericardial effusion
= Major intrathoracic vessels and imaged portion of supra-aortic vessels show normal CT appearance.
= The thoracic skeleton and thoracic soft tissue shadows are normal.

OPINION:-
= *Picture of moderate COVID 19 (CORAD 4).*

Figure 4: Chest CT report of the patient that proved he was a COVID 19 patient

MICROBIOLOGY REPORT

Culture and Sensitivity :

Culture:

- Sample : Pus
- Organism A : *Gram Positive Cocci in grape-like clusters (Staph.aureus)*
- Culture Condition : Aerobic

Sensitivity:

Highly (Organism A) For	Commercial Name
1 Amikcin	Amikin, Likacin
2 Cefatriaxone	Rocephin, Cefatriaxone, Cefotrix
3 Meropenem	Meropenem
4 Sulbactam and Ampicillin	Unictam, Sulbin, Unasyn, Sigmacyn, Ampictam,
5 Azithromycin	Azalide, Azrolid, Aziwok, Xithrone, Zithromax,
6 Linezolid	

Moderate (Organism A) For	Commercial Name
1 Gentamycin	Garamycin, Cidomycin, Refobacin, Epigent,
2 Vancomycin	Vancomycin
3 Erythromycin	
4 Ceftazidime	Cetazime, Fortum, Ceftazidime T3A
5 Cefotaxime	Claforan, Cefotax, Ceforan

Resistant (Organism A) For	Commercial Name
1 Amoxicillin and Clavulanic	Augmentin, Clavucin, Magnabiotic, Curam,
2 Clindamycin	Clindamycin
3 Cefaclor	Ceclor, Cefaclor, Serviclor, Bacticlor

Auto Labs Manager

معامل أوتو لاب للتحاليل الطبية
دكتور/ محمد رضوان
س.ت : ١٧١١٥٤
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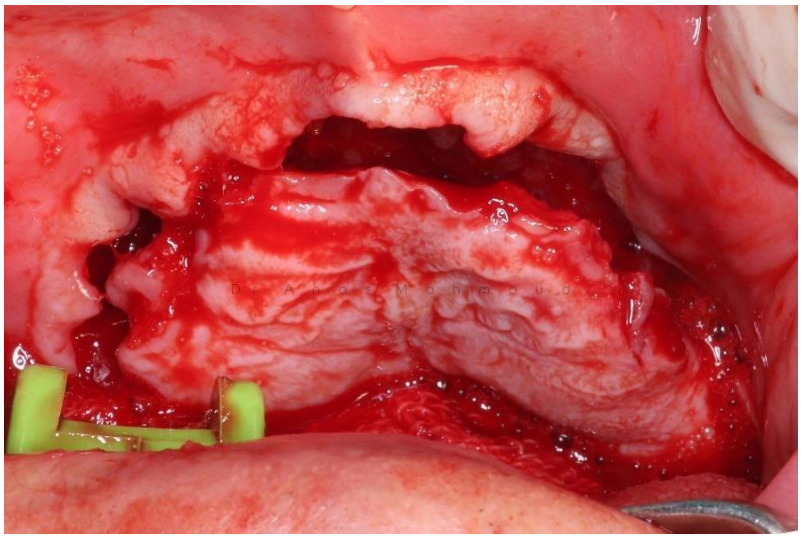

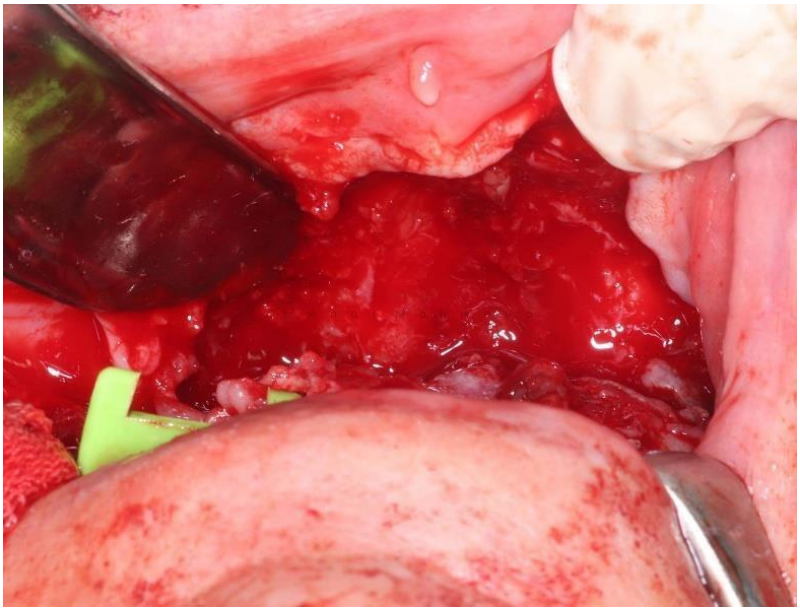

Figure 6 & 7: The Wound After Bone Removal

Figure 8 & 9: The Removed Bone and Involved Teeth

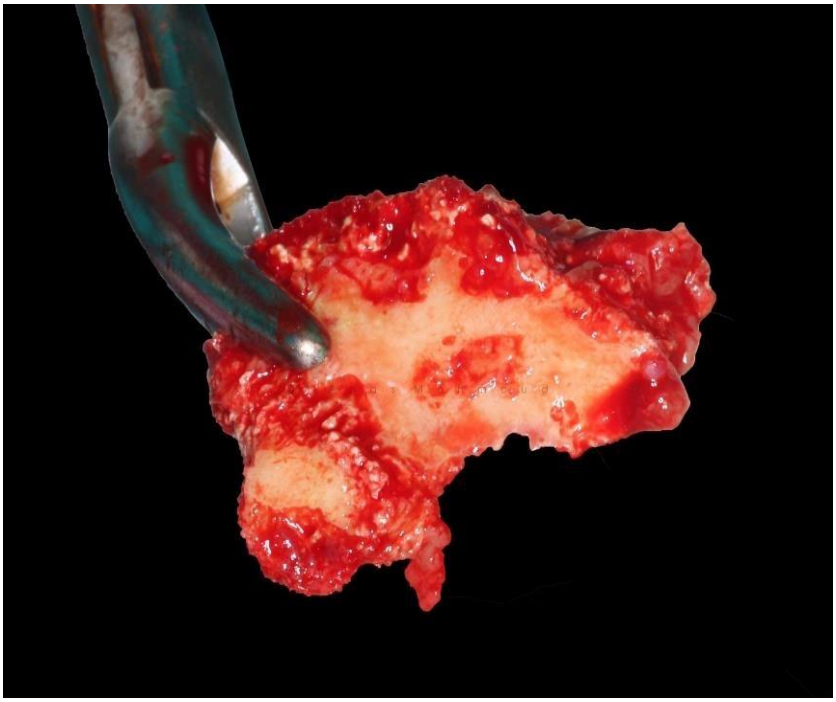

Figure 10: The Removed Bone

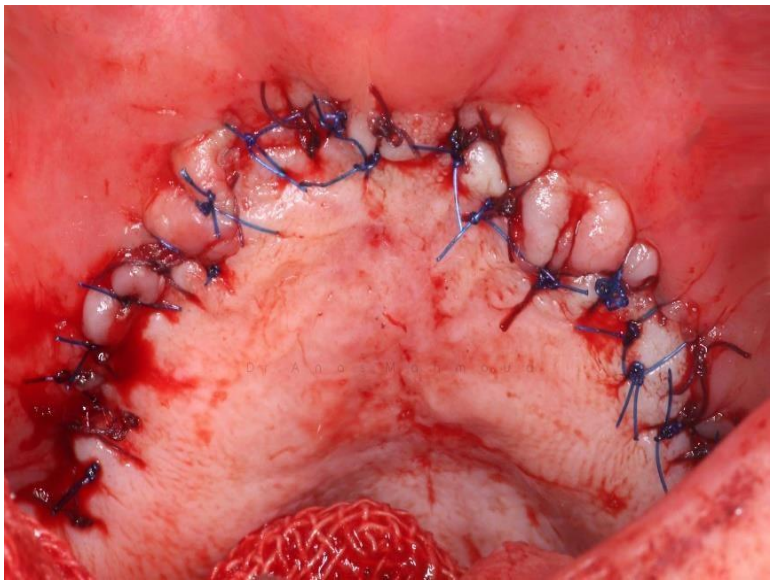

Figure 11: The Wound After Tight Suturing

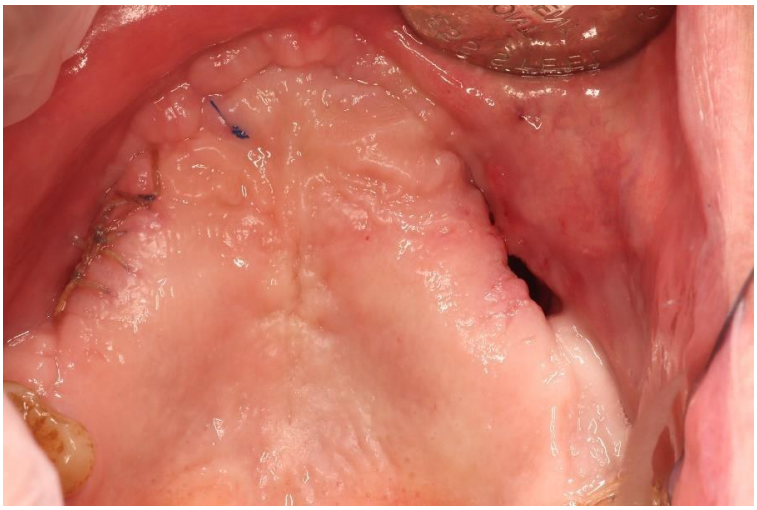

Figure 12: First Follow up visit after 1 week, Oro-antral communication was found

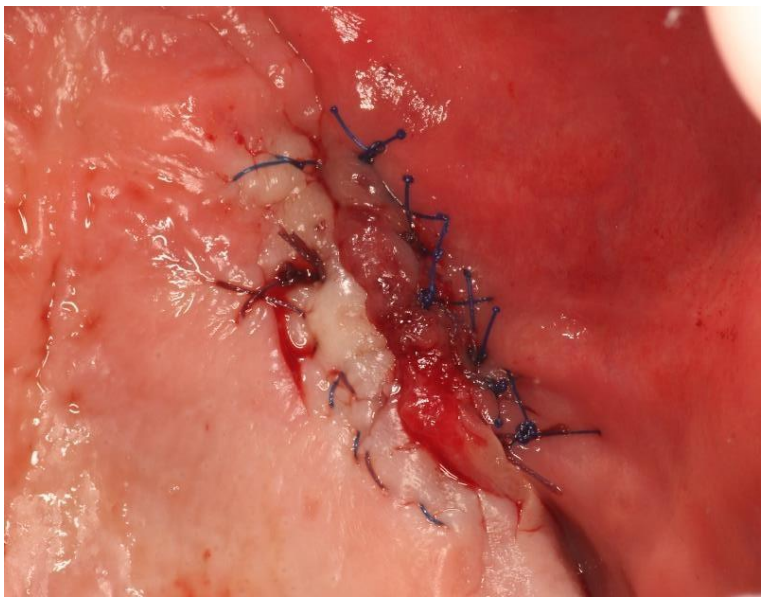

Figure 13: Closure of the Oro-antral communication

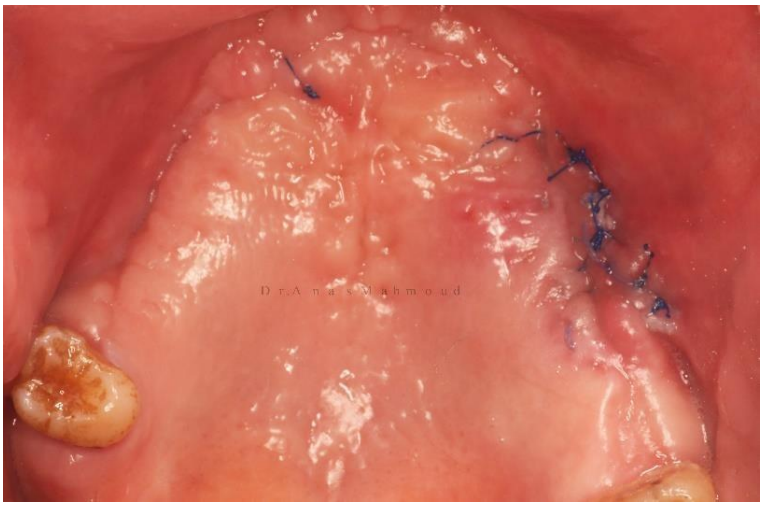

Figure 14: Second Follow Up Visit After 2 Weeks, Complete Closure of The Oro-Antral Communication.

Case 2 report

57-year-old patient presented to the clinic with the major complaint of painless bare alveolus bone after 40 days of extraction of maxillary right 2nd premolar and 1st molar.

Clinical examination:

The posterior right maxilla revealed bare bone with mobility in the 2nd and 3rd molars, as well as movement in the left maxillary central incisor, left maxillary lateral incisor, left maxillary canine, and 1st and 2nd left maxillary premolars. Mobility of the alveolar process extending from the right maxillary tuberosity along the alveolus to the second left maxillary premolar, with no edema or pain on probing.

Medical history:

The patient suffers from uncontrolled hypertension with recent history of COVID-19 that required administration into Intensive Care Unit and Corticosteroids administrations and oxygen therapy.

Management:

When the patient firstly came to the clinic and after clinical examination and precise medical history. Suspicious of osteonecrosis of anterior maxilla and alveolar process as a complication of Mucormyosis.

The surgical intervention was made, extensive bone and soft tissue removal, releasing incision and tight suturing. Post-operative antibiotic administration.

Close follow up 1, 2 weeks then 1 and 2 months to assure healing and manage any complications or recurrence if happened.

In this paper we reported 2 cases of maxilla Mucormycosis without pulmonary involvement in medically compromised patients who received a short course of steroids and oxygen therapy as a treatment of COVID-19 with detailed investigations, management and surgical intervention.

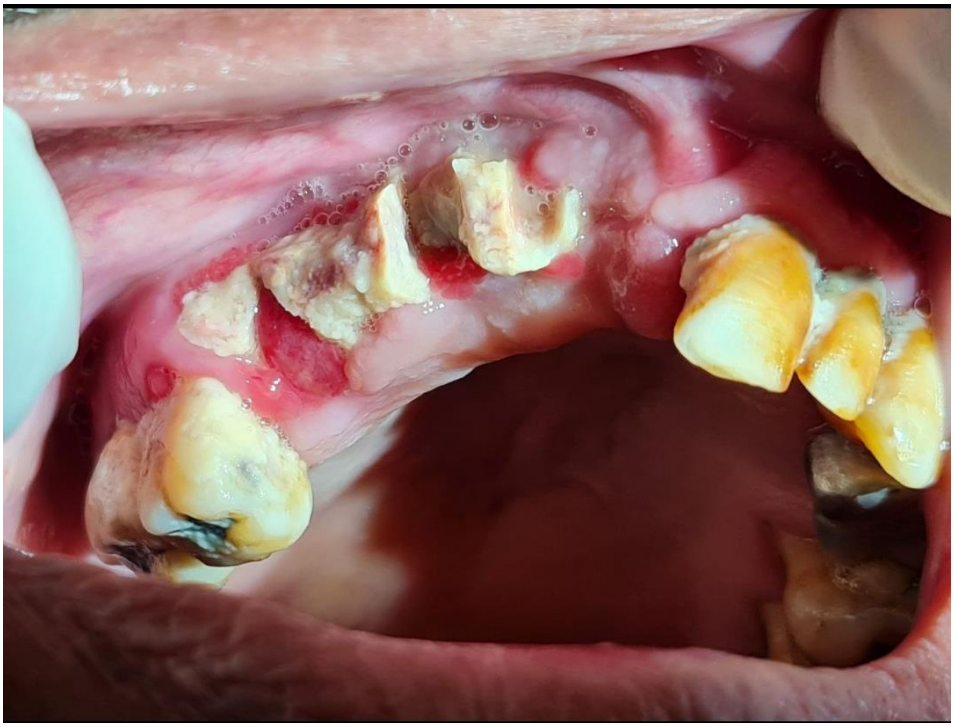

Figure 15: The site of infection in the first visit

Figure 16: Intraoperative removal of necrotic bone

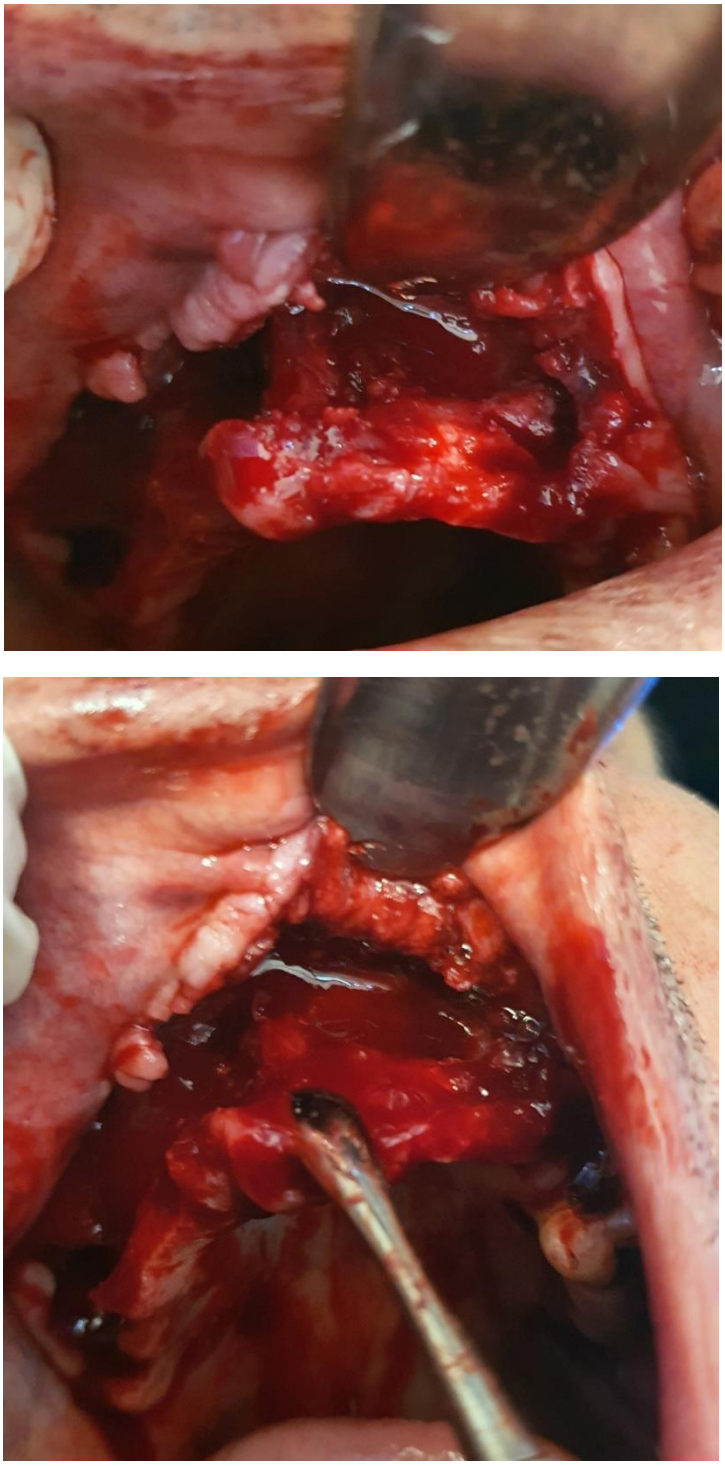

Figure 17: The wound after bone removal

Figure 18 & 19: The removed bone and involved teeth

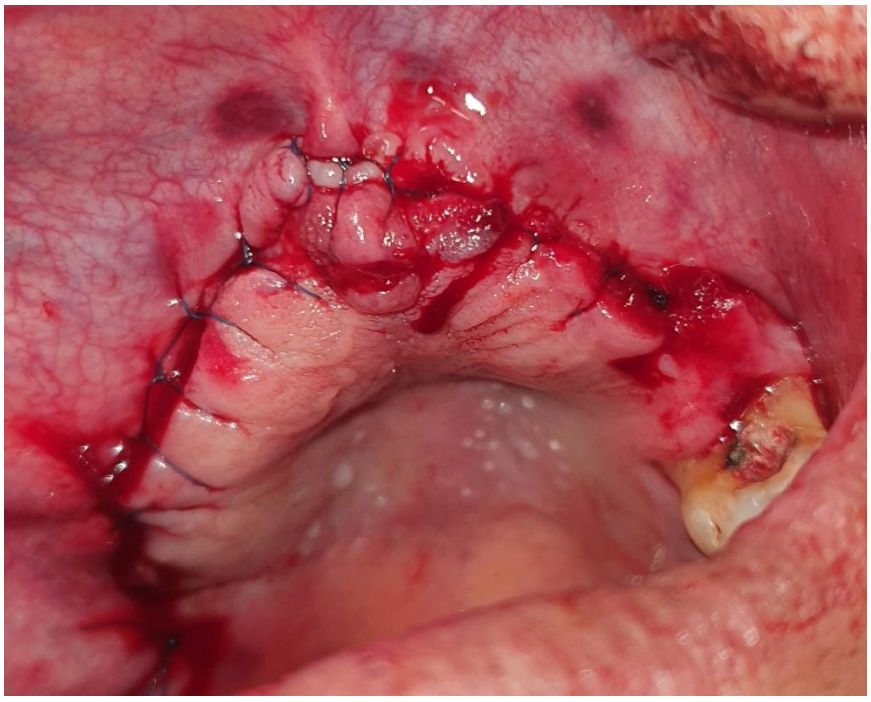

Figure 11: the wound after tight suturing

Discussion

Mucormycosis is an opportunistic, angio-invasive, fungal infection which results in tissue necrosis and thrombosis. In immunocompromised patients, the course is usually rapid and life-threatening (1).

Immunosuppression has an established a correlation with Mucormycosis. 36% of Mucormycosis patients were diabetic patients, Diabetes Mellitus was the most common predisposing factor in one of the largest epidemiological studies conducted so far (16). Hyperglycemia impairs chemotaxis and the fungicidal mechanisms used by phagocytic cells which are the main defensive mechanisms against Mucormycosis. Hyperglycemia also increases the expression of GRP78 (a 78 kDa glucose-regulated protein) which acts as the endothelial receptor for the ligand (spore- coating protein homolog) used by the fungi that cause Mucormycosis (17-19). In cases of acidosis related to hyperglycemia, free iron becomes available in the serum. Fungi that cause Mucormycosis can acquire this excess iron through siderophores (low-molecular-weight chelators) or iron permeases enhancing their virulence (20).

There are multiple forms of Mucormycosis; the rhino-orbito-cerebral form is commonly seen in poorly-controlled diabetes. Pulmonary Mucormycosis usually affects hematopoietic stem cell transplant recipients or patients with prolonged neutropenia and is usually associated with involvement of the sinuses and a high case fatality rate, however; the maxilla is rarely affected (21).

In the largest review of the literature of 929 cases, pulmonary involvement was more than one - half of all sites of infection in patients with malignancy and recipients of bone marrow transplants. The mortality rate of pulmonary Mucormycosis was 76% and 95% when the diseases were disseminated (21).

On the other hand, Corticosteroid's cause impairment in the migration and phagolysosome fusion of bronchoalveolar macrophages. Coupled with the adverse effect of steroid-induced hyperglycemia, a diabetic patient receiving corticosteroids is highly vulnerable to the development of Mucormycosis. There are few reported cases of pulmonary Mucormycosis following short courses (5–14 days) of steroids (22-25).

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