ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 3, Issue – 6, December - 2020, Page No. : 194 - 202

A Unique Association of Aspergillosis and Actinomycosis causing Chronic Destructive Osteomyelitis and Osteonecrosis of the Maxilla

[1]Dr. Paremala K, MDS, Oral Pathology, Assistant Professor, Government Dental College and Hospital, Hyderabad

[2]Dr. Radhika Manoj Bavle, MDS Oral Pathology, Prof and HOD, Department of Oral and Maxillofacial Pathology, Krishnadevaraya College of Dental College and Hospital, Sir MVIT campus, Hunasamarenahalli, via Yelahanka , Bangalore

[3]Dr. Soumya Makarla, MDS Oral Pathology, Reader, Department of Oral and Maxillofacial Pathology and Hospital, Krishnadevaraya College of Dental Sciences, Bangalore

[4]Dr. Sudhakara M, MDS Oral Pathology, Reader, Department of Oral and Maxillofacial Pathology and Hospital, Krishnadevaraya College of Dental Sciences, Bangalore

[5]Dr. Reshma Venugopal, Senior Lecturer, Department of Oral and Maxillofacial Pathology, Krishnadevaraya College of Dental Sciences and Hospital, Bangalore-562157

Corresponding Author: Dr. Reshma Venugopal, Senior Lecturer, Department of Oral and Maxillofacial Pathology, Krishnadevaraya College of Dental Sciences and Hospital, Bangalore-562157

Citation of this Article: Dr. K Paremala, Dr. Radhika Manoj Bavle, Dr. Soumya Makarla, Dr. Sudhakara M, Dr. Reshma Venugopal, "A Unique Association of Aspergillosis and Actinomycosis causing Chronic Destructive Osteomyelitis and Osteonecrosis of the Maxilla", IJDSIR- December - 2020, Vol. – 3, Issue - 6, P. No. 194 – 202.

Type of Publication: Case Report

Conflicts of Interest: Nil

Abstract

Osteomyelitis of the maxilla with osteonecrosis is a rare event in the purview of antibiotics until the patient has co-morbidities viz., diabetes, acquired immunodeficiency virus. Osteomyelitis can be non-specific, or specific when associated with a particular organism. Reports of osteomyelitis caused by multiple organisms are not rare. It is important to recognize such an association early as it is difficult to treat and results in potentially serious consequences. Osteomyelitis is more common in the mandible than the maxilla, as the maxillary bone has a good collateral blood supply. Here we report a unique case of chronic bacterial and fungal osteomyelitis of the left maxilla in a 47-year-old male farmer with uncontrolled Type II diabetes mellitus.

Keywords: Fungal Osteomyelitis, Osteonecrosis, Aspergillosis, Actinomycosis, Maxilla, Diabetic adult, Chronic Suppurative Osteomyelitis

Introduction

Osteomyelitis is defined as inflammation of bone which begins as an infection of the medullary cavity with rapid

involvement of the Haversian systems and extension into the periosteum [1,2].

Jaw osteomyelitis is generally a polymicrobial infection caused mainly due to the spread of infection from invasive openings in the oral cavity or rapid spread in a compromised host. Periapical infection, infected periodontium, extraction sockets, fracture, chronic maxillary sinusitis, etc., are the sources of infection. The patient's age, nutritional status, use of medications such as steroids, chemotherapeutic agents, and compromised vascularity add to the complexity. Immunocompromised state such as age, nutritional status, microvascular diseases, uncontrolled diabetes mellitus, malignancy, chemotherapy, transplantation, use of intravenous drugs, dysfunction of kidney or liver, use of steroids, TNF-α inhibitors alter the immune defense mechanisms and aggravate the condition [2,3,4,5]. The clinical manifestations vary according to the host response.

Uncontrolled diabetes mellitus is one of the major reasons for the spread of infection from teeth and teeth-bearing regions to the bone leading to osteomyelitis. The host defence and vascularity are compromised in this state allowing the spread of infection [2,6,7].

The frequency of occurrence is more in the mandible than in the maxilla. This is due to an extensive collateral blood supply, thin cortices, and interconnecting mesh of trabeculae of the medullary bone in the maxilla. This helps to maintain the vascularity of the jaw that helps to dampen the infections in the maxilla as compared to the mandible [1,7].

In contrast, some studies have cited a higher incidence of maxillary involvement. Two such studies have shown 45.1% and 80.76% involvement of maxilla respectively in uncontrolled diabetes mellitus cases in the Indian population. In a 10-year analysis of the North Karnataka population 52% cases of fungal osteomyelitis and 48% of non-fungal osteomyelitis involving the maxillary bone were evident [7]. According to Peravali RK et al association of diabetes and maxillary osteomyelitis was high and seen in 69% of cases [6].

Osteomyelitis commonly occurs due to bacterial infections. But sometimes fungi, parasites, and viruses can also cause osteomyelitis [3]. The organisms spread through a breach in the mucous membrane either via extraction sockets, fracture of the jaw bone, root canal therapy, pericoronitis, deep periodontal pockets, or caries with periapical infection. The presence of microbes in the marrow tissue causes inflammation, edema leading to compression of the blood vessels resulting in ischemia and osteonecrosis in the later stages [1,2,5,8].

Here we describe a rare case of chronic maxillary osteomyelitis associated with aspergillus fungal infection and actinomycosis bacterial infection in a 47-year-old male patient who presented with uncontrolled diabetes mellitus.

Case Report

A 47- year-old male Indian patient who was a farmer by occupation reported to the Outpatient Department with a chief complaint of pain in the upper lip, right, and left cheek region for four months.

The patient had a history of fever four months back with swelling and numbness in the upper lip and cheek region. Later it was followed by pain, swelling, loosening, and exfoliation of maxillary teeth. The pain was moderate, continuous, and radiating to the forehead. There was pus discharge from the maxillary anterior region and the nose. He had nasal twang and blurring of vision for about 3 months.

The patient's family history was non-significant, but he had a medical history of long-standing type II diabetes mellitus with a random blood sugar level of 284mg/dl which was not treated effectively.

Extra-oral examination on inspection did not show any changes except slight facial asymmetry. On palpation, the lesional area was firm, mildly tender with no rise in the local temperature. The overlying skin appeared normal and had no evidence of sinus openings. The right and left submandibular group of lymph were palpable, firm, and non-tender (***Figure 1A***).

Intra-oral examination revealed a large denuded area of bone on the left maxillary arch of 4.0x 2.0 cms in size, extending anteroposteriorly from the mesial aspect of the maxillary left central incisor (21) to the mesial aspect of the second molar (27) region. The denuded bone and soft tissue swelling extended mediolaterally from the labial vestibule to the midline of the hard palate. No discharge was noted. The exposed bone surface had an ivory-white appearance, was necrotic, mildly tender, and segmental mobility of the alveolar sockets of the missing maxillary teeth 21 to 26 were evident (***Figure 1B***).

On palpation, the soft tissue surrounding the denuded bone was firm in consistency, non-compressible, and mildly tender. The overall hygiene of the patient was poor and Grade II mobility was seen in 11 to 15 teeth.

The orthopantomograph revealed unhealed sockets of the exfoliated teeth and an impacted mesiodens in the 21 region. There was mesial tilting of the 27 and 11 towards the edentulous area. No overt changes were detected in the maxillary sinus region (***Figure 1C***).

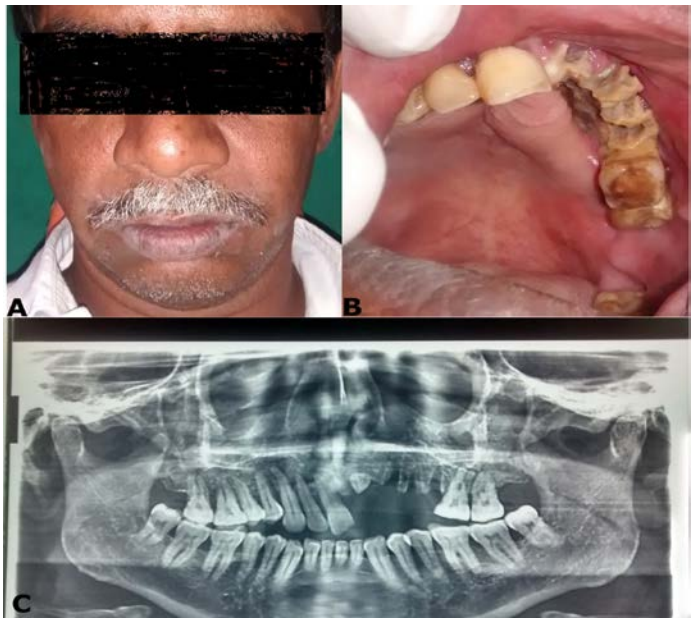

Figure1: A; Extraoral photograph showing slight facial asymmetry, no surface changes noted on the skin. B;Intraoral photograph showing necrotic bone with unhealed alveolar sockets of 21 to 26. The surrounding soft tissue is ulcerated, irregular with inverted margins. C; OPG showing unhealed extraction sockets of missing teeth and an impacted mesiodens in the 21 region.

The occlusal radiograph revealed ill-defined radiolucency at the periapical region of 11 extending till the midline of the palate; impacted mesiodens; and non-healing sockets in the area of 21 to 26 (***Figure 2A***).

On scrape cytological examination, smears revealed clumps of septate hyphae branching at acute angles with few neutrophils in the background (***Figure 2B***). Few bacterial colonies and areas of necrosis were evident suggesting a possible fungal infection.

Incisional biopsy was received to the Department of Oral and Maxillofacial Pathology for histopathological evaluation with a provisional diagnosis of chronic osteomyelitis of the left maxilla.

Two hard tissue and two soft tissue bits were received. The soft tissue bits were creamish white to brownish-black with a firm consistency. The hard tissue bits were

creamish brown in color and hard in consistency. (***Figure 2 C&D***).

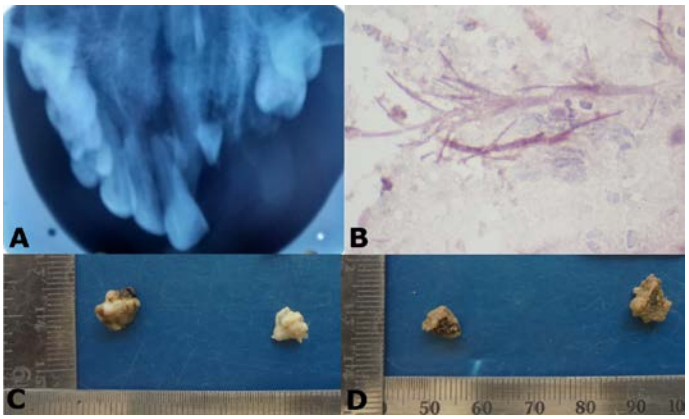

Figure 2: A; The occlusal radiograph revealing ill-defined radiolucency at the periapical area of 11 and unhealed extraction sockets of 21 to 26 (circle). B; The photomicrograph of the cytosmear showing septate fungal hyphae branching at acute angles (black arrow) [PAP stain, x400]. C & D; Gross images of the received incisional hard and soft tissues specimen

The hematoxylin and eosin (H & E) and periodic acid Schiff (PAS) stained tissue sections of the hard tissues revealed non-vital mature bone with empty lacunae associated with a dense conglomeration of microbial colonies (***Figure 3A & B***). High power view of the microbial colonies showed a radial arrangement of filamentous bacteria that were basophilic at the center and eosinophilic at the periphery, giving the "sunray" appearance characteristic of actinomycotic colonies (***Figure 3 C***). PAS stain revealed the filamentous rods ***(Figure 3 D)***. Gram staining of the sections showed a radiating filamentous arrangement of the colonies with central Gram positivity and peripheral eosinophilic clubs ***(Inset: Figure 3E***).

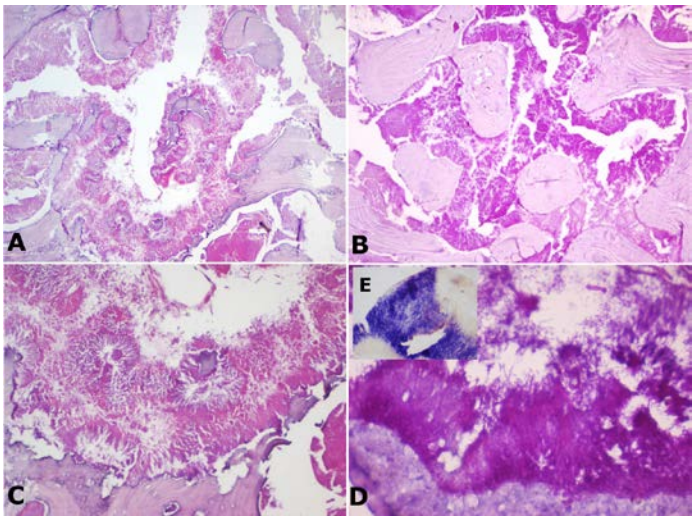

Figure 3: A; Photomicrograph showing non-vital mature bone with empty lacunae. The medullary spaces are filled with dense conglomeration of microbial bacterial colonies [H & E stain x40]. B; Photomicrograph showing radial arrangement of microbial colonies around the necrotic bone [PAS stain, x100]. C; Closer view of the section revealing sun ray arrangement of actinomycotic colonies [H & E stain, x200]. D; High power view of the same showing filamentous bacteria (yellow arrow) arranged radially around the necrotic bone [PAS stain, x400]. Inset: E; Grams stain revealing filamentous arrangement of the actinomycotic bacilli with peripheral eosinophilic club and central gram positive rods [Grams stain, x400].

In many areas, the colonies of actinomycosis were associated with fungal hyphae at the periphery away from the necrotic bone (***Figure 4 A***). High power view of the same showed thin septate fungal hyphae branching at acute angles and refractile fungal spores (***Figure 4 B & C)***.

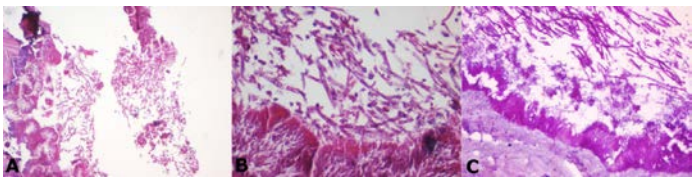

Figure 4: A; Photomicrographs showing actinomycotic colonies close to necrotic bone and associated peripherally placed fungal hyphae [H&E stain, x40]. B; High power

view of the same showing filamentous actinomycotic colonies associated with fungal hyphae and spores [H&E stain, x200]. C; Photomicrograph showing the filamentous actinomycotic colonies and peripheral fungal hyphae branching at acute angles [PAS stain, x100].

The fungal hyphae showed septations, parallel walls, and dichotomous branching at acute angles with the spores confirming it to be Aspergillus ***(Figure 5 A, B & C)***.

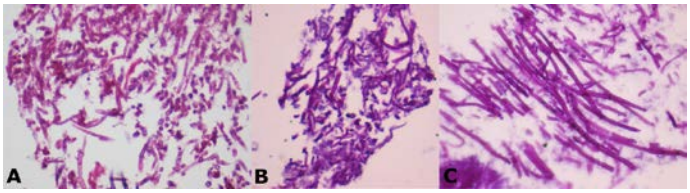

Figure 5: A; Photomicrograph demonstrating sepate fungal hyphae, few of them branching at acute angles along with fungal spores [H&E stain, x200]. B; Photomicrograph depicting the thin, septate fungal hyphae with refractile spores [PAS stain, x100]. C; High power view of the hyphae demonstrating parallel walls, septations, branching at acute angles [PAS stain, x400].

In few areas normal medullary spaces were completely replaced by large clumps of bacterial colonies. Many areas of necrosed bone were evident with a clear demarcation between viable and necrosed bone. There was no evidence of any inflammatory cells in the hard tissue specimen.

Based on the above clinical, radiologic, and histologic examination a final diagnosis of chronic destructive osteomyelitis associated with aspergillus, actinomycosis, and osteonecrosis was given.

The patient was referred to the Physician to control diabetes and to the Oral Surgery Department where the condition was managed by debridement, antibiotics, and antifungal agents. The patient is under regular follow-up for 18 months and is showing good response.

Discussion

Osteomyelitis can be suppurative or non-suppurative. Suppurative osteomyelitis can be further classified as acute, subacute, chronic, or secondary chronic when it begins as acute osteomyelitis and becomes chronic [1]. The condition is termed chronic if it persists for more than a month with the duration ranging from months to years. It presents with low-grade inflammation with periods of exacerbation, dull pain, erythema, swelling, exposed bone, presence of dead bone, new bone apposition, fistulous tracts, and lymph node enlargement [3,5].

The patient in the current case had a history of fever, pain, swelling, numbness of the upper lip, and cheek for four months that was followed by exfoliation of maxillary teeth. A history of pus discharge from the maxillary anterior region and nose with a nasal twang was a point to be appreciated. These features suggest that the condition initially began as an acute lesion and persisted in a chronic state.

Uncontrolled diabetic patients are at higher risk for infectious diseases. They are prone to develop opportunistic diseases due to progressive immunosuppression, increase glucose concentration in mucosal tissues and various body fluids, reduced leukocyte chemotaxis, life span, and phagocytosis; and diminished vascularity that reduces the tissue perfusion [6,9].

As the person ages, the adaptive immune system is hampered with diminished cytokine pattern, reduced clonal expansion, reduced function of antigen-specific T and B cells, and decline in antigen-presenting cell function [9]. This 47-year-old male might have succumbed to osteomyelitis due to reduced immunity related to uncontrolled diabetes and age.

The organisms most commonly involved in jaw osteomyelitis include bacteroides, peptostreptococcus,

microaerophilic streptococcus, Eikenella, Klebsiella, Actinomyces, Candida to name a few. The biofilm of microorganisms acting collectively increases the pathogenicity and progression of osteomyelitis [2,5]. The present case of osteomyelitis is a rare association of aspergillus (fungal) and actinomycotic (bacterial) infection.

Based on the clinical presentation, the differential diagnoses included non-specific osteomyelitis, osteomyelitis associated with mucormycosis due to closeness to the maxillary sinus, and non-specific osteonecrosis of bone with secondary infection.

According to Gamaletsau MN et al, the common radiologic patterns observed in *aspergillus* osteomyelitis are osteolysis, bone destruction, and bone erosion (65%), while the less common changes include periosteal reaction and sequestrum formation [10]. Radiographs in the present case offered little evidence as to the detection of the type of osteomyelitis as only ill-defined radiolucency with unhealed sockets were evident

The gold standard for diagnosing specific organisms affecting osteomyelitis is the histological examination and microbial culture of an abscess if present or of the suspected bone [11]. Histological examination was performed as no draining abscess was detected at the time of examination. The biopsy revealed the entire bone surface to be covered with polymicrobial organisms.

Actinomycetum is a Gram-positive, filamentous, branching, non-acid forming, non-sporing anaerobic bacteria that reside in oral tissues as commensal. The infectious disease manifests when there is a breach in the continuity of the epithelium that leads to the transport of pathogens into tissue layers with an anaerobic environment. The site frequently involved is the cervicofacial region. Actinomyces species could also be responsible for maxillary osteomyelitis in patients with odontogenic maxillary sinusitis [11].

The common species affecting include Actinomyces Israelii. Others such as Actinomyces Naeslundii, Actinomyces Viscosus, and Actinomyces Odontolyticus are identified too. The condition may be rapidly progressing (acute) or slow in progress (chronic). It generally requires symbiosis of other anaerobic streptococci, staphylococci, fusiform or Gram-negative bacilli which create an anaerobic environment; produce toxins or enzymes such as hyaluronidases that break down the connective tissues to aid invasion or inhibit host defences, thus achieving pathogenicity [8,12]. The actinomycotic infection in the present case was also associated with many bacterial colonies and was more close to the necrotic bone.

A study by Kaplan et al has revealed 45 cases of actinomycosis associated with osteomyelitis. [13]. One of the searches has yielded 30 cases of actinomycotic osteomyelitis of the jaws from the period of 1952 to 2011 [12].

The patients with cervicofacial actinomycosis present with multiple draining fistulas with yellow “sulphur granules” and fibrosis leading to indurated swelling of the jaw. Yellowish sulphur granules are constituted by the conglomeration of actinomyces bacterial colonies. The colonies consist of filamentous bacteria aggregated to form a mass with radial arrangement and variation in color between center and periphery of the colony in H & E stain giving a “sunray” appearance [Figure 8]. They are positive for both periodic acid Schiff stain and Gram stain. The colonies are normally seen in connection with mixed inflammatory cells [11, 13]. The patient in the present case did not show suppuration or sulphur granules at the time of presentation, but a history of pus discharge was evident. The sunray colonies were found bound to the

bone and very few inflammatory cells were seen. The inflammatory cells would have been probably affected during the decalcification process, but they were detected in cytosmears.

Culture confirms the diagnosis of actinomycosis but since our case was a polymicrobial disease and also as the literature says that actinomycosis culture is negative in most of the cases, culture studies were not performed [8]. The most common fungal infection is Candida followed by Aspergillus [7]. The most common species of Aspergillus causing infection in humans include A. Israelii. Other species affecting humans include A. naeslundii, A. viscosus, and A. Odontolyticus [8]. Invasive aspergillosis causing osteomyelitis of jaws presents with a mortality rate of 25% [5]. In one of the studies done from 1936 to 2013 aspergillosis associated osteomyelitis of the jaw was reported in 310 cases [2].

Fungal osteomyelitis of jaws is more likely to be invasive as compared to bacterial, if not diagnosed early and treated with appropriate antifungal agents [2]

Aspergillus is the most ubiquitous, aerobic saprophytic fungi. Humans constantly inhale its conidia and these are usually eliminated through the phagocytes that contain nicotinamide adenine di-nucleotide-phosphate (NADPH) oxidase. Activated NADPH oxidase helps in the production of reactive oxygen species that destroy the organism. In neutrophils, this antimicrobial activity is linked with the activation of intracellular proteases [2, 5, 12]. The patient was a farmer by occupation which increases the risk of exposure to the fungal spores from the environment. The immunocompromised state as with the current case due to diabetes and added actinomycotic infection would have lead to disease progression.

The aspergillus hyphae are quite characteristic showing narrow septate hyphae of 3–6 μm in size having dichotomous branching between 45° and 90°. The spores of aspergillus bud at 45-degree angle [7]. The typical aspergillus hyphae and spores were identified away from the necrosed bone closer to the aerobic conditions in the present case.

The presentation of the microorganism here was characteristic with anaerobic actinomyces identified close to the necrosed bone where an anaerobic environment would be prevalent and the fungal hyphae were close to the surface where an aerobic condition was conducive. Areas of resorption of mature bone, non-vital, and necrotic bone were evident.

Aspergillus and actinomycosis associated osteomyelitis is a rare event with only three cases reported till date. The present case was similar to the case reported by Vinay et al where the aspergillus and actinomycosis osteomyelitis was reported in a 38-year old male farmer who had uncontrolled diabetes and involved the left maxilla. In contrast and comparison with the present case, the aspergillus organism in Vinay et al case was found among the necrotic material and isolated masses of actinomycotic colonies were found [14].

The differential of mucormycosis was ruled out as the morphology of hyphae were not broad, not branching at 90 degrees, and were septate [7]. The present case was of specific osteomyelitis associated with osteonecrosis. The organisms involved were mainly actinomyces and aspergillus.

The other differentials that can be considered include Fusarium infection. The hyphae of fusarium are hyaline, septate, and are 3-8 microns in diameter. They branch at acute/ right angles. They produce fusiform macroconidia (hyaline, multicellular, banana-like clusters with foot cells at the base of the macroconidium) and microconidia (hyaline, unicellular, ovoid to cylindrical in slimy head or chains) that are characteristic and are not seen in aspergillus [15].

The treatment modalities of chronic osteomyelitis vary from a range of simple non-invasive approaches to more invasive radical treatment. This simple approach is by using pharmacological antibacterial and antifungal medications. The surgical treatment varies from debridement, curettage, sequestrectomy, and resection. Because most oral microorganisms are can form biofilms, treatment of chronic osteomyelitis requires removal of bone sequestration, curettage, debridement, and systemic antimicrobials for weeks [5].

Conclusion

Chronic osteomyelitis associated with osteonecrosis commonly presents with polymicrobial biofilm formation which requires early detection, and appropriate management. The correction of underlying systemic condition, debridement and use of specific antimicrobials control the magnitude of mortality and morbidity. The present case was a unique association of actinomycosis and aspergillus infection which requires a combination of anaerobic and aerobic environment, a rare event as literature search yielded only three such cases with the present case being the fourth and was associated with osteonecrosis.

Reference

1. Topazian RG, Goldberg MH and HuppJR. Oral and Maxillofacial Infections, WB Saunders, Philadelphia, Pa, USA, 4th edition, 2002.
2. Arani R, Shareef SNHA, Khanam HMK. Mucormycotic Osteomyelitis Involving the Maxilla: A Rare Case Report and Review of the Literature. Case Reports in Infectious Diseases 2019;2019:1-6. DOI: https://doi.org/10.1155/2019/8459296
3. Prasad KC, Prasad SC, Mouli N, Agarwal S. Osteomyelitis in the head and neck. Acta Otolaryngol 2007;127:194–205. DOI: 10.1080/00016480600818054
4. Braddley JW. Clinical risk factors for invasive aspergillosis. Medical Mycology 2011, 49(Suppl. 1), S7–S12. DOI: 10.3109/13693786.2010.505204
5. Dym H and Zeidan J. Microbiology of Acute and Chronic Osteomyelitis and Antibiotic Treatment. Dent Clin N Am 2017;61: 271–282. DOI: http://dx.doi.org/10.1016/j.cden.2016.12.001
6. Peravali RK, Jayade B, Joshi A, Shirganvi M, Rao CB, Gopalkrishnan K. Osteomyelitis of Maxilla in Poorly Controlled Diabetics in a Rural Indian Population J. Maxillofac. Oral Surg 2012;11(1):57–66. DOI: 10.1007/s12663-011-0283-0
7. Urs AB, Singh H, Mohanty S, Sharma P. Fungal osteomyelitis of maxillofacial bones-Rare presentation. J Oral Maxillofac Pathol 2016;20:546-547. DOI: 10.4103/0973-029X.190966
8. Curia M M, Diba L L, Kowalskib L P, Landmanc G. Manginid C. Opportunistic actinomycosis in osteoradionecrosis of the jaws in patients affected by head and neck cancer: incidence and clinical significance. Oral Oncology 2000;36: 294-299. DOI: https://doi.org/10.1016/S1368-8375(99)00080-9
9. Rajagopalan S. Serious infections in elderly patients with diabetes mellitus. Clin Infect Dis 2005;40:990-996. DOI: https://doi.org/10.1086/427690
10. Maria N. Gamaletsou MN, Rammaert B, Bueno MA, Moriyama B, Sipsas NV, Kontoyiannis DP, et al. Aspergillus Osteomyelitis: Epidemiology, Clinical Manifestations, Management, and Outcome. J Infect 2014; 68(5): 478–493. DOI: http://dx.doi.org/10.1016/j.jinf.2013.12.008
11. Valour F, Sénéchal A, Dupieux C, Karsenty J, Lustig S, Breton P, et al. Actinomycosis: etiology, clinical features, diagnosis, treatment, and management. Infection and Drug Resistance 2014;7: 183–197. DOI: http://dx.doi.org/10.2147/IDR.S39601

12. Sezer B, GünizAkdeniz B, Günbay S, Hilmioğlu-Polat S,Başdemir G. Actinomycotic osteomyelitis of the jaws: Report of four cases and a review of the literature. Journal of Dental Sciences 2017;12:301-307. DOI: http://dx.doi.org/10.1016/j.jds.2013.02.031
13. Kaplan I, Anavi K, Anavi Y, Calderon S, Schwartz-Arad D, Teicher S et al. The clinical spectrum of Actinomyces-associated lesions of the oral mucosa and jawbones: correlations with histomorphometric analysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:738-746. DOI: doi:10.1016/j.tripleo.2009.06.019
14. Vinay BH, Mohan A, Haritha P, Lakshmi KR. A rare coexistence of aspergillosis with actinomycosis. J Oral Maxillofac Pathol 2017;21:277-81. DOI: 10.4103/jomfp.JOMFP_66_17
15. Kudur MH, Prakash P Y, Savitha M. Fusarium solani causing quasi-invasive infection of the foot in an immunocompetent middle-aged man from South India. Indian J Dermatol 2013;58:241. DOI: 10.4103/0019-5154.110852