Case study

A RARE CASE REPORT OF OSTEORADIONECROSIS MANDIBLE AFTER IRRADIATION FOR BREAST CANCER

ABSTRACT

Management of irradiated patients with cancer in the head and neck region is a challenging scenario. Radiotherapy promotes cellular and vascular insufficiency that results in a low response rate in the healing. Consequently, surgical procedures in irradiated tissues present high rates of complication. Osteoradionecrosis (ORN) is the most severe sequelae caused by radiotherapy. ORN can occur due to multiple reasons, of which periodontal disease, traumatic injury induced by ill-fitting dentures and trauma after surgery or tooth extraction are the most common. The management of this side effect is difficult and can result in bone or soft tissue loss, affecting the quality of life since majority of patients with ORN have various comorbidities associated. In this article we present a case report of osteoradionecrosis secondary to irradiation for breast cancer which is not frequently reported in literature.

Key words: Osteoradionecrosis, radiation, breast, mandible

INTRODUCTION

Radiotherapy is one of the important treatment modality in the management of malignant disease of the head and neck. Radiotherapy destroys all the cells with a high turnover rate. [1]. Even though bone is radio-resistant compared with other tissues, radiotherapy will seriously compromise in its blood supply and reparative ability. Osteoradionecrosis (ORN) is one of the most severe complications of radiation therapy [2]. Marx (1983) defined ORN as an area greater than 1 cm of exposed bone in a field of irradiation that failed to show any evidence of healing for at least 6 months [3]. Since majority of patients with ORN have various comorbidities associated, it is difficult to treat and often leads to poor outcome and deformity. ORN can occur due to various reasons, of which periodontal disease, traumatic injury induced by ill-fitting dentures and trauma after surgery or tooth extraction are the most common [2]. ORN is seen to be dependent on the technique of the RT used, in particular—the radiation dose to the bone. A total dosage of approximately 6500 to 7000 uGy or greater, particularly to the floor of the mouth and mandible significantly show elevated incidence of ORN of the mandible [3]. Dose rates in excess of 0. 55 uGy/hour have also been seen to elevate the risk of ORN. ORN of mandible secondary to breast irradiation is not frequently reported in literature since site of irradiation in breast cancer is chest wall which is distant from mandible and this makes our case report unique.

CASE REPORT

A 73 year old lady reported to our department with complaints of pain and swelling in the lower right back tooth region since three months duration. She was diabetic, dislipidemic and hypertensive. Patient also gave a history of breast cancer two year back (T2N2M1). For this she underwent left radical mastectomy and adjuvant chest wall RT with 5000 cGy in 25 fractions. This was followed by adjuvant

chemotherapy with 8 cycles of 5-florourasil, epirubicin, and cyclophosphamide after surgery. Dental extraction of 47 was done 3 months after the radiation therapy. Since then she gives a history of continuous pus discharge from the extraction socket (Fig.1). She first consulted a local dental clinic and was given antibiotic course for one week. The symptoms subsided after antibiotic therapy. However the symptoms had aggravated again.

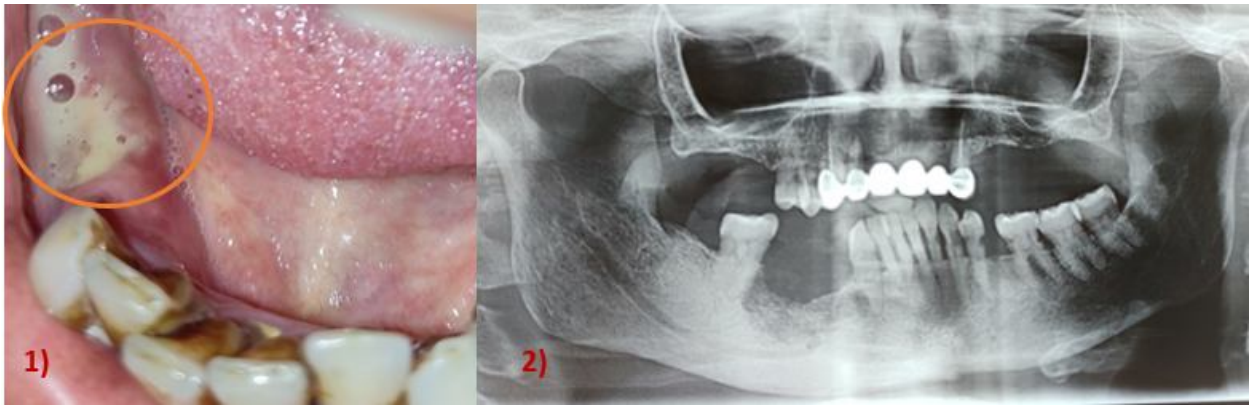

Fig: 1 – Pus discharge from extraction socket, Fig: 2 - OPG One year extraction

On examination, a non-healing extraction site was seen in relation to 47 with pus discharging from the extraction socket with obliteration of buccal vestibule and erythematous swollen area from 45 to 48. Paresthesia in relation to lateral one third of right lower lip was also noted. The site was non tender on palpation.

Investigations

The pus was sent for culture and sensitivity, which revealed presence of aerobic streptococcus viridian's species (alpha haemolytic). Routine blood examinations revealed a slight elevation in creatinine level. CRP was also elevated slightly. An OPG (Fig. 2) was taken which showed moderate bone loss in relation to extraction site. CT mandible revealed ill-defined oblong area of mixed sclerosis and intramedullary lucency involving the body of mandible on right side with cortical defects and sequestrum.

Management:

Initially a conservative management was planned and patient was given ampicillin 500mg, 6 hourly for 7 days, pentoxifyllin 400mg three times daily, and tocopherol 1000 IU daily therapy for 6 months. But even after long term medical management, symptoms didn't subside. Hence surgical management under GA was planned. Prior to surgery, the site was irrigated daily with saline-betadine solution in 1:1 ratio, Tab Pentoxyfilline 400mg TID and Cap Evion 600mg BD was given for one week. Daily irrigation reduced the pus discharge. After substantial decrease in pus discharge, surgery was performed under GA. Following intraoral debridement, sequestrectomy and saucerization, a small pediatric nasogastric feeding tube 6 to 10 inches long in length was placed against the bony bed and secured in the vestibule with 4-0 silk sutures (Fig 3, 4, 5). Local drug delivery with gentamycin was given through the infant nasogastric tube for one week. Along with that Inj Accuzone plus 1.5g IV BD, pentoxyfilline and evion was administred.

The patient was discharged after one week. At that time the surgical site has healed completely and the patient is in periodic follow up since then.

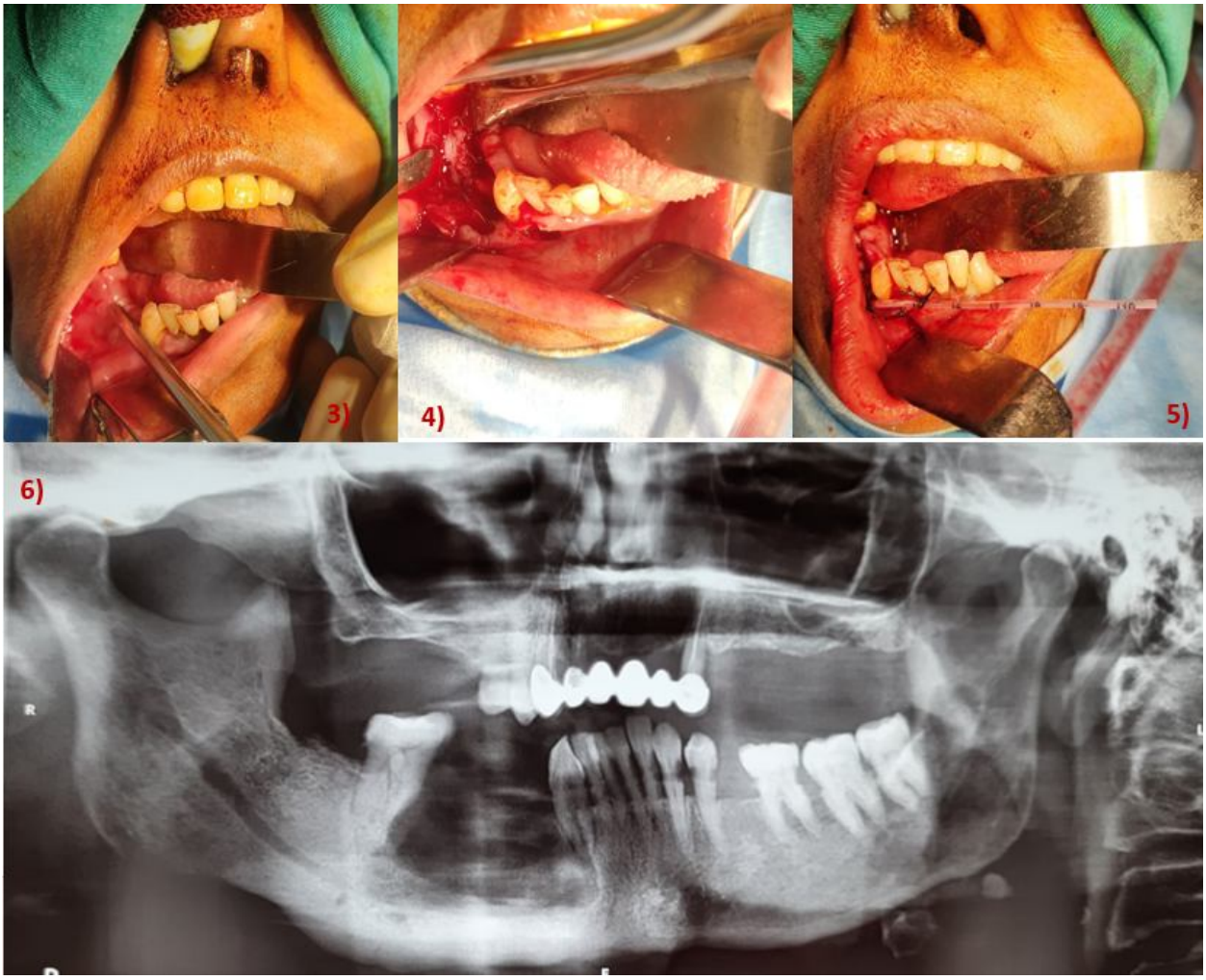

Fig: 3 – Site at the time of surgery, Fig: 4 – After sequestrectomy

Fig: 5 – After suturing, Fig: 6 – Post op OPG

DISCUSSION

Malignant diseases of maxillofacial region are treated by (i) radiation therapy, (ii) surgery, (iii) chemotherapy, and (iv)combination therapy. Radiation often has serious effects on hard and soft tissues. Because of its inorganic composition, bone absorbs more energy than soft tissue and is more susceptible to radiation induced injuries. The effects of radiation on bone depend on the following four factors, viz: 1. Quality of radiation 2. Quantity of radiation 3. The location and extent of lesion 4. Condition of teeth and periodontium.

The late and major complication of therapeutic radiotherapy for head and neck cancer is osteoradionecrosis. Osteoradionecrosis was considered an infection initiated by injury to irradiated

bone before 20th century. Marx [4, 5] has shown that it is a chronic, non-healing wound caused by hypoxia, hypocellularity and hypovascularity of irradiated tissue. Before 1960's only ortho voltage irradiation was the available treatment modality which was highly deleterious to bone and the incidence of ORN was about to be 37% [6]. But shift from orthovoltage to megavoltage, targeted irradiation, collimation, dose fractionation etc. reduced the incidence to 2 to 5 percent [7]. Initially ORN was thought to be a triad of radiation, trauma and infection. Marx et al. [8] have shown that microorganisms are merely contaminants and trauma is only one of several factors involved in the disease.

Irradiation in chest wall for breast cancer usually do not cause ORN mandible. But if a supraclavicular field of irradiation is done in such cases, this may cause ORN of mandible as the irradiated field is in proximity with mandible.

Incidence:

ORN is common in mandible among facial bones which account about 2-3% [9, 10]. The second common bone involved in ORN is temporal bone.

Classification:

The following are the most accepted classification system of ORN.

Table: 1. List of different symptoms and treatment by Epstein et al - 1987 [11]

Stage	Description	Symptoms	Treatment
I Ia Ib	Resolved, healed No pathologic fracture Pathologic fracture	None	Follow-up, prevention of recurrence Reconstructed
II	Chronic, persistent non-progressive	None, or controlled	Local wound care Antiseptics/antibiotics, analgesics, hyperbaric oxygen (if indicated)
III	Active, progressive	Progressive	Local wound care Antiseptics/antibiotics, analgesics, hyperbaric oxygen (if indicated)

Table: 2 List of different symptoms and treatment by Marx - 1983 [3]

Stage	Description	Symtoms	Treatment
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Pathophysiology:

Marx has described the three H principle in the development of ORN.

(i) Hypocellularity,

(ii) Hypovascularity of the irradiated tissues and

(iii) Hypoxia.

But now the fibroatrophic theory (2014)[15] is gaining much importance which states that fibroblast populations undergo total cellular depletion and reduced ability to produce and secrete collagen into the surrounding tissue in response to radiation exposure. The sequence in the development of ORN is given below:

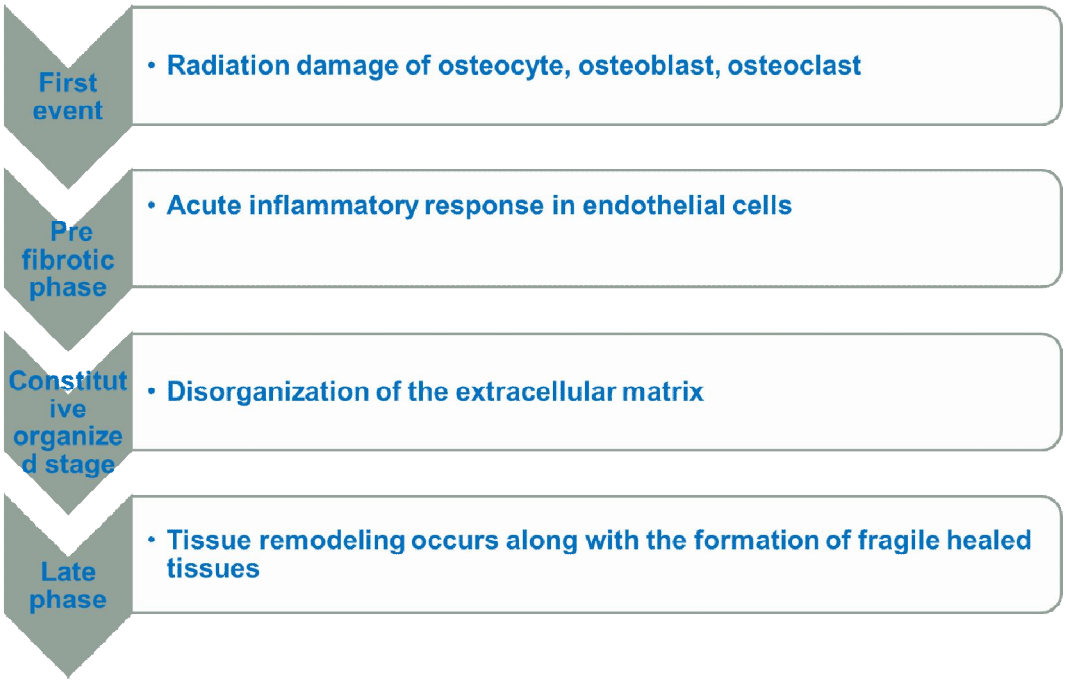

Image 1: Flow chart describing the fibroatrophic theory

Clinical features:

Severe deep boring pain with evidence of exposed bone are the chief presenting features. There may be associated trismus, fetid breath, pyrexia, soft tissue abscesses and persistently draining sinuses. Exposed bone is frequently associated with intraoral/extraoral fistulae. The exposed bone often has rough surface that abrades adjacent soft tissue and causes further discomfort.

Radiographic Features:

Very little radiographic change occurs in the early stages of the disease. The characteristic changes seen in osteomyelitis of non-irradiated bone (sequestra and involucra) occur late or not at all in irradiated bone because of severely compromised blood supply. Initial blood flow assays with nuclear isotope

technetium-99 methylene diphosphate scanning can be of some benefit in assessing regional perfusion of the afflicted areas.

Management:

There is no universally accepted treatment for ORN. The management of ORN remains controversial, both radical and conservative treatments have been reported. Conservative treatment include systemic antibiotics, selective rinsing with topical antiseptics, and selective removal of small sequestra, curettage and local debridement. Radical treatment is indicated, where ORN is refractory to conservative treatment. HBO therapy was once one of the mainstays of treatment. But now it's not included as a definitive treatment modality and is used only as an adjunct [12, 13]. Circumscribed debridement can be performed in small necrotic areas, whereas large necrotic areas should be surgically removed [14]. All these procedures should be done as atraumatically as possible. Also the periosteum covering the intact bone should be preserved. Bone resection is performed, if there is persistent pain, infection or pathological fracture. It is preferably done intraorally, to avoid possibility of orocutaneous fistula in radiation-compromised skin. Studies have shown that combined use of pentoxifylline-tocopherol therapy has been effective in the management of septic ORN of the mandible. Because there is currently no standard medical treatment, this approach constitutes a useful alternative to existing therapies in treating ORN. The combinations of these two drugs act synergistically and are readily available, well tolerated and inexpensive [15]. Recently the use of PENTOCLO therapy is widely accepted which emphasizes on the combination of pentoxifilline- tocopherol-clodronate regimen [16]. However the use of clodronate is debatable as it may precipitate chemonecrosis/BRON J [17, 18, 19, 20].

Prevention:

Pre irradiation dental care of the teeth in direct beam of radiation should be performed. Non-restorable and periodontally compromised teeth should be extracted. Radiation therapy is delayed by 10 to 14 days to allow initial healing. Restoration of teeth, topical fluoride application and periodontal therapy should be completed before irradiation. If extraction is unavoidable after irradiation, the number should be limited to a minimum of one or two per appointment. Also extraction should be done atraumatically and without raising extensive flaps. It is mandatory to do extractions under antibiotic prophylaxis. Prophylactic use of pentoxifylline and tocopherol in such patients shows excellent results [21]. Time interval of extraction after irradiation has an important role in precipitation of ORN. As the time period increases chance of developing ORN also increases [21].

SUMMARY AND CONCLUSION

This case report highlights the need of proper precautions that should be taken before extractions and other surgical procedures in mandible for who had undergone chest wall irradiation. ORN of mandible secondary to chest wall irradiation is not common. However, if there is a history of supraclavicular field of irradiation, the possibility of development of ORN of mandible is very high.

REFERENCES

1. Nabil S, Samman N. Incidence and prevention of osteoradionecrosis after dental extraction in irradiated patients: a systematic review. Int J Oral Maxillofac Surg. 2011 Mar;40(3):229-43.
2. Beumer J, Harrison R, Sanders B, Kurrasch M. Osteoradionecrosis: predisposing factors and outcomes of therapy. Head Neck Surg 1984: 6: 819– 827.

3. Marx RE. Osteoradionecrosis: a new concept of its pathophysiology. J Oral Maxillofac Surg. 1983;41(5):283-8.
4. Marx RE. Chronic osteomyelitis of jaws, Oral Maxillofac Surg Clin North Am. 1991;3:367.
5. Marx RE. A new concept in the treatment of osteoradionecrosis. J Oral Maxillofac Surg. 1983;41(6):351-7.
6. Mark A Engleman, Gayle Woloschak, William Small Jr. Radiation-induced skeletal injury. In: William Small Jr, Gayle W (Eds). Radiation Toxicity: A practical Guide, Volume 128. US: Springer. 2006.pp.155-69.
7. Lauren O'Malley, et al. Improvement of radiological penumbra using intermediate energy photons (IEP) for stereotactic radiosurgery. Phys Med Biol. 2006;51:2537-48.
8. Marx RE, Carlson ER, Smith BR, et al. isolation of actinomyces species and Eiikenella corrodens from patients with chronic diffuse scelerosing osteomyelitis. JOMS. 1994;52:2
9. Clayman L. Clinical controversies in oral and maxillofacial surgery: Part II. Management of dental extractions in irradiated jaws: a protocol without hyperbaric oxygen therapy. J Oral Maxillofac Surg. 1997;55:275-8.
10. Bras J, de Jonge HK, van Merkesteyn JP. Osteoradionecrosis of the mandible: pathogenesis. Am J Otolaryngol. 1990;11(4):244-50.
11. Epstein JB, Wong FL, Stevenson-Moore P: Osteoradionecrosis clinical experience and a proposal for classification. J Oral Maxillofac Surg 1987, 45:104–110.
12. Annane D, Depondt J, Aubert P, Villart M, Gehanno P, Gajdos P, et al. Hyperbaric oxygen therapy for radionecrosis of the jaw: a randomized, placebo-controlled, double-blind trial from the ORN96 study group. J Clin Oncol. 2004;22(24):4893–900.
13. Sultan A, Hanna GJ, Margalit DN, Chau N, Goguen LA, Marty FM, et al. The use of hyperbaric oxygen for the prevention and Management of Osteoradionecrosis of the jaw: a Dana-Farber/ Brigham and Women's Cancer center multidisciplinary guideline. Oncologist. 2017;22(3):343–50.
14. Pitak-Arnnop P, Sader R, Dhanuthai K, Masaratana P, Bertolus C, Chaine A, et al. Management of osteoradionecrosis of the jaws: an analysis of evidence. Eur J Surg Oncol. 2008;34(10):1123–34.
15. Delanian S, Lefaix JL: The radiation-induced fibroatrophic process: therapeutic perspective via the antioxidant pathway. Radiother Oncol 2014, 73:119–131.
16. Medical treatment of osteoradionecrosis of the mandible by PENTOCLO: Preliminary results : Robard M, Y.Louis,D.Blanchard E,.Babin: European Annals of Otorhinolaryngology, Head and Neck Diseases,Volume 131, Issue 6 , December 2014, Pages 333-33.
17. Hagelauer N, Ziebart T, Pabst AM, Walter C. Bisphosphonates inhibit cell functions of HUVECs, fibroblasts and osteogenic cells via inhibition of protein geranylgeranylation. Clin Oral Investig. 2015;19(5):1079–91.
18. Ruggiero SL, Dodson TB, Fantasia J, Goodday R, Aghaloo T, Mehrotra B, et al. American association of oral and maxillofacial surgeons position paper on medication-related osteonecrosis of the jaw--2014 update. J Oral Maxillofac Surg. 2014;72(10):1938–56.
19. Rugani P, Walter C, Kirnbauer B, Acham S, Begus-Nahrman Y, Jakse N. Prevalence of medication-related osteonecrosis of the jaw in patients with breast cancer, prostate cancer, and multiple myeloma. Dent J (Basel). 2016;4(4):32.

20. Pabst AM, Ziebart T, Ackermann M, Konerding MA, Walter C. Bisphosphonates' antiangiogenic potency in the development of bisphosphonate-associated osteonecrosis of the jaws: influence on microvessel sprouting in an in vivo 3D Matrigel assay. Clin Oral Investig. 2014;18(3):1015–22.
21. Aggarwal K, Goutam m, Singh M, Kharat N, Singh V, Vyas S, et al. Prophylactic use of pentoxifylline and tocopherol in patients undergoing dental extractions following radiotherapy for head and neck cancer. Niger J Surg 2017;23:130-3.