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Bilateral Osteoradionecrosis of Mandible: A Case Report

Dr. Tejashree Mantri[1], Dr. Anita Munde[2], Dr. Safia Shoeb[3], Dr. Sudharani Biradar[4]

P.G. Student, Department of oral Medicine and Radiology, Rural Dental College, PIMS, Loni, Maharashtra, India[1]

Professor, Department of oral Medicine and Radiology, Rural Dental College, PIMS, Loni, Maharashtra, India[2]

H.O.D & Professor, Department of oral Medicine and Radiology, Rural Dental College, PIMS, Loni, Maharashtra, India[3]

Senior Lecturer, Department of oral Medicine and Radiology, Rural Dental College, PIMS, Loni, Maharashtra, India4

ABSTRACT: Osteoradionecrosis (ORN) defines exposed irradiated bone, which fails to heal over a period of 3–6 months without evidence of residual or recurrent tumor. It is a long term and serious complication of therapeutic radiotherapy for head and neck cancer. The pathogenesis of ORN has been proposed relating it to a fibroatrophic mechanism including free radical formation, endothelial dysfunction, inflammation, microvascular thrombosis leading to bone and tissue necrosis. Risk factors mainly include radiation related risk factors, surgery, tobacco and alcohol abuse. Removing of diseased teeth after radiotherapy is generally considered the main risk factor in ORN. Prevention of ORN is based on the preventive extractions of decayed or periodontally compromised teeth before radiotherapy. Based on the clinical staging various therapeutic protocols have been suggested. We here report a case of Bilateral mandibular ORN with discussion of clinical features, pathogenesis, preventive measures, and management of ORN.

KEYWORDS: Osteoradionecrosis, pathogenesis, prevention, risk factors.

I. INTRODUCTION

Osteoradionecrosis (ORN) describes the process where irradiated bone undergoes necrosis and becomes exposed through soft tissue. The first report of ORN of the jaws after radiation therapy was published in 1992 by Regaurd. Ewing in 1926 first recognized and reported the bone changes associated with radiotherapy (RT) and described this disease state as radiation osteitis. [1] Since several theories have been propounded to explain its cause but the most widely accepted theory is of hypoxia, hypovascularity, and hypocellularity. [2] ORN ranges from small asymptomatic bone exposures that remain stable for months and heals with conservative management, to severe necrosis with pathologic fracture necessitating surgical intervention and reconstruction.

The mandible is affected more commonly than any other bones of the head and neck region. The incidence of ORN of mandible is reported to be between 2% and 22%. ORN is rare after radiation of less than 60Gy. With the older radiation techniques, the rate of ORN was reported to be between 5% and 15%, [1] while with newer techniques such as IMRT, brachytherapy, 3D conformal RT, stereotactic RT, radiofrequency ablation, radioimmunotherapy have decreased rate to 6% or less.

II. CASE REPORT

A 65 year old male patient reported to the department of Oral Medicine and Radiology with a chief complaint of numbness in lower lip and chin since 2 months. Patient gave a history of malignancy of larynx, for which he received radiotherapy (35 cycles) and chemotherapy, 6 years back. Patient started experiencing difficulty in mastication, deglutition, dryness of mouth and reduced mouth opening since 2 months. Patient was habitual for bidi smoking since 35 yrs. Medical and dental histories were not significant.

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On extraoral examination face was bilaterally symmetrical (fig.1) and there was loss of sensation with lower lip and chin region on pricking with the probe. Bilateral solitary submandibular lymph nodes were palpable which were, firm, mobile, approximately 1x1cm in size and tender.

Intra oral examination revealed upper and lower partial edentulous arches. There was exposure of alveolar bone in the right and left mandibular posterior region extending from first molar to third molar region along with pus discharge. The mucosa in the same region was inflamed and tender. There was presence of deep cervical caries in upper right anteriors and premolars. Root pieces were seen with upper left premolars, molars and lower anteriors. (fig: 2,3) Radiographic examination (OPG and PA mandible) revealed ill defined radiolucency with right and left posterior region of mandible extending from first molar to third molar. There was presence of radiopaque dense bone masses within the radiolucency with mandibular right and left posterior region suggestive of sequestrum formation. Thinning of left inferior border of mandible was seen. [fig: 4, 5]

Depending upon the clinical and radiological features provisional diagnosis of bilateral ORN (stage II B according to Schwartz and Kagan classification) of mandible was made. Patient was treated by conservative therapy which included antibiotics (Cap. Amoxycillin 500mg t.i.d. for 15 days and Tab. Metronidazole 400mg t.i.d. for 5 days) along with curettage and sequestrectomy of bone. Excised bone specimen was sent for histopathological examination which showed features of parakeratinised stratified squamous epithelium with dysplastic features, connective tissue was fibrocellular with blood vessels, extravasated blood elements, overall features were suggestive of "chronic inflammatory lesion".[Fig. 6,7]

Final diagnosis was made as Bilateral ORN of mandible (Stage IIB according to Schwartz and Kagan classification). Patient was on regular follow up for 6 months with no signs of recurrence. (fig.8)

Discussion

Osteoradionecrosis is the most serious clinical complication that occurs in a bone after irradiation. The bone becomes hypovascular, hypocellular, hypomineralised. [3]

When ORN develops, it starts as a small area of mucosal breakdown with exposure of the underlying bone, and progressively patient starts developing trismus, neuropathic pain, and chronic drainage. Additionally, patients also experience collateral damage from radiation therapy (i.e. xerostomia, chronic trismus, dysgeusia, dysphagia, and decreased tongue mobility).These problems, in combination with symptoms from ORN, often leave patients physically and emotionally disabled. [4]

The mandible is affected more often than any other bones of head and neck region. The mandible receives blood supply comparatively less than other facial bones. Posterior mandible has denser bone with higher mineral content and thus higher absorbed radiation dose. Also mandible is more likely in the field of radiation for oropharyngeal cancers. [1, 5]

ORN pathophysiology remains controversial with various theories put forward.
There is classic triad described by Meyer in the pathophysiology of ORN includes Radiation, trauma and infections. The above theory was improved by Marx showing it as the hypoxic-hypocellular-hypovascular theory. It occurs in 4 step sequence in which after radiation exposure there is formation of hypoxic-hypocellular-hypovascular tissue leads to excess collagen lysis and cellular death which eventually leads to chronic nonhealing wound. [2]

The most recent theory is radiation fibroatropic theory suggesting activation and dysregulation of fibroblastic activity of the previously radiated area which leads to progression of ORN. The hypothesis focuses on 3 phases which are Prefibrotic phase, Constitutive organized phase, Late Fibroatrophic phase.

The fibroatrophic theory described by Delanian and Lefaix, proposes that radiation induce unavoidable sequelae to high dose RT and proposes that fibroblast proliferation undergo total cellular depletion due to radiation exposure and shows reduced ability to produce collagen into the surrounding tissue. [4]

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There are several classification systems which determine the severity of ORN to guide treatment. Marx's classification system (1983) was widely used but it was based on clinical response to hyperbaric oxygen therapy (HBOT). More recently, Kagan and Schwartz (2002) described a three stage clinical staging system. This staging system differs significantly from the system created by Marx because the disease is classified based on clinical and radiologic findings and treatment is determined based on the stage. **(Table 1)** [4]. Radiation related risk factors of ORN include: total dose, photon energy, field size, and fractionation. [5].Intensity Modulated Radiotherapy (IMRT), brachytherapy, helical tomotherapy could be the next advance in reducing rate of ORN. [6, 7]

Diseased tooth extractions (odontogenic and periodontal disease), denture trauma after irradiation, [8] abuse of alcohol and tobacco are also considered as risk factors for ORN. [6, 9] Other factors associated with ORN are location of primary tumor in tongue, floor of mouth, alveolar ridge, reteromolar trigone, tonsil, stage III/IV cancer, doses above 60Gy of radiation, poor nutritional status which could affect wound healing.

Table 1: Clinical staging of ORN

Stage	Description	Treatment
I	Superficial involvement, only cortical bone exposed & minimal soft tissue ulceration	Majority improve with conservative management
II A. Minimal soft tissue ulceration B. Soft tissue necrosis	Localised involvement of mandible, exposed cortical and medullary bone are necrotic & possible orocutaneus fistula	Majority improve with conservative management, surgical procedures, or hyperbaric oxygen therapy
III A. Minimal soft tissue ulceration B. Soft tissue necrosis	Diffuse involvement of the mandible, including the lower border. Pathologic fracture may occur & possible orocutaneus fistula	Require surgical intervention, resection, and reconstruction

Prevention of ORN is an extremely important part of the comprehensive management of patients who undergo external beam radiation therapy to the head and neck. All diseased teeth should be extracted 21 days before initiation of radiation therapy. All patients should be instructed on meticulous oral hygiene and fluoride should be applied to the dentition daily via custom moulded trays. Patients should undergo weekly check up during RT and monthly follow ups for the first six months. Following early post treatment patient should visit their dentists for every four months. Modifications in RT such as IMRT, brachytherapy, 3D conformal RT, stereotactic RT, radiofrequency ablation, radioimmunotherapy can also be used for reducing rate of ORN. [10, 11]

Management of ORN depends upon stage of disease. Most oro-pharyngeal cancer patients have undergone major surgery before ORN occurs, so there should be avoidance of any additional jaw surgery. Up to 60% of the early and localized cases of ORN resolve with medication (topical and systemic) and wound care (saline irrigation, sequestrectomy and curretage) only. [4, 6, 10]

ORN is managed with topical antibiotic (tetracycline) or antiseptic (chorhexidine) rinses. Systemically penicillin is the antibiotic of choice which can be given orally at a dose of 500mg 4 times daily for 2-4 weeks.

Mainous et al. were first to suggest the use of hyperbaric oxygen (HBO) therapy for ORN management which is usually carried out for a period of 20-30 dives at 100% oxygen and 2-2.5 atmospheres of pressure. It has been advocated for pre-operative and post-operative treatment in patients having teeth extracted or other operations. If surgery is required postsurgical HBO therapy of 10 dives is recommended. [2]

The results of HBO in treating ORN are not much convincing when it is used alone. [4, 7].The development of myocutaneous flaps and the use of microvascular free bone flaps allows modifications in the extent of the surgical ablation of extensive ORN. The replacement of the dead bone with a vascularised bone-containing flap will allow for restoration of the mandibular continuity and provide non irradiated soft-tissue coverage with blood supply. [6, 8]

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There are other novel innovations in management of ORN which are 1200 mg/d pentoxifylline (PTX) for 6 months, combination of PTX and tocopherol (vitamin E). PTX is an antioxidant methylxanthine derivative with an anti-tumor necrosis factor effect. Alpha-tocopherol (vitamin E) scavenges free radicals generated during oxidative stress and protects cell membranes against lipid peroxidation. Vitamin E also has well-established antioxidant properties. These two drugs act synergistically as potent antifibrotic agents. Therapeutic ultrasound, bFGF, BMP-1 & BMP-2, distraction osteogenesis are also used in the management of ORN. [6]

Fig.1:Extraoral photograph

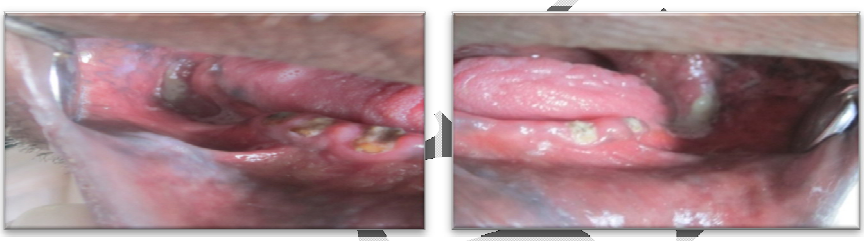

Fig. 2: Clinical photograph showing bone exposure and pus discharge with right mandibular posterior region
Fig.3: Clinical photograph showing bone exposure and pus discharge with left mandibular posterior region

Fig 4: OPG showing mixed radiopaque and radiolucent lesion bilaterally
Fig 5: PA mandible showing bilateral destruction of mandible

Fig.6- Intraoperative photograph
Fig.7- Excised specimen of bone

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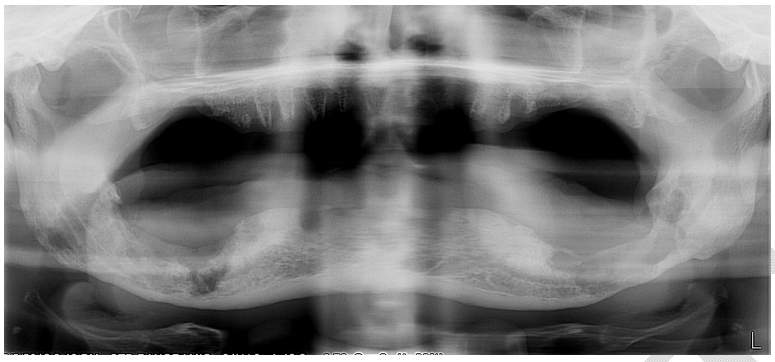

Fig.8: Postoperative radiograph

III. CONCLUSION

Recent advances in the understanding of ORN pathogenesis have opened new perspectives in the medical management of mild to moderate ORN. In severe, extensive and long established ORN, particularly with a pathological fracture, free tissue surgical transfer is the treatment of choice.

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BIOGRAPHY

I am Dr.Tejashree Mantri, 3rd year PG student from Dept of Oral Medicine and Radiology, RDC, PIMS, Loni. I am pursuing my MDS in the same college and is my last year. I have keen interest in writing articles related to my field and exploring new dimensions in the cases.