



Risk assessment for osteoradionecrosis of the jaws in patients with head and neck cancer

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Abstract

Objectives. To identify the potential risk factors for the occurrence of osteoradionecrosis (ORN) of the jaws among patients who have been treated with radiotherapy for head and neck malignancy.

Methods. The study comprised of 231 patients treated with radiotherapy for head and neck malignancy at a tertiary referral center. The following details were recorded for each patient: age, gender, histopathological diagnosis, clinical staging, tumor site, treatment modality, radiation dose, radiation field, number of fractions, type of accelerator used, radiation area and duration of follow-up. Patient's tobacco, alcohol habit history, and history of extraction of teeth before/during/after radiotherapy were also noted.

Results. Thirteen patients had osteoradionecrosis (frequency 5.62%). Among the radiotherapy variables assessed, increased radiation area was found to be significantly associated with the occurrence of osteoradionecrosis. Among the 13 ORN cases, 10 (76.9%) had a history of tobacco consumption, 8 (61.5%) had a time interval between radiotherapy and occurrence of ORN of less than 1-year duration.

Conclusions. We found a low cumulative incidence of osteoradionecrosis and a tendency to occur within a year of starting radiotherapy. Patients of older age, those with a prior tobacco habit may be considered more liable to develop osteoradionecrosis. A larger radiation field may also put patients at hazard for developing osteoradionecrosis.

Keywords: carcinoma, complications, malignancy, mandible, necrosis, oral cavity

Introduction

The management of head and neck cancer remains a challenge. Despite advances in treatment protocols, about two-thirds of patients require adjuvant therapy in the form of radiotherapy (RT) or chemo-radiotherapy for better regional control [1-3]. Patients treated with radiotherapy are prone to sequelae: radiation, induced mucositis, degeneration of major salivary glands leading to xerostomia and its consequences, a decrease in micro-vascularization during or shortly after treatment, and fibrosis of the muscles of mastication and osteoradionecrosis (ORN) as a long term effect [4-8].

Osteoradionecrosis is a critical

side effect of radiotherapy. The definition of osteoradionecrosis is “the presence of exposed bone in an irradiated field, which fails to heal within three months” [9]. It is a debilitating condition affecting the patient's general health and quality of life. Early presentation, within two years, is associated with treatment-induced trauma (bone resection) whereas late presentation is secondary to traumatic dento-alveolar procedures like extraction and alveoloplasty [10].

The incidence of ORN varies widely in literature, ranging from 1% to 37% [11]. The main predisposing factors are site of the primary tumor, radiation technique used, radiation dose, and dental status [12]. Only a small proportion of

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patients go on to develop ORN following radiotherapy, and this number is thought to be falling. This, in part, is due to a better understanding of the etiology of the condition and multidisciplinary approach. Other factors include developments in radiotherapy and radiotherapy protocols, better patient education, and the institution of preventive measures [13].

Hence, keeping these developments in mind, the objective of our study was to evaluate potential risk factors for the occurrence of ORN.

Materials and methods

A retrospective analysis of medical records of 231 patients was performed. These patients had received treatment for head and neck cancer at a university hospital, either alone or in combination with surgery and chemotherapy. The medical records were assessed for the occurrence of osteoradionecrosis in the oropharyngeal region. Data on the patients' demographics, histopathology and clinical diagnosis and staging of tumor, the tumor site, oncology treatment modality (surgery or chemotherapy or radiation), radiotherapy data - dose(Gy), radiation field (the area towards which the radiotherapy was directed.), radiation area (the physical field size expressed in sq. cm) number of fractions, type of accelerator used, duration of follow – up) and associated systemic conditions were reviewed using a structured proforma.

Patient's tobacco habit history and history of extraction of teeth before/during/after radiotherapy was also recorded. The exclusion criteria were - patients having radiographic evidence of bone destruction by a tumor on presentation, recurrence or metachronous malignant lesion involving bone close to the primary malignancy. Institutional ethics committee clearance was obtained.

The conventional treatment protocol for the management of head and neck carcinomas with radiotherapy in our center is 66 Gy given in 33 fractions over six and half weeks, with lateral, parallel – opposed beam configuration using wedges. Linear accelerator (Electa 1500 precise treatment system® Canada) was used to provide radiation therapy to 204 patients while 59 patients were treated with cobalt 60 machine (Theratron 780 C® Canada).

The five year follow up protocol for patients treated with head and neck malignancy in our hospital is: once a month for the first three months, once in two months for the next eight months, biannually for next two years and then annually once for three years. Dental extractions are also electively done in cases where teeth have periodontal involvement or have gross carious lesions with poor prognosis. All extraction procedures are done at least 3 to 4 weeks before the commencement

of radiotherapy. Bivariate analysis was done using T-test. Statistical analysis was carried out using statistical software for social sciences (SPSS) version 13.

Results

A total of 231 patient records were studied. The prevalence of ORN in our study was 5.62%, i.e. 13 out of 231 patients who were treated with RT, either alone or in combination with surgery and chemotherapy, developed ORN. Squamous cell carcinoma was the most common histopathologic diagnosis, accounting for 95.4% (n= 220) of the patients. Almost 47% were also treated with chemotherapy. The youngest patient in the study was 21 years old, and the oldest 90 years old, with a mean age of 55. 26 years. There were 180 (77.9%) men and 51 (22%) women in the study population. Ten (4.32%) men and three (1.29%) women had developed ORN. Twelve patients (4%) had a recurrence of their primary malignancy.

The most common tumor site was tongue (28.1%) followed by buccal mucosa (17.3%) oropharynx (11.3%), and alveolus (7.4%). About 57% of the patients had clinical stage IV disease, 24.7% were in stage III, and 11.7% in stage II. Mandible was more commonly affected, with the body of the mandible being the most common site. Two patients with ORN had multiple site involvement – anterior mandible and right and left posterior maxilla, bringing the total number of sites to 14. Eight patients (61.5%) with stage IV disease, four patients (30.8%) with stage III and one patient (7.7%) with stage II disease developed ORN. A majority of patients had a radiation dose of more than 66 grays (75.32%) and the number of fractions less than 33 (96.10%). A total of 61.5% (n=8), 15.4% (n=2), 7.7% (n=1) and 15.4% (n=2) patients developed ORN in the first, second, third and fourth year after treatment respectively (Table I).

There was no significant association between ORN occurrence and duration of radiotherapy, radiation dosage with either the type of accelerator used or the number of fractions. A statistically significant association was however observed between ORN occurrence and the size of the area irradiated, where the mean radiation area (208±6.3 sq.cm) was significantly larger among those patients who developed ORN than those who did not (190.76±59.25 sq.cm) (Table II).

Nearly 77% of patients had a history of tobacco consumption. All patients who had ORN had undergone dental extractions. A few patients had extractions only before radiotherapy and a small number both before and after radiotherapy (Table III).

Table I. Distribution of patients with ORN in relation to site, age, cancer and radiotherapy (RT) variables.

	Particulars	Number of patients	Number of ORN cases
Age	11-20	3	0
	21-30	6	0
	31-40	20	1
	41-50	48	4
	51-60	69	0
	61-70	52	5
	71-80	30	2
	81-90	3	1
Anatomic site of cancer	Tongue	65	1
	Buccal mucosa	40	5
	Oropharynx	26	0
	Pyrimiform fossa	21	0
	Alveolus	17	4
	Tonsil	9	0
	Floor of the mouth	8	2
	Others	45	1
Stage of Cancer	I	6	0
	II	27	1
	III	57	4
	IV	131	8
	Unknown	10	0
RT variable- Radiation dose	≤66 Gy	57	4
	≥66 Gy	174	9
RT variable - Number of fractions	≥33	222	12
	≤33	11	1
RT variable - Duration	≤6 weeks	99	6
	≥6 weeks	132	7

Table II. Comparison of RT variables in relation to radiotherapy and occurrence of ORN.

ORN	Cobalt (radiation dosage in grays)	Linear (radiation dosage in grays)	Weeks	Radiation Area (Sq.cm)
Present	14.5 ± 26.4	53.1 ± 19.9	5.8 ± 1.1	208 ± 6.3
Absent	5.07 ± 18.3	46.0 ± 27.1	5.2 ± 1.6	190.7 ± 59.2
P Value	0.105	0.628	0.234	0.04

p ≤ 0.05 = statistically significant

Table III. Extraction history, Tobacco/Alcohol habit prevalence, treatment modality and time interval between RT and ORN occurrence among ORN patients.

Variables	Details	N	%
History of extraction	Only before RT	6	46.1
	During RT	0	0
	Both before and after RT	5	38.4
	Only After RT	2	15.3
Tobacco/Alcohol habits	No Habits	3	23.0
	Smoking Only	0	0
	Chewing Only	4	30.7
	Alcohol Only	0	0
	Smoking and chewing tobacco	2	15.3
	Smoking and alcohol	2	15.3
	Chewing tobacco and alcohol	2	15.3
Treatment Modality	Surgery + Chemotherapy + Radiotherapy	4	30.7
	Only Radiotherapy	5	53.8
	Chemotherapy +Radiotherapy	4	30.7
Distribution of ORN according to time interval after RT	≤1 year	8	61.5
	> 1 year and < 2 years	2	15.3
	> 2 years and < 3 years	1	7.6
	> 3 years	2	15.3

RT: Radiotherapy

Discussion

We found that the incidence of ORN was 5.62%. There is a wide variation in the incidence reported in the literature (1.0% to 37%). This may be attributed to differences in the study populations, length of follow up, and in the selection of the population [14]. In the present study, ORN was observed more frequently in older individuals. This observation is in agreement with the findings by Marx et al [9]. We found a majority of patients with ORN had a primary tumor site in the buccal mucosa and alveolus. This finding is similar to other studies [15-17] that state that oral cavity cancers, specifically cancers involving buccal mucosa, have the highest potential to develop ORN.

In eleven of our patients with ORN, extractions were done at least one month before radiotherapy, thus providing adequate time for healing of extraction sites. Six of them had extractions done post-radiotherapy (time period 8 to 24 months). Also, five of these patients underwent jaw resection surgeries (hemi-mandibulectomy/maxillectomy) along with RT. There was an overlapping of patient groups (extraction both before and after radiotherapy), resulting in dilution of any possible association with ORN. The duration between radiotherapy and occurrence of ORN was less than one year in the majority of our patient cohort with ORN and agrees with previous reports [15,18,19]. We also found that patients who were treated with a larger radiation field were liable to develop ORN.

Tobacco abuse has been identified to increase the likelihood of ORN by numerous studies [5,14,20]. We found a majority of the ORN patients to have a history of tobacco consumption. The consumption of tobacco is in many forms - of betel quid, gutkha, khaini, zarda, and so forth in this part of the world. Hence, chewing rather than the smoking form of tobacco was a more common habit among the cases of ORN.

The most common site involved by ORN in our study was the body of the mandible. Other investigators reported similar findings. [21-24]. The higher susceptibility of the mandible is due to the nature of its compact bone and reduced blood supply. In the mandible, the premolar, molar, and retromolar regions are the most vulnerable site for the radiation-induced microvascular disease [25]. In our study, the mandibular molar area was affected in 12 of the 13 patients with ORN. This finding is consistent with the report by Beumer et al [17].

Some patients were lost for follow up as they continued the treatment elsewhere. Data were incomplete or unclear in some of the patient records. In such cases, patients/ treating doctors were contacted and missing data obtained.

Conclusion

We found a low prevalence of osteoradionecrosis and a possible link between the use of chewing tobacco and the occurrence of ORN. Osteoradionecrosis can be

a cruel blow to patients and their families who endure the treatment of cancer and its morbid side-effects. Better radiotherapy protocols, multidisciplinary preventive care, and reconstructive surgery can improve the quality of their lives.

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