CASE REPORT

Bilateral osteoradionecrosis of the jaw – A rare case report

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Abstract
Osteoradionecrosis (ORN) is among the extensive and most solemn oral complications of radiotherapy of head and neck malignancies with a tardy radiation-induced injury, occurring most commonly in mandible with the most striking features of necrosis of bone and its failure to heal. Unlike other complications, the exact etiology of its occurrence, risk factors are not known, but the theory of hypoxia, hypovascularity, and hypocellularity is considered to be the most widely accepted theory till now. This article presents a clinical case of bilateral ORN of the mandible, occurring with exposed and infected bone, necrotic process that extended through body of the mandible and traumatic extraction was considered to be the etiology of exposed bone. Due to the stage of the condition, a decision for surgical treatment accompanied with antibiotics was made. Proper oral hygiene and frequent dental checks ups should be performed by irradiated patients and patients with osteoradionecrosis.

Introduction
Radiotherapy (RT) is one of the frequently used primary therapeutic modality for the treatment of head and neck malignancies, adjuvant or neoadjuvant in aggregation with concurrent chemotherapy or as palliative treatment for late stage and unresectable head and neck malignancies. Even though it is seen that curing rates have been increased in irradiated patient but these patients are more vulnerable to secondary effects also and oral cavity and oropharynx are the most common sites for radiation-induced adverse effects.

Depending on duration, complications of RT has been broadly classified as early and long-term. As the name suggests early complications are very frequent, chiefly the oral mucositis which is the most common and stressful complication of malignancy treatment and may have lower the quality of life of the patient.

Long-term complications of head and neck RT include dry mouth (xerostomia), loss of taste, limitation of mouth opening (trismus), progressive periodontal attachment loss, dental caries, microvascular alteration, and soft tissue necrosis, and which is not very frequently, but one of the wickedest, osteoradionecrosis (ORN). In severe cases, even death can occur.

The ORN is defined as the exposure of bone tissue irradiated on one or more areas of the mandible or maxilla, which does not heal for more than 3 months without signs of residual disease or relapse (not caused by tumor recurrence). It may occur in one-third of patients irradiated on the head and neck, but most commonly its establishment is observed after tooth extractions, oral surgery or due to irritation caused by maladapted dentures.

ORN is characterized by irradiated bone undergoing necrosis and then exposing through soft tissue. In 1992, Regaurd reported for the first time the occurrence of ORN of the jaws after radiation therapy. In 1926, Ewing first documented and described the bone undergoing changes accompanying with RT and designated this condition as “radiation osteitis”. Meyer classified ORN as one distinct type of osteomyelitis. Titterington also used the term “osteomyelitis of irradiated bone” describing the association of ORN to osteomyelitis. Although numerous theories have been promulgated to elucidate its etiology but the utmost expansively acknowledged theory is of hypoxia, hypovascularity, and hypocellularity. Its management also varies according to the severity which ranges from small asymptomatic exposure of the bone which remains stable for months and repairs with conservative management, to severe necrosis with pathologic fracture demanding surgical intervention and reconstruction. ORN patients have to compromise their quality of life leading to serious clinical symptoms such as chronic spontaneous pain, dysphagia, and facial deformation.

For the prevention of this complication, the ORN patient may show its recovery.
by considering the risk factors and its pathophysiology but sometimes may also occur naturally, unconnected to trauma.[15,16] The mandible is the most commonly affected site than any other bones of the head and neck region and its prevalence is reported to be between 2% and 22% and depending on the techniques used comparatively in older times was between 5% and 15%, to new advancement in techniques such as IMRT, brachytherapy, 3D conformal RT, stereotactic RT, radiofrequency ablation, and radioimmunotherapy have declined rate to 6% or less.[15]

Although there are various theories been reported to elucidate the pathophysiology of osteoradionecrosis but recently Delanian and Lefaix one proposed another theory which states that ORN occurs due to a radiation-induced fibrotrophic mechanism, which includes the formation of free radicals, endothelial dysfunction, inflammation, microvascular thrombosis, fibrosis, remodeling, and finally necrosis of bone and soft tissues.[17,18] Its clinical manifestations include pain, swelling, erythema of soft tissue, necrotic bone exposure, trismus, ulceration, cervical lymphadenopathy, bone sequestration, paresthesia, fistula, and pathological fracture. ORN risk is dependent on the following factors as dose, technique (external or brachytherapy) and volume of irradiated tissue, location, and histological tumor grade. Other predisposing factors include total radiation dose, photon energy, brachytherapy, field size, fractionation, periodontitis, pre-irradiation bone surgery, poor oral hygiene, alcohol and tobacco use, dental extractions, tumor size, location, and stage, proximity of tumor to bone, lack of HBO therapy, increased time since radiation, lack of radiation shields, and edentulousness.[19,22]

Out of those above mentioned predisposing factors, dental extractions immediately before or after RT are considered to be the main triggering factor of osteoradionecrosis and its occurrence is about 2-18% whereas the spontaneous occurrence in the absence of any traumatic event is reported in 35% of cases.[4,5] Clinical management of osteoradionecrosis includes the use of local or systemic antibiotics, pain control, and surgery in severe cases.[14] Additional therapies have been recommended as the use hyperbaric oxygen therapy and ultrasound, and drugs that increase blood perfusion as pentoxifylline, vitamin E, and clodronate.[6,14,15]

Case Report

A 70-years-old male reported to the dental outpatient department with the complaint of pain on the lower jaw since 1 years. He reported being a cigarette smoker for 40 years and an alcoholic person for 25 years, whose consumption he had stopped for 7 and 3 years, respectively. The patient was diagnosed with squamous cell carcinoma of the base of the tongue on the right side around 6 years back somewhere else, with an impression of an ulceroproliferative growth crossing the midline and involving both the vallecula and reaching up to the lingual surface of epiglottis and was indicated for RT and chemotherapy. Patient was advised for OPG and all the required pre-operative extractions as well as oral prophylaxis was done. This subject reported having undergone a surgical treatment with the radical neck dissection on the right region, associated with 30 RT sessions in a telecobalotherapy unit (total of 7,200 cGy), in addition to 4 chemotherapy sessions. The patient complained of pain and swelling 3 years after RT in 23, 24, 25 and then later on after a period of 2 years he again complained of pain and swelling in 36, 37 region and were extracted and seeing the overall condition, multiple carious teeth total extraction was advised. No systemic disease or chronic conditions were present.

Extraorally, facial asymmetry was noticed on the left side due to the single diffuse swelling in the left lower part of the face approximately measuring about 3.5 × 3.5 cm extending anteroposteriorly from the corner of the mouth to 2 cm away from the angle of the mandible and superoinferiorly 4 cm below the Ala-tragus line to the inferior border of the mandible without any change in coloration on comparing to the other normal side [Figures 1 and 2]. On palpation, the swelling was firm in consistency, tender, local rise in temperature elicited, and fixed to the underlying structure. On lymph node examination, there was the presence of a well circumscribed mobile lymph node enlargement on right side, measuring about 1 cm x 1 cm in size approximately, soft in consistency, nontender and fixed suggestive of submandibular lymph node enlargement.

Intraorally, a prominent bone exposure was appreciated in the alveolar ridge of 36 and 46 measuring about 3 × 3 cm on left side and 1.5 × 1.5 cm on right side resulting in a crater like a defect with irregular erythematous borders and a presence of foul smell on opening the mouth [Figures 3 and 4]. On palpation, alveolar ridge was continuous, nontender. On correlating history and clinical findings, we gave osteomyelitis in edentulous 35, 36, 45, and 46 regions as a provisional diagnosis. Clinical differential diagnosis could be actinomycosis, tuberculous infection, and intraosseous carcinoma. The patient was subjected to radiological investigation.

Panoramic radiograph revealed, bilaterally gross pathological changes in the mandible with extensive radiolucency and bone rarefaction bilaterally. There was a widening of the inferior alveolar canal with a change in trabecular pattern of bone of mandible and displaced coronoid process [Figure 5]. The patient was subjected to surgical management. The pathological site was surgically opened under GA and fragments removed.

On histological examination, decalcified hard tissue section shows matured bone with lacunae devoid of osteocytes which are a sign of necrosis.

Based on the history, clinical, radiological, laboratory, and histopathological investigations, final diagnosis of osteoradionecrosis in the edentulous 34, 35, 36, 46, and 47 teeth region was made.

Discussion

Throughout the years ORN has acknowledged with many descriptions, and hence it is occasionally problematic to
Different authors have different opinions regarding the time of exposure, some recommend a 2 month period before ORN can be diagnosed, or even 3 months and 6 months. ORN typically advances during the first 6-12 months after RT.\cite{4,17,21,23-28} Berger and Symington reported two late presentations, one 45 years after a radium implant, and another 38 years after external beam treatment.\cite{28}

Although there are various risk factors, but the dental extractions immediately before or after RT are considered to be the main triggering factor of osteoradionecrosis. Consequently, various factors should be considered while performing tooth extractions in irradiated patients such as the type of treatment, radiation area, tumor prognosis and knowledge of the radiation dose, since at doses lower than 60 Gy the risk is minimal but in this case, the radiated dose given was 70 Gy.\cite{4,11} Similarly, the dental condition of the patient should be considered.\cite{5,6} The patients with the following conditions should undergo extractions: Teeth with a poor prognosis due to advanced carious lesions, with a questionable pulp status or advanced symptomatic pulpal involvement; periodontal disease especially with advanced bone loss, residual root tips not fully covered by the alveolar bone, and a high risk for radiation caries.\cite{4,29} The first method to prevent either future tooth extractions or ORN should occur previously to the beginning of the oncotherapy, by performing an adaptation of the oral environment to decrease the infection.\cite{1,3,6,23} In this

**Figure 1:** Profile picture showing facial asymmetry

**Figure 2:** Lateral profile of a patient

**Figure 3:** Intraorally exposed bone of left side

**Figure 4:** Intraorally exposed bone of right side

**Figure 5:** Panoramic radiograph depicting rarefaction of the bone
case, this adjustment was carried out, however, carries eventually evolved, largely compromising the tooth structure and oral health. Another important factor for extracting questionable teeth is a lack of motivation which may lead poor oral hygiene required for dental maintenance, which may cause infections, increasing, thus, the risk of ORN.\cite{34,35} This was an important factor considered in this case since the poor oral hygiene of the patient was worsened by avulsion. The quality of life of the patient is another fact to be respected, and the dental treatment plan should be resolve by the conditions in which the patient is at each moment.\cite{36} In case the extraction is the decision made, other actions should be employed to prevent ORN advancement is antibiotic prophylaxis which is the most common initiative to prevent infections in compromised tissues; penicillin and clindamycin being the most used antimicrobials.\cite{4,30} Due to its easy administration, availability and wide acceptance among surgeons and patients, this approach has been relevant for planning and carrying out extractions in irradiated patients.\cite{4,30}

In this case, clindamycin 300 mg was the antibiotic used for 7 days because of its increased tissue diffusion capacity. However, it was changed to amoxicillin 500 mg for 7 days post-surgical procedure due to gastrointestinal side effects shown.

As ORN pathophysiology remains debatable, Meyer designated the pathophysiology of ORN by a classic triad as radiation, trauma, and infections. The above theory was improvised by Marx suggesting it as the hypoxic, hypovascular, and hypovascular theory which states that after radiation exposure there is a formation of hypoxic-hypovascular hypovascular tissue which will cause excess collagen lysis and cellular death leading to chronic nonhealing wound and the most recent theory is the radiation fibroatrophy theory pronouncing the activation and dysregulation of fibroblastic activity of the previously radiated area which leads to progression of ORN.\cite{31,32} Prevention of ORN is an enormously noteworthy part of the complete management of patients who undergo external beam radiation therapy to the head and neck malignancies. As per protocol, all the indicated teeth should be extracted 21 days before initiation of radiation therapy and patients should be instructed on meticulous oral hygiene and fluoride should be applied to the dentition daily via custom molded trays and should undergo weekly check-up during RT and monthly follow-ups for the first 6 months and then following early post-treatment patient should visit their dentists for every 4 months.\cite{33}

Osteoradionecrosis is a disease that requires excessive consideration and a multidisciplinary association, which involves the patient, general dentists, specialist in maxillofacial surgery and specialist in oncology and RT.

Our case was diagnosed as a second class of ORN, which postulates that localised involvement of mandible, exposed cortical and medullary bone are necrotic bone. In the both sites of the mandible ORN was induced by local trauma after tooth extraction. Although it was mentioned earlier, the patient had undergone complete tooth extraction in both maxilla and mandible, it is observed that in the upper jaw healed slowly, but successfully, with no evidence of necrotic bone. The mandible is a common site for developing ORN because of its structure and vascularization manner. It is a compact bone with greater density than that maxilla which is a porous cancellous bone. Consequently, mandible absorbs more photons during radiation, which leads to pathological vascular changes. It is the best explanation why the mandible is more susceptible to ORN than the maxilla. Once if the bone gets necrosed, condition will get worsen with time if not treated. Microorganisms will play a major role only in secondary infection cases in which it may lead to serious osteomyelitis. If conservative treatment has not succeeded, a surgical approach is suggested. It is the only option in patients with the late stage of ORN. The extension of surgical removing of bone tissue depends on the severity of necrosis. However, removing of all necrotic tissue is strongly recommended.\cite{34}

**Conclusion**

Although there are many complications of radiation therapy but osteoradionecrosis is a noteworthy complication of radiation therapy in head and neck malignancies. For the prevention and improvement in the prognosis of this complication, its risk factors and the underlying pathophysiology should be better understood.

This case report shows that it is very important and critical for irradiated patients and patients with osteoradionecrosis to perform appropriate oral hygiene and frequent dental check-ups. If tooth extraction is indicated, prevention should be planned. Antibiotics and hyperbaric oxygen therapy are recommended before and after the extraction or operation, regarding to accepted protocols. Great attention should be paid to these patients several years after RT.

**References**

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