

Osteoradionecrosis of Jaw: An Institutional Experience

Abstract

Aims and Objectives: Osteoradionecrosis (ORN) of the jaw is a significant yet rare complication of radiotherapy (RT) associated with the management of head-and-neck malignancies. Recent decrease in the incidence of ORN following RT to the head and neck is being mainly attributed to refinement in RT techniques and improvement in our understanding of this morbid disease. The aim of this study is to assess the patients with ORN following head-and-neck RT to determine the various contributing risk factors involved in the development of ORN. **Subjects and Methods:** A retrospective data review from 2003 onward was conducted on the cases of ORN which presented to the Department of Dental and Oral Surgery, Christian Medical College, Vellore. Details of the patients with regard to the site of primary malignancy, type of treatment provided - RT alone or in combination of surgery and chemotherapy, dose of RT, presenting complaint, duration between the RT and presentation of ORN, and method of management considered were evaluated. **Results:** A total of 25 patients were evaluated. The average age of the 25 patients in our study was 58 years. Oropharynx (about 50%) was the leading site of primary malignancy. More than half of the patients in the study (52%) had undergone radical RT for the primary malignancy and all the patients were given >60 Gy dose of RT. About 48% of the patients in the study reported with pus discharge as their chief complaint. The average intervening time period from completion of RT to the presentation of ORN was 48 months. The mandibular alveolus was the most common site for ORN. Twelve of the 25 cases in the study were managed conservatively with only 3 patients requiring major resection. **Conclusion:** Due to its rare presentation, ORN still remains a challenge for the clinician in its management. Our study revealed that radical RT and concurrent chemo-RT for the oropharyngeal and base of the tongue malignancies have a higher risk of developing ORN. Patients subjected to the dose of RT above 60 Gy for head-and-neck malignancies have an increased risk of future ORN; henceforth, newer modality treatment like intensity-modulated RT regimen is recommended for such sites. Most of the patients in the study were satisfactorily managed of the symptoms with conservative modality treatment; hence, it is recommended to consider for surgical methods only in severe end-stage form of ORN.

Keywords: Management of osteoradionecrosis of jaw, osteoradionecrosis of the jaw, preradiotherapy dental clearance

Introduction

Osteoradionecrosis (ORN)^[1] of the jaw is a significant yet rare complication of radiotherapy (RT) associated with the management of head-and-neck malignancies. The associated risk factors are multifactorial.^[2] Various theories regarding the pathophysiology have been proposed. These include the radiation, trauma and infection theory^[3] by Meyer in 1970, hypoxia, hypovascularity and hypocellularity by Marx in 1983,^[4] and recently, the radiation-induced fibroatrophic theory.^[5] Complexity in diagnosing of ORN is attributed to a wide plethora of presenting clinical features ranging from asymptomatic

bone exposures that remain stable for months to severe necrosis that necessitates surgical intervention and reconstruction. Management of ORN of the jaws still remains controversial.^[6] Conservative methods of management include observation and follow-up, antibiotic and analgesic therapy for acute exacerbations,^[7] hyperbaric oxygen therapy,^[8] pentoxifylline, and tocopherol drug therapy,^[9] whereas surgical procedures may vary from locoregional debridement to resection^[7] of the affected bone. This study is an attempt to help analyze and contribute to the understanding of this morbid disease. This study aims to assess the patients with ORN following head-and-neck RT to determine the various correlating risk factors involved in the development of ORN.

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**Saurabh Kumar,
Catherine
Chandran,
Rabin Chacko,
J. S. Jesija,
Arun Paul**

*Department of Dental and Oral
Surgery, Christian Medical
College and Hospital, Vellore,
Tamil Nadu, India*

Address for correspondence:
Dr. Saurabh Kumar,
Room Number 130, First
Floor OPD Block, Christian
Medical College and Hospital,
Vellore - 632 004, Tamil Nadu,
India.
E-mail: dr.s.kumar.bds@gmail.
com

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Subjects and Methods

A retrospective review was conducted on the documented cases of ORN from January 2003 to April 2017 in the Department of Dental and Oral Surgery, Christian Medical College, Vellore. The details were collected from the Department's Electronic Documentation System and also by reviewing the charts from the Medical Records Department. Demographic data, the primary site of malignancy, presenting complaints, region of disease, time of presentation, details on RT, and modes of management of ORN were assessed and documented. Further, analysis was carried out on the collected data to draw further correlation among various parameters to determine risk factors responsible for the development of ORN.

Results

Demographic data analysis revealed that the average age of the patients in the study was 58 years. The age range varied between 35 and 76 years of age [Figure 1]. A quarter of the patients included in the study were female [Figure 2]. The primary site of malignancy was the base of tongue in 6 out of the 25 patients [Figure 3]. This was closely followed by tonsil in 5 out of the 25 patients. Other sites included were the mandible, tongue, larynx, and floor of the mouth. To summarize, those exposed to RT for malignancy of the oropharynx appeared to be more prone to develop ORN of the jaws [Figure 4]. This was followed by the oral cavity and the mandible.

In this study, most of the patients presented with not just a single symptom or complaint but often multiple [Figure 5]. However, the most frequent complaint was pus discharge (50%). This was followed by an equal number of patients presenting with extraoral sinus opening and pain (24%). Other complaints included were swelling, pathological fracture, nonhealing extraction site, and bone exposure. Five of the patients were asymptomatic and had reported for their regular review. ORN was identified in these patients on clinical or radiological examination. With regard to the site of presentation of ORN [Figure 6], the mandibular alveolus was the most common presentation. This was closely followed by the mandibular body (40%). Two patients had ORN of the maxilla. The average time duration between completion of RT and the time of presentation was 48 months [Figure 7].

More than half of the patients in the study (52%) had undergone radical RT for the primary malignancy. Thirty-six percent of the patients had had adjuvant chemotherapy [Figure 8], and an equal number of patients (1 each) had undergone brachytherapy, intensity-modulated RT (IMRT), and high-frequency RT. Patients managed with radical RT received a dose of 60 Gy in 30 fractions, patients who underwent concurrent chemo-RT received 66 Gy in 33 fractions, 1 patient with brachytherapy received 10 × 6 Gy high-dose rated (HDR) regimen, 1 patient who underwent hyperfractionated

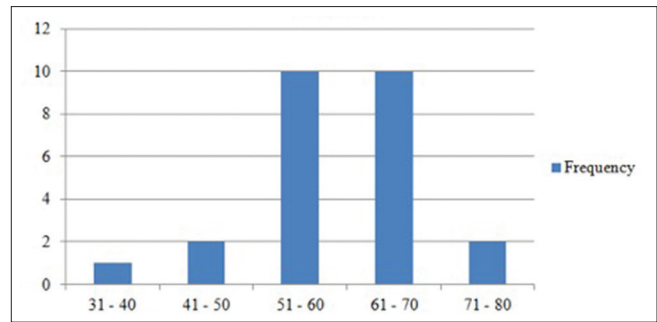


Figure 1: Age distribution

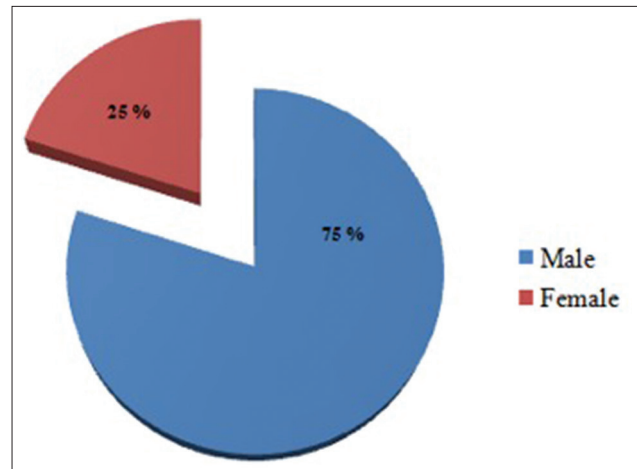


Figure 2: Gender distribution

Primary site	Number of cases
Base of tongue	6
Tonsil	5
Mandible	4
Tongue	3
Buccal mucosa	3
Larynx	1
Floor of mouth	1
Posterior maxilla	2

Figure 3: Primary site of cancer

regimen had 54 Gy in 36 fractions, and the patient with IMRT who developed ORN had 70 Gy in 33 fractions [Figure 8].

Twelve of the 25 cases in the study were managed conservatively [Figure 9], and rest of the patients were either managed with local debridement or surgical removal of foreign body (implants), dental extraction, and sequestrectomy along with long-term antibiotics. Three patients required major surgery in the form of hemimandibulectomy.

Discussion

Marx was the first to explain ORN in 1983 as a triad of hypoxia–hypocellularity–hypovascularity.^[8]Advances

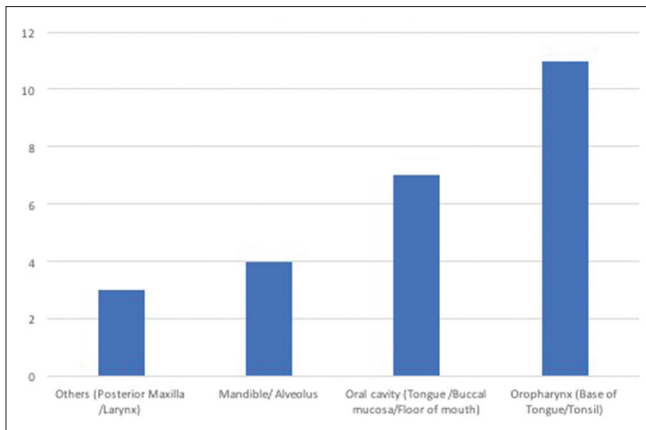


Figure 4: Region of malignancy

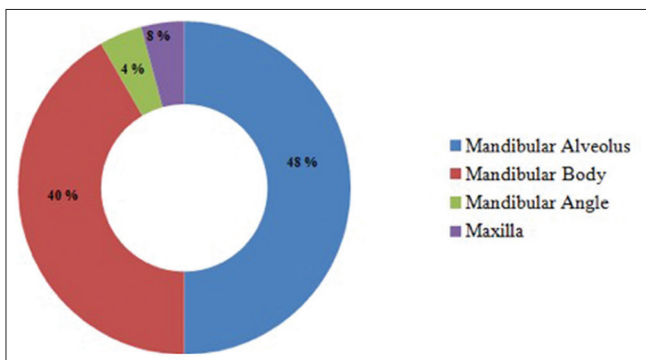


Figure 6: Site of osteoradionecrosis of the jaw

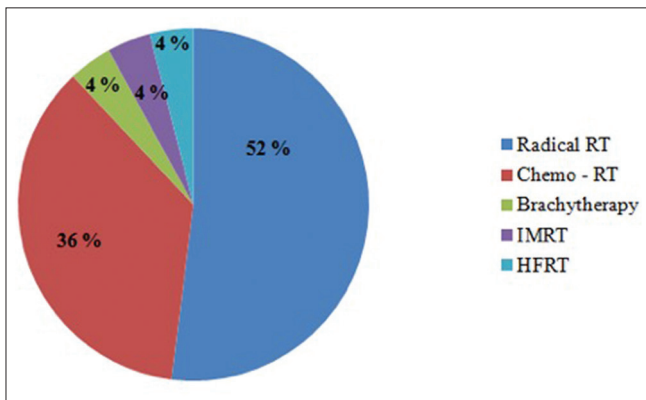


Figure 8: Type of radiotherapy modality (radical radiotherapy, chemoradiotherapy, brachytherapy, intensity-modulated radiotherapy, and hyperfractionated radiotherapy)

in cellular and molecular biology have led to the latest proposal: radiation-induced fibrosis.^[5] Harris appropriately defined ORN as a condition wherein an “irradiated bone becomes devitalized and exposed through the overlying skin or mucosa and persists without healing for 3 months in the absence of tumor recurrence.”^[1] The reported incidence of ORN varies from 2% to 22%.^[10]

Our institution, a tertiary medical center catering to suburban South Indian population annually reports more than a thousand cases of head-and-neck malignancies in a

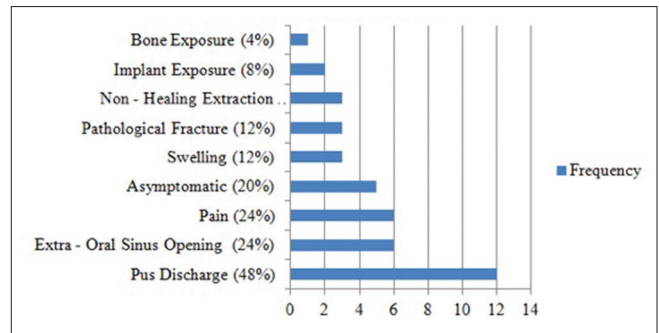


Figure 5: Clinical features at the time of presentation of osteoradionecrosis

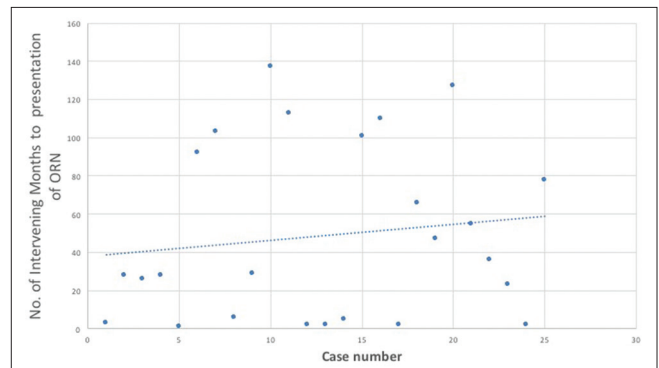


Figure 7: Intervening time of presentation of osteoradionecrosis

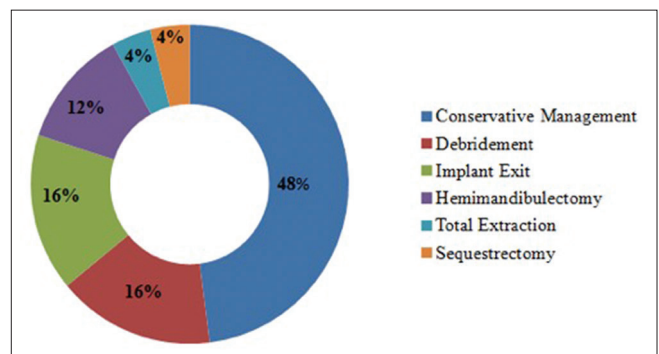


Figure 9: Management of osteoradiotherapy

year. Most of them undergo combined modality treatment that includes both surgery and RT. On regular follow-up visits, only a select few have been diagnosed with ORN. Retrospective evaluation of data from our institutional database revealed 25 followed up cases of ORN of the jaw in patients who had undergone RT for head-and-neck malignancy between 1995 and 2016. The mean age in our sample of 25 patients was 58 years. On the whole, the patients ranged between 35 and 57 years of age. Equal number of patients fell within the fifth and the sixth decades of life. Three-quarters (75%) of the ORN sample were men owing probably to their increased cultural exposure to adverse habits such as tobacco chewing and alcohol intake. Literature reports no statistical correlation of ORN to either gender.^[11]

The diagnosis of ORN was based primarily on clinical signs and symptoms. Generally, ulceration or necrosis of mucosa with exposure of necrotic bone for longer than 3 months with prior history of radiation is considered as ORN. Other symptoms included were pain, trismus, suppuration, halitosis, and associated neurologic symptoms.^[12] In our sample, pus discharge (48%) was the leading complaint on presentation. Few patients were totally asymptomatic and it was review radiographs that pointed to the presence of disease. Some patients had developed pus discharge in earlier stages while others at later stages. Diagnosis of septic ORN is easier as examination usually reveals extra/intraoral draining fistulae. However, a biopsy is essential to rule out malignancy. Pathological jaw fracture was also reported resulting due to localized weakened skeleton [Figures 10-22]

Multiple risk factors have been indicted in ORN. Tumor-related factors include primary site, T stage, and proximity of the tumor to the bone; radiation-related factors include dose and type of radiation (external beam RT, IMRT, brachytherapy, etc.). Nutritional status, continued substance abuse (tobacco and alcohol), type of dentition, and oral hygiene are patient-related factors that can contribute to the development of ORN. The patients in the sample were evaluated based on primary site of malignancy into oropharynx, oral cavity, mandible, and others, about 50% of patients fell within the oropharynx group and more specifically, and individuals treated with RT for cancer of the base of the tongue had high incidence of ORN. Our findings correlated with the report by Owosho et al. that malignancies of the oropharynx were more prone to the development of ORN and in particular those having lesions of the tongue.^[13]

In our sample, the mandible was the site of ORN in most of the cases. This was again in correlation with the study at the Memorial Sloan Kettering Cancer Center.^[13] Malignancies of the oropharynx showed higher risk of developing ORN in most of the cases as these malignancies are managed with higher doses of radiation. Posterior mandible more often falls within the trough zone of radiation of the oropharynx. This might also account for the higher proportion of mandibular ORN seen in oropharyngeal malignancies. Posterior maxilla was the site commonly affected in cases with maxillary ORN, which was also in correlation with the aforementioned study.^[13]

About 52% (13) of patients with ORN in our sample had undergone radical RT. Patients managed with radical RT received a dose of 60 Gy in 30 fractions, 36% (9) patients who underwent concurrent chemo-RT received 66 Gy in 33 fractions, 1 patient with brachytherapy received 10 × 6 Gy HDR regimen, 1 patient who underwent hyperfractionated regimen had 54 Gy in 36 fractions, and the patient with IMRT who developed ORN had 70 Gy in 33 fractions. Hence, it again substantiated that radiation dose of above 60 Gy is associated with high risk of the development of ORN. From the study, it was, henceforth, inferred that the



Figure 10: Case 1: Pus discharge from posterior mandible



Figure 11: Case 1: Orthopantomogram showing osteomyelitic bone in the left angle with pathologic fracture



Figure 12: Case 2: Intraoral asymptomatic bone exposure

risk of developing ORN is higher in patients treated with radical RT and concurrent chemo-RT as compared with IMRT. The mean intervening duration between RT and the presentation of the patient with symptoms in our study was 48 months [Figure 7] contrary to as reported by Fan *et al.*,^[9] who in 2014 published a schematic timetable on the duration of the latent period and the onset of ORN and mentioned that early presentation of ORN within 2 years is related to high dose of RT (>70 Gy), whereas late presentation was affected due to secondary trauma and delayed wound healing within compromised tissue.^[9]



Figure 13: Case 2: Orthopantomogram showing osteomyelitic changes in the left posterior alveolus

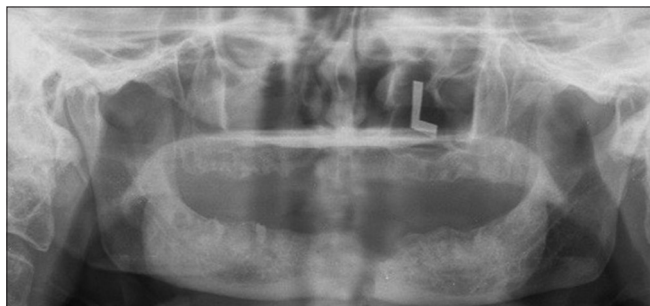


Figure 15: Case 3: Orthopantomogram showing osteomyelitic changes in the lower anterior alveolus



Figure 17: Case 4: Intraoral bone exposure in the posterior maxilla



Figure 14: Case 3: Pus discharge with associated symptoms of pain



Figure 16: Case 4: Patient with sinus in the right cheek region

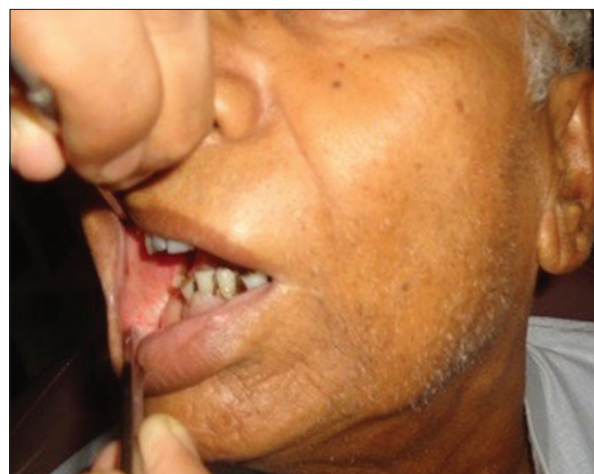


Figure 18: Case 5: Patient presenting with severe trismus

Currently, the management of ORN remains largely conservative in nature. These include antibiotic therapy,^[7] HBO therapy,^[8] and pentoxifylline and tocopherol combination drug therapy.^[14] Ultrasound has been shown to increase angiogenesis and stimulate collagen and bone production. Reports of ultrasound being used for the management of ORN can also be found in literature.^[7] Surgical procedures include local debridement, sequestrectomy, decortication, and resection (segmental/marginal). Most of the patients in our study were largely managed conservatively with symptomatic management.^[7,11] Only three of our patients underwent major resection and the rest underwent minor surgical procedures followed with antibiotics. In case of extensive jaw surgery, good reconstruction options in the form of free fibular flap,^[15] cancellous bone grafting, and distraction osteogenesis^[16] are available.

At present, the focus is on the prevention of ORN. Various strategies have been recommended in literature.^[6] Most of them include pre-RT counseling, oral prophylaxis, removal of foci of infection (extraction of teeth with poor

prognosis), use of sialogogues or salivary substitutes, and regular dental follow-up. Attempt at reducing the incidence and prevention of ORN remains a priority. In our department, patients planned for RT toward the management of head-and-neck malignancies undergo pre-RT counseling. Patients are explained to regarding the



Figure 19: Case 5: Orthopantomogram showing fracture mandible



Figure 21: Case 6: Intraoral extensive exposed sequestered bone in the mandible



Figure 20: Case 6: Patient presenting with extraoral draining sinus



Figure 22: Case 6: Orthopantomogram showing extensive osteoradionecrosis of mandible

importance of good oral hygiene maintenance, the need for the removal of teeth with poor prognosis, the complications of RT, and post-RT oral care. RT is initiated only after dental clearance. Similar protocols are also being followed at other centers.^[17,18] Precaution, prevention protocols, and refinement in RT techniques are key in decreasing levels of the incidence of ORN.

Conclusion

Due to its rare presentation, ORN still remains a challenge for the clinician in its management. Our study revealed that radical RT and concurrent chemo-RT for the oropharyngeal and base of the tongue malignancies have a higher incidence of developing ORN. Patients subjected to the dose of RT above 60 Gy for head-and-neck malignancies have an increased risk of future ORN; henceforth, newer modality treatment like IMRT regimen is recommended for such sites. Most of the patients in the study were satisfactorily managed of the symptoms with conservative modality treatment; hence, it is recommended to consider for surgical methods only in severe end-stage form of ORN.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and

other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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