Case Report

Osteoradionecrosis of the mandible: A report of three cases

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ABSTRACT

Osteoradionecrosis of the mandible is one of the most serious and severe complications of radiation therapy for head and neck malignancies. In this condition, there is a nonhealing wound persistent for 3 months or more characterized by the irradiated bone getting exposed and devitalized with loss of the overlying skin or mucosa. Here, we present a report of three cases which reported to the department of oral medicine and radiology.

Key words: Oral cancer, osteoradionecrosis, radiotherapy, sequestra

INTRODUCTION

One of the most serious and severe complications of management of head and neck cancers with radiotherapy is Osteoradionecrosis (ORN). ORN is defined as an area of exposed irradiated bone tissue that fails to heal over a period of 3 months without a residual or recurrent tumor.[1] The total incidence of ORN after tooth extraction in irradiated patients as found in a study was 7%.[2] Tooth extraction is the most common cause of trauma induced ORN in the jaws (60-89%).[3] When ORN develops, it starts with the loss of oral mucosa and exposure of the underlying bone. As it progresses, patients often develop the trismus, neuropathic pain, and chronic drainage. In addition, these patients usually experience the other complications of radiation therapy as well (i.e. xerostomia, chronic trismus, dysgeusia, dysphagia, decreased tongue mobility). This spectrum of conditions, often leave patients with physical and emotional stress.

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CASE REPORT

Case 1

A 65-year-old male patient reported to the outpatient department with a chief complaint of a growth present in his left cheek region for the past 3 months. On clinical intra-oral examination, upon inspection, a growth with irregular ulcerated surface measuring approximately 3.5 cm at the maximum dimension was noted in the left lower buccal vestibule. The mucosa overlying the growth was reddish pink in color with a greyish white slough-like appearance in the center. On palpation, the growth was rubbery firm in consistency with surrounding induration. A provisional diagnosis of a malignant growth w.r.t. the left lower buccal vestibule was given. The patient underwent all routine blood investigations and was taken up for an incisional biopsy which proved the growth to be a well-differentiated squamous cell carcinoma of the left lower vestibule. The patient was then referred to the Oncology Department wherein radiation therapy was planned as an initial treatment modality. He was again referred back to us for pre radiation therapy dental opinion when we advised extraction of all upper and lower left side teeth. After the extraction and oral prophylaxis, patient was referred to the Department of Radiotherapy again. The patient returned to us 5 months later with a complaint of pain and pus discharge from the left lower side of the face. On clinical examination, exposed bone of the left body of mandible was seen with clear pus-like exudate. The region was tender on palpation. Intra-oral examination was not

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completely possible due to reduced mouth opening. A left lateral oblique radiograph of the body of mandible was taken which revealed a pathological fracture of the left body of mandible [Figure 1]. A sterile squab culture of the discharge revealed no growth. A diagnosis of ORN of the left body of mandible was made. The patient was then kept on tablet clindamycin, 300 mg, qid, tablet ibuprofen, 400 mg and paracetamol, 325 mg combination and tablet ranitidine, 150 mg for 7 days and referred to the Department of Oral and Maxillofacial Surgery for further management.

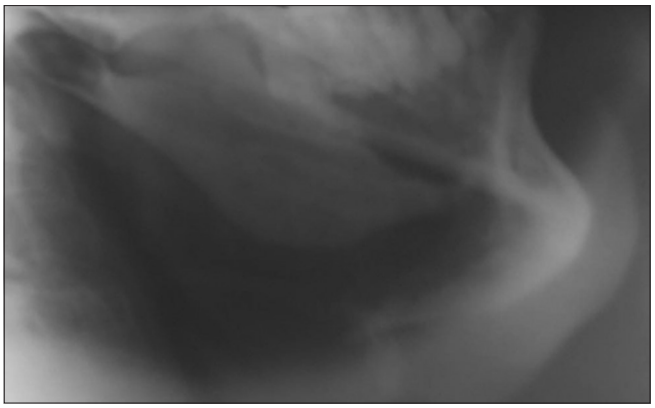

Figure 1: Lateral oblique radiograph of left body of mandible

Case 2

A 60-year-old female patient reported to our department with a complaint of severe pain in the lower right lip region for the past few days. On further enquiry, patient gave a history of having reported to a primary health center with a complaint of a nonhealing ulcer 8 months back. A biopsy was performed, and the lesion was histopathologically diagnosed as well-differentiated squamous cell carcinoma of the lower lip. The patient was referred to the regional cancer institute wherein extraction of lower anterior teeth was done. Fifteen days post extraction patient went in for radiotherapy of the lower lip. When the patient reported to us, clinically, a fistula on the right side just below the lower lip was noted. The lower lip and its labial mucosa were severely deformed. The alveolar mucosa overlying the anterior mandible was shrivelled and also missing from some areas exposing the bone. The orthopantomogram (OPG) revealed moth-eaten appearance of bone in the mandible from tooth no 32 to 45 [Figure 2]. The mandibular occlusal radiograph revealed a diffuse radiolucency in the right mandibular parasymphysis region with intact cortical plates. Soft tissue radiolucency was noted suggestive of the oro- cutaneous fistula [Figure 3]. A diagnosis of ORN was made, and patient was kept on tablet clindamycin, 300 mg, qid and tablet ibuprofen, 400 mg and paracetamol, 325 mg combination and tablet ranitidine, 150 mg for 7 days. Patient was also prescribed an herbal mouthwash (Himalaya HiOra) and antioxidant tablets as supportive care and further referred to the Department of Oral and Maxillofacial Surgery for surgical management.

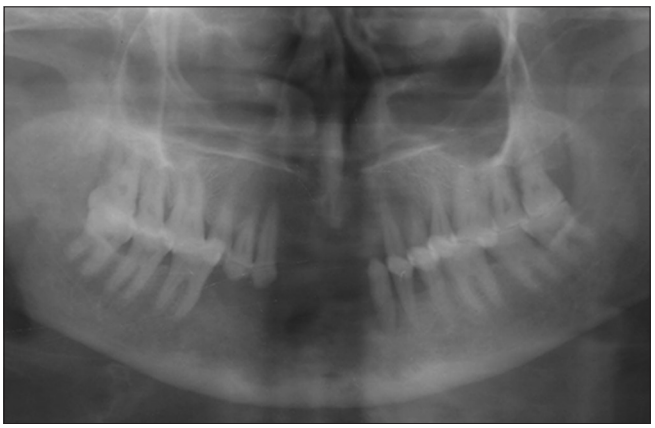

Figure 2: Case 2 - Orthopantomogram

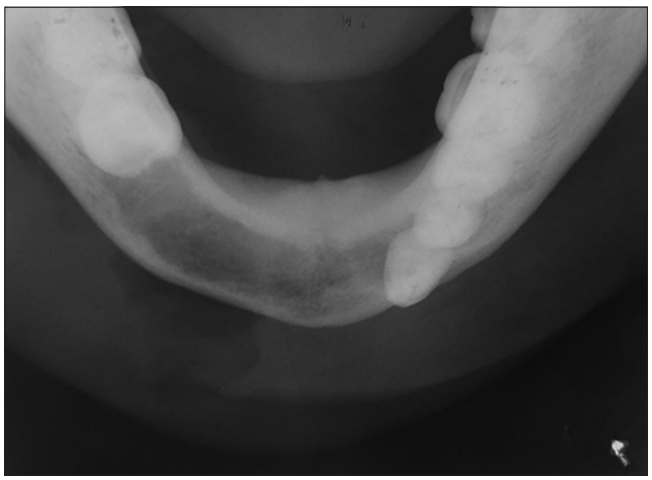

Figure 3: Case 2 - Mandibular occlusal radiograph showing oro- cutaneous fistula

Case 3

A 69-year-old male patient reported to our department with a chief complaint of pain in the right lower back tooth region for the past few days. Past medical history revealed patient had undergone radiotherapy for carcinoma of tonsils in the year 2006. Intra-oral examination revealed exposed bone in the right lower posterior tooth region in relation to 48 of size 2 cm × 1 cm. The exposed bone was mobile, and a necrotic yellowish covering was present over the surface. OPG revealed altered trabecular pattern in the right side of the maxilla and mandible. An irregular radiolucency with severely altered bony pattern was present in the right posterior body of the mandible. Computed tomography (CT) scan revealed intramedullary lucency in distal body and angle of mandible with disorganized/destroyed medullary trabeculae associated with air pockets, sclerotic dead medullary sequestra, and cortical break/fracture [Figure 4]. The patient was referred to the Department of Oral and Maxillofacial Surgery wherein sequestrectomy with curettage (under general anesthesia)

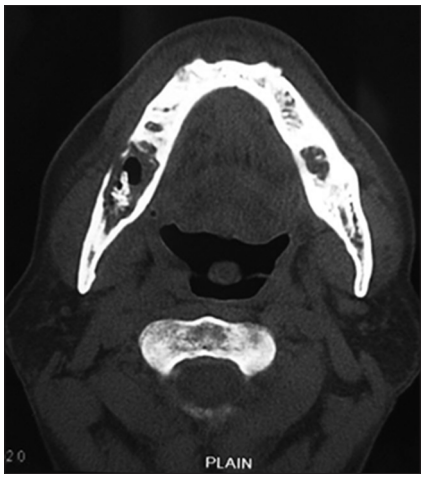

Figure 4: Case 3 - CT image, axial section

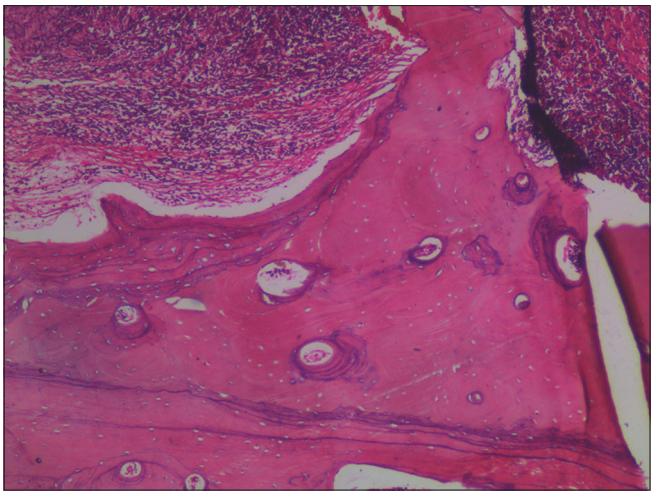

Figure 5: Case 3 - Photomicrograph, H and E, ×4

was done, followed by placement of surgical packs on a weekly basis. The histopathological picture revealed cortical bone with empty lacunae, with many reversal lines and fibrocellular connective tissue showing inflammatory cell infiltrate [Figure 5]. The site healed considerably, and the patient has been on regular follow-up ever since.

DISCUSSION

The disease cancer not only causes severe physical and emotional burden to the patient and his family, but its treatment as well can lead to a lot of sufferings. The management of cancer can be done either with chemotherapy, radiotherapy, surgery, or various combinations of these. Head and neck cancers are usually managed with a combination of surgery and radiotherapy.

Treatment with radiation therapy may either be curative or palliative. Until the advent of newer technologies like intensity-modulated radiation therapy and helical tomotherapy, radiation doses in the range of 60-65 Gy were given which also led to increased exposure to the adjacent normal tissues. But with these new technologies up to 72 Gy can be given. This sort of radiation exposure along with the various risk factors can lead to the development of ORN. The various risk factors which could lead to this dreaded condition are - primary site of the tumor, extent of mandible included in primary radiation field, state of dentition, poor oral hygiene, radiation dose >60 Gy, use of brachytherapy, nutritional status, concomitant chemo-radiation, ill-fitting tissue borne prosthesis resulting in chronic trauma, acute trauma from surgical procedures to the jaw, and advanced stage tumors.

The pathophysiological basis for the development of ORN initially as stated by Marx was considered to be a theory of hypoxia, hypocellularity and hypovascularity (HHH). A new hypothesis proposes that ORN occurs by a radiation-induced fibro-atrophic mechanism, including free radical formation, endothelial dysfunction, inflammation, microvascular thrombosis, fibrosis, and remodeling, and finally bone and tissue necrosis.[3] The key event in the progression of ORN is, therefore, the activation and dysregulation of fibroblastic activity that lead to atrophic tissue within the previously irradiated area.[4]

Diagnosis of ORN is mostly done based on medical history and clinical examination with a little help from radiographs. A histopathological examination is not usually necessary as a biopsy leads to additional trauma of the already irradiated and diseased tissue. Clinically, exposure of the bone with loss of the overlying soft tissues is seen. There may be a continuous exudate from the lesion which may be secondarily infected. In the three cases reported, sterile swab cultures revealed no growth of any aerobic organisms suggesting microbial invasion might not play a role in the etiopathogenesis of the condition. Radiographs/CT scans reveal a radiopaque/hyperdense area surrounded by a radiolucent/hypodense or normal density region which is suggestive of dead necrotic bone, the sequestra.

In the first two cases reported, timing of extraction of teeth in the irradiated site could have led to the development of ORN. Adequate time has to be given for the extraction site to heal before beginning the radiotherapy, but not at the expense of rapid growth of the tumor.

Extraction of teeth in the area to be irradiated or already irradiated is considered to be the main risk factor in the development of ORN. Although the risk is increased when tooth extractions are performed after irradiation, few studies show an increased risk of ORN development when extractions are performed before radiotherapy.[5]

Marx's classification system, based on response to therapy, has three stages through which patients are advanced until

the ORN is resolved. Stage I ORN treatment involves primary hyperbaric oxygen (HBO) therapy, regardless of prior treatment. Treatment in Stage II involves a combination of trans-oral debridement or sequestrectomy, with a primary mucosal repair, followed by additional HBO therapy. Stage III involves a definitive surgical extirpation of all the diseased bone, primary wound closure, and external fixation followed by additional HBO therapy (20 dives). Ten weeks after resection of diseased bone, a staged reconstruction is performed with autogenous cancellous bone packed into a freeze-dried allogenic bone carrier. Additional postoperative HBO (10 dives) is then administered for completion of this protocol. Maxillo-mandibular fixation is maintained for 8 weeks. Patients who present with a pathologic fracture, oro-cutaneous fistula, or radiographic evidence of bony resorption of the lower border of the mandible are immediately classified as Stage III disease, bypassing the protocol for Stages I and II disease.[6] According to this system, cases 1 and 2 would fall under Stage III.

Hyperbaric oxygen has been utilized as an adjunctive treatment modality in the management of ORN since the 1960s. The basis for applying HBO to ORN is an extension of Marx's theory that ORN is the result of tissue HHH.[7] The purpose of HBO is to increase the blood-tissue oxygen gradient, which enhances the diffusion of oxygen into hypoxic tissues. The increased oxygen supply stimulates fibroblast proliferation, angiogenesis, and collagen formation.[1,8] In addition, the increased oxygen tension is bactericidal and bacteriostatic.

Initially, treatment of ORN with HBO yielded favorable results. In 1976 Hart and Mainous reported successful results in 69 patients treated with HBO as an adjunctive measure for ORN.[9] In 1981 Mansfield *et al*. reported that 11 of 12 patients with refractory ORN responded favorably to HBO.[10] In 1983, Marx reported that 58 patients with refractory ORN were successfully treated with his published protocol.[7] In 1985, Kraut reported three cases in which HBO was used successfully as a prophylactic measure before and after dental extraction to prevent the development of ORN.[11]

Recently a lot of authors and clinicians have started questioning the use of HBO in the treatment of ORN. In 1993 Mounsey *et al*. in a study of 41 patients with ORN treated with HBO found that HBO was beneficial in the treatment of mild ORN but a combination of surgery and HBO is necessary for more advanced ORN.[12] In 2000, Maier *et al*. in their experience of treating 41 patients with advanced ORN concluded that the patients with advanced ORN who were treated with debridement and antibiotics alone were just as likely to recover as those who were treated with debridement, antibiotics, and postoperative HBO.[13] In 2003, Gal *et al*. reported their experience with 30 patients with Marx Stage III ORN, who were treated with radical resection and an osteocutaneous free flap reconstruction without the use of perioperative HBO. They reported a 97% overall success rate for the treatment of Stage III disease without the use of HBO therapy. They stated that in advanced disease, they felt that HBO will only delay more definitive therapy.[14]

From these various studies, it is evident that advanced ORN requires aggressive surgical therapy, and that HBO alone has minimal if any benefit in the treatment of advanced ORN. The use of HBO in early and intermediate ORN remains important because the benefit seems clear based on numerous retrospective studies. The side effects of HBO are transient myopia, middle ear barotrauma and seizures.[15]

Nowadays, treatment of ORN is based on the clinical, radiological and CT findings, which help to determine the stage of the disease as early, intermediate, or advanced stage disease.

Stage I disease represents small, superficial, localized bone resorption with cutaneous or mucosal dehiscence. Early stage ORN is approached conservatively with local wound care (oral rinses), HBO therapy with 20 dives and antibiotic therapy to quell the super-infection that is often present. If patients show definitive improvement, an additional 10 dives of HBO is given to allow for additional healing of the surrounding soft tissue. Patients that do not show signs of healing undergo a trans-oral debridement and additional HBO therapy. This approach of 20/10 differs from Marx's protocol where a 30/10 protocol is recommended.

Stage II disease represents larger and deeper areas of bone resorption. Cortical and medullary bone are involved, and the mucosal, or cutaneous areas of breakdown are moderate in size. This stage of ORN is approached with antibiotics, trans-oral debridement or sequestrectomy, and HBO therapy (20 dives preoperatively and 10 postoperative dives). All necrotic bone is debrided to a base of bleeding bone, and a primary mucosal closure is performed. If the mucosa is unable to be closed primarily, a soft tissue flap can be utilized for coverage. All patients receive an additional 10 dives of HBO postoperatively. Patients that develop wound problems or repeat bone exposure are then treated with aggressive surgical extirpation of all diseased hard and soft tissue and an immediate reconstruction with a well-vascularized free tissue transfer. Again, this approach differs from Marx's protocol in that only 20 preoperative dives are performed prior to surgical debridement. Marx's Stage II protocol utilizes up to 60 total dives pre- and post-operatively.

Stage III ORN is defined by full thickness devitalization of bone, resorption of the inferior border of the mandible, fistula or a pathological fracture. These patients are treated with aggressive surgical extirpation of all diseased hard and soft tissue, and then immediate reconstruction is performed using free tissue transfer.

Management of ORN from a dental perspective aims at preventing the development of ORN with thorough pre radiation therapy assessment of the patient, wherein all teeth with deep carious lesions or a hopeless periodontal prognosis are extracted. A minimum period of 3 weeks should be given before the commencement of radiotherapy after extraction of teeth. Later, oral prophylaxis should be performed followed by fabrication of special trays for delivery of topical fluoride gels. This topical fluoride application will help in the prevention of the development of new carious lesions. The patient should then be followed-up regularly during the period of radiation therapy and also at monthly intervals after that. Maintenance of good oral hygiene should be emphasized to all patients. Any surgical intervention after radiotherapy should be avoided, but if necessary, extractions should be done at least 4 months after completion of radiotherapy.

CONCLUSION

Osteoradionecrosis can be referred to as a condition which is easy to diagnose but difficult to manage/cure. With the ever increasing burden of cancer on society, complications associated with its treatment only add to the distress of the patients. As part of the healthcare team, it is essential that dental practitioners establish a previous history of radiotherapy to the jaws and chalk out a proper dental treatment plan in conjunction with the oncology team to prevent any such complications.

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