

Actinomycotic osteomyelitis of the maxilla in a female patient: A rare case report with the review of the literature

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Abstract

Actinomycotic osteomyelitis is a rare chronic suppurative, granulomatous, fibrosing saprophytic infection. It is an endogenous infection caused by the *Actinomyces* species, which are part of the normal oral microflora. There is a male predilection for this type of infection, with the male to female ratio of 4:1. Though the etiopathogenesis of the infection is unclear, it is mostly attributed to the disruption of the normal oral microflora and the invasion of the microorganism into deeper tissues through a break in the mucosal barrier due to damage from trauma, extraction or previous injury. The portal of entry can be through the pulpal, periodontal or mucosal route, causing the purulent and necrotic infection of soft tissue, bone, or both. The diagnosis is usually considered when there is a persistent infection without the presence of regional lymphadenopathy and is usually confirmed through the histopathological depiction of the bacterial colonies – ‘ray fungus’ – as obtaining the positive culture of the causative microorganisms is difficult and is reported to be effective in less than 50%. Patients with such infections are managed with surgical debridement, followed by antibiotic therapy for a longer time period. Recent advances have been emphasized for an early diagnosis and a better prognosis of the therapy.

Therefore, this paper aimed to present a rare case of actinomycotic osteomyelitis of the maxilla in a 45-year-old female patient, and also to review the literature on this rare infection.

Keywords: bacterial infections, osteomyelitis, actinomycosis, maxilla, *Actinomyces*

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Introduction

Actinomycosis is a rare chronic suppurative, granulomatous, fibrosing saprophytic infection caused by the commensal oral and pharyngeal *Actinomycetaceae* family of bacteria. It is a specific chronic inflammation of soft tissue and rarely of bone.¹ The actinomycotic species are non-acid fast, slow-growing, Gram-positive, anaerobic or microaerophilic bacteria resembling fungi. The *Actinomyces* species resemble both bacteria and fungi, but most of the basic characteristics suggest that in fact, they are bacteria. Unlike fungi, they do not have sterols in their cell walls and are susceptible to antibacterial pharmacotherapeutic agents.² The principal micro-organism involved in this infection is *Actinomyces israelii* (*A. israelii*),³ although other species, like *A. viscosus*, *A. naeslundii*, *A. meyeri*, and *A. odontolyticus*, are identified occasionally. *Actinomyces* cause this infection particularly when there is a break in the normal mucosal barrier because of any trauma, extraction, surgery, or a preceding infection.⁴ The presence of this break and the devitalized tissue pave the way for the deeper invasion of tissues causing infection.

Actinomycosis is a polymicrobial infection involving the association of other companion bacteria, which are frequently Gram-negative fusiform bacilli, anaerobic streptococci or staphylococci, and facultative anaerobic bacilli that form a mutual/symbiotic anaerobic environment in the body, enabling the growth of the *Actinomyces* species.⁵ Thereby, these co-pathogens increase the invasive power of the *Actinomyces* species by releasing enzymes or toxins, or by suppressing the host defensive mechanisms, resulting in the early manifestations of the infection and the failure of the therapy.⁵

Actinomycosis involving bone is rare but possible. Osteomyelitis occurs secondary to the primary infection and the infection spreads through direct invasion into the surrounding adjacent tissues. It burrows through the anatomical planes, unlike the other infections which follow it, creating a lobular 'pseudotumor'.⁶ Actinomycotic osteomyelitis of the jaws, especially of the maxilla, is a very rare occurrence because of the abundant blood supply and cancellous architecture of bone as compared to the mandible. There are only very few cases reported in the literature involving the maxilla in a female patient.^{3,7-9} Thus, our article is another example of a report of a rare case of actinomycotic osteomyelitis involving the maxilla in a 45-year-old female patient.

Case report

A 45-year-old female patient, a farmer, reported to the Department of Oral Medicine and Radiology with the chief complaint of pain, a bad breath and a growth in the left posterior region of the maxilla (Fig. 1A), along with



Fig. 1. Facial view at day 1 (A), 2 days postoperatively (B) and 1 month postoperatively (C)

headache for the past 2 months. Further, when recording a detailed history, the patient revealed that 2 months before she had a continuous dull pain that aggravated during mastication and subsided at rest. The patient visited a medical practitioner, who administered an intraoral injection on the palate, for which she had no record. After 15 days since the injection administration, the patient started experiencing a continuous sharp pain that aggravated on mastication, followed by the occurrence of a growth in the injected area. After this, the patient visited an ENT specialist, who prescribed her analgesics and vitamin supplements, and advised her to perform blood tests; the results were reported to be within normal limits. The patient was further referred to our Department, as there was not much improvement. The patient also had a history of fever, which occurred one and a half months before. There was no history of change in the size of the patch for the past one and a half months, as reported by the patient.

The patient had no relevant medical, dental and family history. She had also stopped brushing her teeth with a toothbrush 2 months before and had been using her fingers to clean her teeth. The extraoral examination revealed a single submandibular lymph node, palpable on both the right and left side, 1 cm × 1 cm in size, round in shape, mobile, and tender on palpation.

During the intraoral soft tissue examination, an irregular greenish-white patch of size 6 cm × 3 cm on the upper left palatal mucosa was observed, extending from the mesial aspect of tooth 22 to the distal aspect of tooth 27 antero-posteriorly, and from the midline to the palatal marginal gingiva in the 2nd quadrant mediolaterally (Fig. 2A). A bony sequestrum was present on the buccal aspect in relation to the posterior teeth, involving the marginal gingiva and a width of 1 cm of the attached gingiva in relation to teeth 24 and 25 (Fig. 2B). The surrounding area appeared to be inflamed and erythematous. Severe halitosis was present. On palpation, the patchy growth was tender, firm, with a rough surface. When retracting the patchy growth, it could be easily raised, revealing an ulcerative denuded area underneath it. During the examination of the gingiva, generalized gingival inflammation, generalized marginal gingival erythema and bleeding on probing were present.

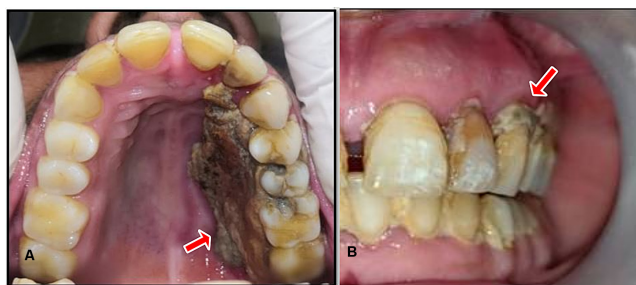


Fig. 2. Intraoral clinical presentation at day 1
A – maxillary occlusal view; B – cropped frontal view.

Other hard tissue findings included deep caries in teeth 25 and 26 with tenderness on percussion, dental caries in teeth 37, 47 and 48, Miller class III mobility of teeth 24, 25 and 27, Miller class I mobility of teeth 23 and 26, the crowding of the mandibular anterior teeth, stains – +++, and calculus – ++.

The intraoral periapical radiographs of the maxillary left posterior region, an orthopantomogram, plain computed tomography (CT) – the paranasal sinus (PNS) view, and the incisional biopsy of the palatal mucosa were advised.

The intraoral periapical radiographs divulged deep dental caries in teeth 25 and 26, and apical periodontitis in teeth 24, 25, 26, and 27. The orthopantomogram revealed deep dental caries in 25 and 26. The plain CT (PNS) exposed the erosion and destruction of the upper left alveolar ridge in the premolar and molar region, extending to the pterygoid plates, and superiorly involving the floor of the left maxillary sinus and the left lateral margin of the hard palate (Fig. 3). It also showed a few air pockets noted in the adjacent soft tissue, a deviation in the nasal septum toward the left side, the left osteomeatal complex block, the left concha bullosa; hypodense mucosal thickening in the maxillary sinuses bilaterally, sphenoidal sinuses, and ethmoidal air cells suggestive of sinusitis.

The incisional biopsy was performed and the patient was prescribed a broad-spectrum antibiotic (ciprofloxacin 500 mg b.i.d.) as well as analgesics (paracetamol 325 mg + aceclofenac 100 mg b.i.d.) for 7 days. The histopathological examination under $\times 400$ magnification revealed features suggestive of osteomyelitis with a bacterial and fungal infection, such as necrotic tissue at the periphery with the loss of architecture and the presence of abundant microbial colonization and loose edematous connective tissue in the center, Gram-positive cocci in pairs and chains infiltrating deeper tissues, the non-viable necrotic interconnected trabeculae with the absence of osteocytes and osteoblasts in lacunae, bony trabeculae of irregular ragged borders, necrotic marrow tissue, extravasated red blood cells (RBCs), and chronic inflammatory cell infiltration. After 7 days since the incisional biopsy, an obvious bony sequestrum with the surrounding inflamed mucosa was noted in the same region (Fig. 4).



Fig. 3. Axial sections of plain computed tomography (CT) – the paranasal sinus (PNS) view showing the destruction of bone involving both the lingual and buccal cortical plates (A, B), and a coronal section depicting extension to the floor of the left maxillary sinus (C)



Fig. 4. Intraoral clinical presentation after 7 days since the initial biopsy showing an obvious bony sequestrum with the surrounding inflamed erythematous mucosa

The patient was referred for necessary surgical therapy. Preoperatively, the patient was prescribed the intravenous (i.v.) injection of cefixime 1 g b.i.d., the i.v. injection of metronidazole 100 mL in normal saline (NS) t.i.d. and the i.v. injection of diclofenac 150 mg b.i.d. for 5 days. Sequestrectomy, thorough debridement, curettage, and the extraction of teeth 21–28 (Fig. 5), followed by wound closure with Vicryl® 3-0 sutures (Ethicon, Inc., Somerville, USA) were performed under general anesthesia, and the excised tissue was sent for a histopathological examination again. The patient was prescribed a postoperative broad-spectrum antibiotic (amoxicillin 500 mg t.i.d.) for 2 months and analgesics (paracetamol 325 mg + aceclofenac 100 mg b.i.d.) for 10 days.

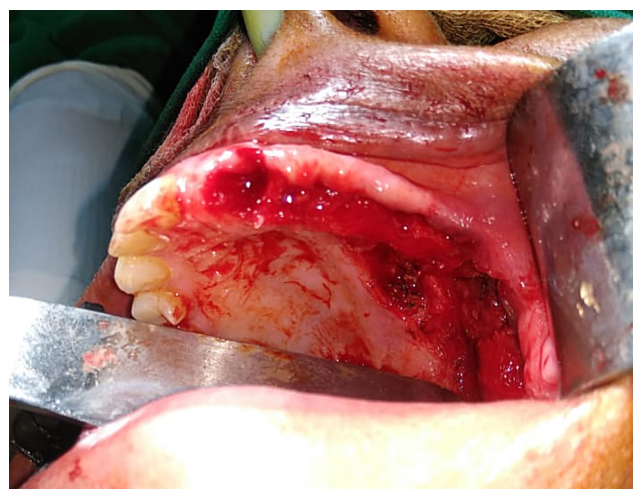


Fig. 5. Intraoperative photograph

The second histopathological examination of the excisional biopsy tissue under $\times 400$ magnification revealed features suggestive of actinomycotic osteomyelitis, like necrotic trabeculae with ragged borders and the absence of osteocytes and osteoblasts in lacunae (Fig. 6A), numerous multinucleated osteoclasts in Howship's lacunae at the periphery of bony trabeculae, central necrotic marrow tissue with extravasated RBCs and chronic inflammatory cell infiltration, bacterial colonies in some areas, where individual colonies appeared round or lobulated, and were made up of a meshwork of peripheral radiating filaments that were hematoxyphilic, along with the eosinophilic peripheral club-shaped ends of the filaments (Fig. 6B). Figures 6C and 6D depict the filaments under $\times 1,000$ magnification and the periodic acid–Schiff (PAS) staining of the actinomycotic colonies under $\times 100$ magnification, respectively.

Satisfactory healing was observed at the 2-day, 1-week and 1-month postoperative follow-ups of the patient (Fig. 1B,1C,7,8) as well as the alleviation of symptoms. The patient was referred for prosthetic rehabilitation after 3 months of the healing period.

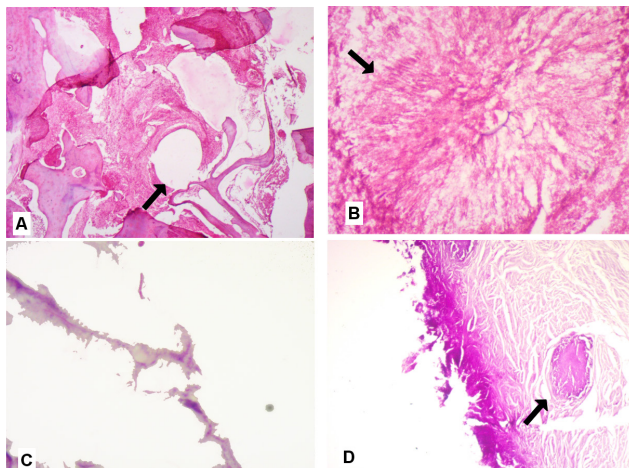


Fig. 6. Histopathological sections depicting necrotic bone with the actinomycotic colonies under $\times 40$ magnification (A), the 'ray fungus' appearance under $\times 400$ magnification (B), filaments under $\times 1,000$ magnification (C), and the periodic acid–Schiff (PAS) staining of the actinomycotic colonies under $\times 100$ magnification (D).

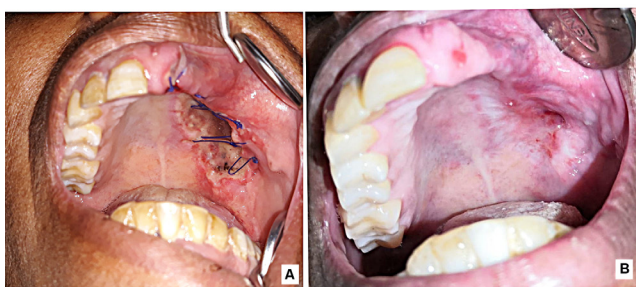


Fig. 7. Intraoral clinical presentation at 2 days postoperatively (A) and 1 month postoperatively (B).



Fig. 8. Orthopantomogram at 1 month postoperatively.

Discussion with the review of the literature

Primary actinomycotic osteomyelitis is a rare condition that accounts for only 12% of the cases.¹⁰ In the cervico-facial region, it commonly affects the chin and the angle of the mandible, but rarely the maxilla, as in the present case, as well as the temporomandibular joint (TMJ). The mandible to maxilla prevalence ratio is 4:1.^{11,12} The incidence of the *Actinomyces* infection is 53.6% in the mandible, followed by 16.4% in cheeks, 5.7% in the maxilla, and 0.3% in TMJ.¹³

Actinomycotic osteomyelitis is attributed to the invasion of the species, which are normally present in the gingival fluid, dentin cavities and palatine tonsils, on mucosal surfaces, and at post-extraction sites, into deeper mucosal tissues. Although the pathogenesis is unclear, the infection is manifested mainly when there is disruption in the composition of the normal microflora, leading to a chronic primary infection, which results in the pathological changes of bone.¹¹

This condition develops only in the presence of certain predisposing circumstances, like immunosuppression, diabetes, the prolonged use of corticosteroids, smoking, alcoholism, and most importantly a break in the epithelium from injury due to trauma or extraction. Also, sinusitis can evolve into such an infection after dental extraction, as reported in the literature.¹⁴ In the present case, the infection could be attributed to trauma to the palatal tissues during the administration of an intraoral injection or the pre-existing sinusitis (chronic inflammation). *Actinomyces* lack the ability to produce the tissue-decomposing enzymes (hyaluronidases), and hence they rely on other co-pathogens, which are the possible source of hyaluronidases, to establish pathogenicity. It could be observed also in the present case, along with the actinomycotic colonies. The most common area of involvement is the head and neck region, accounting for 55% of the cases, although the ophthalmic, neurological, abdominal, respiratory, and urogenital involvement has been reported as well.⁶ The most commonly affected age group is between

30 and 60 years, which is in accordance with the present case, and the male to female ratio is 4:1, substantiating the case to be an extremely rare one.^{10,15–17}

The infection is clinically manifested as an acute or chronic presentation, with the former being less common. An acute infection is characterized by floating swelling, which is painful, along with a rise in temperature and a tendency to rapidly spread into tissues, resembling an odontogenic infection.¹⁴ A chronic infection is characterized by a progressive, slow increase in volume due to the burrowing of the microorganisms, with or without painful symptoms, and is associated with a slight rise in temperature; it may take weeks, months, or even years for it to develop, and the infection may be accompanied by normal hematological findings and the absence of malaise, as reported in the present case.^{10,14,18}

Only a limited number of cases of actinomycotic osteomyelitis have been reported in the literature.^{2,19} Despite the patient's history and the physical examination being essential in the diagnosis of any disease, the radiographic examination, the bacterial culture examination, and the histopathological examination of tissues and secretions from the affected site are necessary for the diagnosis of actinomycotic osteomyelitis.^{8,11,16}

The radiographic examination can be helpful in determining the extent of invasion into bone, even in the presence of the edema of tissues.²⁰ Computed tomography can help determine the extent of osteolysis and the formation of fibrous tissue in the infected area, and scintigraphy with gallium can help differentiate the inflammatory changes from neoplasms and assess the effectiveness of treatment. However, no imaging modality can be regarded as a sole method of investigation to confirm the diagnosis of actinomycotic osteomyelitis.^{10,11}

The diagnosis depends not only on the clinical findings and the demonstration of microorganisms in the tissue sections or smear, but also upon their culture, which is difficult to obtain in 50% of the cases for numerous reasons.²¹ The culturing of the bacteria should be preferably performed when the patient has not been on antimicrobial therapy for at least 7–10 days before the procedure, as otherwise it may interfere with the diagnosis, making it obscure. The histopathological features include a granulomatous appearance with the characteristic round or lobulate colonies of microorganisms within the central abscess formation, which occur as floating in the sea of polymorphonuclear leukocytes, often associated with multinucleated giant cells and macrophages, especially around the periphery. This appearance is the basis of the term 'ray fungus', which is frequently used.²² All the above-mentioned findings are in accordance with the present case. In the current case, the culturing of the microorganisms was not done, and the diagnosis was based on the morbid anatomical, radiographic and histopathological examinations, especially hematoxylin and eosin (H&E) and PAS staining, rather than the identification of the microorganisms

by culture. The need for the careful handling of the specimens to obtain a positive anaerobic culture is well emphasized. However, the histopathological examination is also strongly recommended.²³ The *Actinomyces* species stain heavily with the H&E, PAS and Giemsa stains. Also, the Grocott–Gömöri methenamine silver (GMS) staining is helpful for the demonstration of filaments.²⁴

Nucleic acid probes and the polymerase chain reaction (PCR) are advisable for the rapid and accurate detection of the microorganisms, as the diagnosis is difficult when it is based only on the clinical and direct identification and/or isolation of the responsible microorganism, which is a laborious process. Molecular testing is considered as the appropriate method for the diagnosis of actinomycotic osteomyelitis of the jaws.²⁵ It has been recommended for the PCR analysis of *A. israelii* to have a higher sensitivity that the specimen undergoes mild decalcification with ethylenediaminetetraacetic acid (EDTA)²⁵ rather than with trichloroacetic acid.²⁶ The same diagnostic approach has also been recommended for the bone biopsies done for the histological examination.²⁵ On the other hand, although the PCR testing overweighs the conventional identification procedure in terms of identification of slow-growing and non-cultivable microorganisms, the method is expensive and it requires an experienced hand to perform the analysis.

Actinomycotic osteomyelitis often demands vigorous treatment once a sound diagnosis is set. The initial treatment consists of the administration of high doses of penicillin, either orally or intravenously, depending on the severity of the infection, although there may be a necessity of surgical management if there is any tissue necrosis or involvement of bone.²⁰ All abscesses should be surgically disrupted and penetrated with a hemostat, regardless of their size. Prolonged antibiotic therapy, preferably with penicillin, is recommended after the removal of the foci of infection by draining abscesses, sequestrectomy and/or the excochleation, saucerization and excision of the fibrous/granulation tissue until the exposure of healthy tissue,^{12,25} which was done in the present case. Other effective antibiotics include erythromycin, clindamycin, tetracycline, minocycline, cephaloridine, and imipenem.^{10,27,28} Penicillin can be administered by i.v. infusion in doses ranging from 3 million to 12 million units daily or as an oral dose of 2–4 g per day for a period of 3–12 months, depending on the host response to the infection. Administering antibiotics for an additional period is recommended, as the lysis of the *Actinomyces* species takes place at a slower rate than in the case of most other bacteria.²⁸ The prognosis for a satisfactory resolution is excellent and the recurrence is rare,^{3,29,30} as demonstrated in the present case. Sometimes maxillofacial reconstruction may be necessary when there is a substantial soft and hard tissue loss, which was not necessary in the present case. The secondary surgical repair or the reconstruction and replacement of the teeth can be attempted once we are confident with the complete resolution and healing of the infection.

Conclusions

Despite a diagnostic dilemma with regard to mucormycosis in presentation, after following a meticulous diagnostic protocol, the current case turned out to be a case of actinomycotic osteomyelitis. The treatment of actinomycotic osteomyelitis, which is a rare and unusual occurrence, is a challenging task. However, it can be overcome with surgical and prolonged antibiotic therapy, and a complete resolution can be achieved, as demonstrated in the present case. The diagnosis of actinomycotic osteomyelitis should be considered in relation to persistent oral infections, as progressive actinomycosis, especially in the maxilla, is likely to lead to serious consequences in the skull base and intracranial involvement. The early diagnosis of actinomycotic osteomyelitis can improve the prognosis and the outcomes of the therapy, thus preventing serious consequences in patients.

Ethics approval and consent to participate

The ethical clearance was obtained from the Research and Ethics Committee, KLE Vishwanath Katti Institute of Dental Sciences, Belagavi, India, with the reference number 20/07/2020/074. Also, the authors declare that the written informed consent was obtained from the patient.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

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