DOI: 10.7860/JCDR/2024/73191.19956

Case Report

Dentistry Section

A Case of Pernicious Complication of Radiotherapy: Osteoradionecrosis of Mandible with Extensive Bilateral Involvement following Dental Extraction

PULKIT KHANDELWAL[1], HARISH SALUJA[2], SEEMIT SHAH[3], ANUJ DADHICH[4]

ABSTRACT

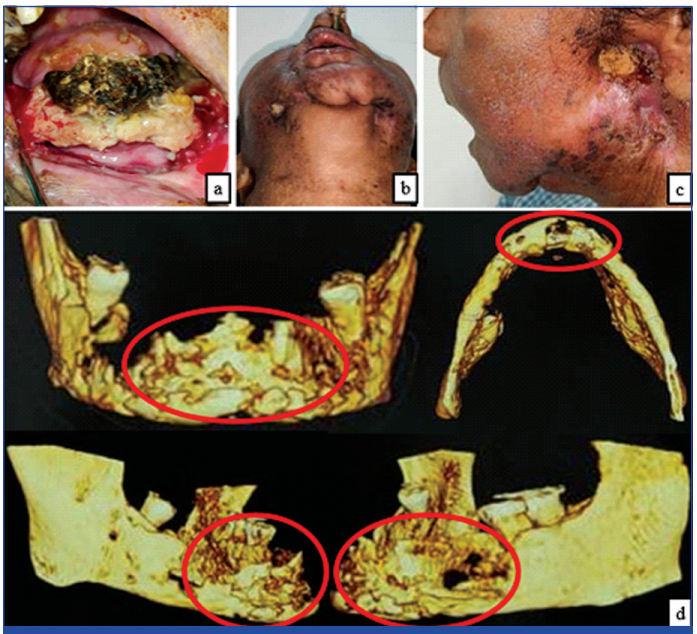
Osteoradionecrosis (ORN) is a condition of bone necrosis following mucosal breakdown after radiotherapy. It can lead to significant reduction in quality of life. ORN, particularly in the mandible, is a severe long-term complication of radiotherapy for head and neck cancer. ORN causes ulceration of oral mucosa with exposure of necrotic bone, pain, trismus and suppuration leading to chronic infection and non-healing wounds. Radiation-induced fibrosis, chronic infection, fistulae and necrotic tissues make the treatment challenging. We report a case of mandibular ORN in a 50-year-old female following dental extraction. Devitalised alveolar bone of the mandible was exposed intraorally through ulcerated mucosa from body-to-body region with multiple cutaneous fistulae. The necrosed bone was surgically debrided and healing was uneventful at the time of discharge. The patient was referred for Hyperbaric Oxygen Therapy (HBOT) for further management. Prevention of ORN is important for proper management of patients who undergo radiation therapy to head and neck region.

Keywords: Carcinoma, Necrosis, Oxygen, Surgery, Therapy

CASE REPORT

A 50-year-old female reported to the Department of Oral and Maxillofacial Surgery, Rural Dental College with a one-year history of irregular blackish bony projections in her mouth and pus discharge. The patient was diagnosed as a case of well differentiated squamous cell carcinoma of tongue two-year-ago and chemoradiation treatment was administered at that time. She received 70 Gray of external-beam radiation in 35 daily fractions over two months, alongside six cycles of Cisplatin and 5-Fluorouracil chemotherapy. The tongue lesion resolved completely post-treatment without the need for surgery. She underwent extraction of four lower anterior teeth (four incisors) after six months of radiotherapy. Since then, the wound at the extraction sockets was not healing. Within two months, she noticed bony exposure in lower jaw intraorally with pus discharge. Bony exposure kept increasing in size and subsequently underwent necrosis. She reported with exposed bone, continuous dull pain, foul odour, dysphagia, speech difficulties, and inability to close her mouth, making oral intake impossible.

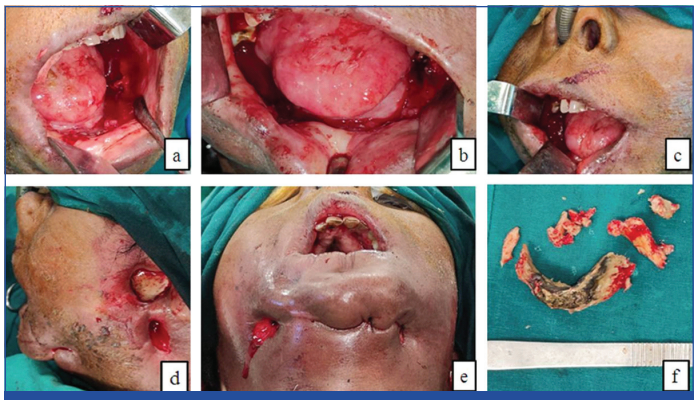
Systemic examination was insignificant and there was no history of any medical illness such as diabetes, hypertension, asthma, epilepsy, thyroid disorder, etc. On examination, exposed devitalised alveolar bone of the mandible was present through ulcerated mucosa from body-to-body region and pus discharge was evident [Table/Fig-1a]. The skin was inflamed, erythematous and irradiated. Multiple scars of sinuses were present in submental region, bilateral submandibular region [Table/Fig-1b] and left pre-auricular region [Table/Fig-1c] with exposed bone. Ryle's tube was in situ. Based on the history and clinical examination, provisional diagnosis of Stage III Osteoradionecrosis (ORN) of the mandible was made. Computed Tomography (CT) scan was suggestive of extensive osteolytic areas, ill-defined cortical interruptions, bony fragmentation, bone resorption and extensive sequestra formation extending from body-to-body region of the mandible [Table/Fig-1d]. Blood investigations were done and all findings were within normal limit {Haemoglobin (Hb)- 12.8 g/dL, White Blood Cell (WBC) count- 7600/microlitre, Red Blood Cell (RBC) count- 4.56 million/mm^3, Platelet count- 2.54 lacs/microL, Triiodothyronine (T3)-1.3 ng/mL, Tetraiodothyronine/Thyroxine (T4)- 6.7 microgram/dL, Thyroid Stimulating Hormone (TSH)- 2.734 microIU/mL, Total bilirubin- 0.86 mg/dL, Serum urea- 25 mg/dL, Serum Creatinine- 0.9 mg/dL, Calcium- 8.5 mg/dL, Fasting Blood Sugar Level (FBSL)- 98 mg/dL}. Patient and her relatives were informed about the condition and need for treatment. Informed consent was obtained.



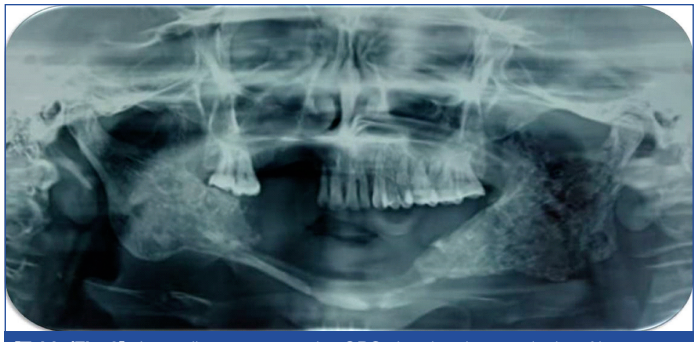
[Table/Fig-1]: Preoperative photographs: a) Exposed necrosed alveolar bone of the mandible from body-to-body region with evident pus discharge; b) Sinus present in submental region and submandibular region bilaterally; c) Sinus present in left pre-auricular region with exposed irradiated bone; d) CT scan showing extensive osteolytic areas ill-defined cortical interruptions, bony fragmentation, bone resorption and extensive sequestra formation extending from body-to-body region of the mandible (encircled in red).

The patient was admitted, and preoperative antibiotic treatment was initiated immediately. Intravenous medications (Inj. Augmentin 1.2 g i.v. BD, Inj. Metronidazole 500 mg/100 mL i.v. TDS, and

Inj. Paracetamol 1g TDS) were administered preoperatively for one day. Surgery was performed under general anaesthesia. Sequestrectomy was performed, necrotic bone was excised and bony margins were freshened till bleeding appeared [Table/Fig-2a-c]. Extra-oral sinuses were curetted from left preauricular region [Table/Fig-2d], submental and submandibular region [Table/Fig-2e]. Excised specimen [Table/Fig-2f] was sent for histopathological examination and was reported as Stage III ORN [1]. Specimens were stained with Haematoxylin and Eosin (H&E) and then observed under a Zeiss light microscope (100 x magnification). Necrotic bone showed no osteoclasts in resorption lacunae, reactive bone formation was present on the lateral cortical bone and fibrosis was present in the bone marrow. Postoperative Orthopantomogram (OPG) showed that continuity of the lower border of the mandible was maintained and there was no residual necrotic bone in the mandible [Table/Fig-3]. Intravenous medications (Inj. Augmentin 1.2 g i.v. BD, Inj. Metronidazole 500 mg/100 mL i.v. TDS, and Inj. Paracetamol 1g TDS) were administered for five days followed by oral administration (Tab. Augmentin 625 mg TDS, Tab Metronidazole 400 mg TDS, and Tab Ketorolac 10 mg TDS) for the next two days. Local wound support dressing with antiseptic ointment (10% betadine) was done twice daily. The patient was advised to take only liquid/soft diet orally. She was discharged uneventfully after one week. Oral medications were prescribed for one more week. She was referred for Hyperbaric Oxygen Therapy (HBOT) to a higher centre for further management.



[Table/Fig-2]: Operative photographs: a-c) Sequestrectomy performed and necrotic bone excised; d) Extra-oral sinuses curetted from left preauricular region; e) Extra-oral sinuses curetted from submental and submandibular region; f) Specimen of necrosed bone excised.



[Table/Fig-3]: Immediate postoperative OPG showing that continuity of lower border of the mandible is maintained with no iatrogenic/pathological fracture or residual necrotic bone in the mandible.

DISCUSSION

Treatment of oral cancer mainly includes surgery and radiotherapy. Sometimes, chemotherapy may be required. The most dreaded complication of radiotherapy is ORN. It is a severe delayed radiation-induced injury where irradiated bone undergoes irreversible tissue damage, necrosis and becomes exposed through soft-tissue [1,2]. ORN is defined as exposed irradiated bone that fails to heal over a period of six months without evidence of persisting or recurrent tumour [3]. In 1926, Ewing first reported osseous changes associated with radiotherapy and described this condition as radiation osteitis [2]. Incidence of ORN of the mandible is reported to be around 2-22% [4]. It mostly occurs after trauma following dental extractions and appears between six months to five years following radiotherapy [1]. It is predominant in the mandible than maxilla (ratio-24:1) due to restricted localised blood supply, more dense bone and higher absorption of radiation during radiotherapy [5]. Numerous factors associated with development of ORN includes high dose of radiotherapy (>70 Gray), type of radiotherapy, fractionation [6], poor oral hygiene, dental extractions, trauma to irradiated region, alcohol and tobacco abuse, etc., [7]. Radiotherapy, particularly at high doses, severely affects hard and soft-tissues, leading to endarteritis, tissue hypoxia, hypovascularity, and ultimately, chronic non healing wounds [3].

The ORN in early stages may be asymptomatic. Clinical signs and symptoms of ORN include ulceration of the mucosa with exposure of necrotic bone for longer than three months, pain, trismus and suppuration. Other symptoms include dysesthesia, halitosis, dysgeusia, food impaction and physical irritation of adjacent tissues [2]. In severe cases, multiple fistulae from oral mucosa or skin, complete devitalisation of bone and pathological fractures can occur [8]. In external beam radiation therapy, osseous changes usually appear in the body of the mandible, whereas in brachytherapy, lingual or buccal surface of the mandible is affected [9]. Prerequisites for diagnosis of ORN include: (i) History of radiotherapy of affected bone; (ii) No recurrence of lesion; (iii) presence of mucosal breakdown or failure of healing causing bone exposure; and (iv) necrosis of involved bone [10]. The radiographic features of ORN include localised or extensive osteolytic areas, sequestra formation and/or fracture [10,11]. The treatment of ORN includes antibiotic therapy, local wound irrigation, debridement, sequestrectomy and HBOT [12,13]. Recently, vascular directed therapy (pentoxifylline) and antioxidant therapy have been recommended in treating superficial cases of ORN [12]. [Table/Fig-4] summarises few case reports published in the literature regarding management of ORN [2,12,14,15].

S. No.	Authors	Chief complaints	History of radiotherapy	Clinical findings	Treatment
1.	Rathy R et al., [2]	Exposed bony fragments since 7 months and history of pus discharge from the right side of cheek 2 months back	History of radiotherapy for squamous cell carcinoma of right buccal mucosa 4 years back	Exposed necrotic bone found from right lower retromolar area extending toward midline	Antibiotics and sequestrectomy
2.	Kahenasa N et al., [12]	Severe left mandibular painand exposed lingual plate in left posterior mandible	History of radiotherapy for tonsillar and base of tongue cancer 6 months ago	ORN of the left posterior lingual mandibular cortex	6 months of pentoxifylline 400 mg BD and tocopherol 1000 IU every day
3.	Moraes PC et al., [14]	Pain in the mandible, difficulty in swallowing and extraoral fistulae	History of extraction of tooth 47 after 5 years of radiotherapy treatment for squamous cell carcinoma of the lip	Bone exposure and fistula formation at the right mandibular second molar	Conservative non-operative therapy, including long-term antibiotic therapy (Chloramphenicol 500 mg, TDS for 12 days) and daily irrigation with chlorhexidine 0.12 mouthrinses
4.	Dorsaf T et al., [15]	Severe pain due to a purulent lesion on the right side of the submandibular region	History of radiotherapy for undifferentiated carcinoma of the nasopharynx 8 years ago	Painful, purulent and indurated lesion of right submandibular region	Pentoxifylline (Torental) 800 mg/day, Tocopherol 1000 IU/day for 2 weeks, Paracetamol 3 g/day Chlorhexidine mouthwashes 4 times/day, Pilocarpine 4 mg 5 times daily

[Table/Fig-4]: A few case reports published in the literature regarding management of ORN [2,12,14,15].

The HBOT is recommended as adjunctive therapy along with surgery for effective management of ORN by promoting the healing process [16]. The patient is exposed to 100% oxygen at 2.4 atmospheres absolute for 90 minutes at depth during one dive of HBOT. In Stage-I ORN, patients receive 30 dives of HBOT. Patients who respond to HBOT alone (Stage-I responder) demonstrate softening of irradiated tissues and spontaneous sequestration of exposed bone with formation of granulation tissue. Each Stage I responder undergoes an additional 10 HBOT sessions [1,10]. If healing doesn't occur after three months, the condition is advanced to Stage-II. Alveolar sequestrectomy is performed and additional 20 HBOT dives are given (total of 60 dives). If wound dehiscence or failure to heal again occurs, the patient is advanced to Stage-III [1]. Treatment commences with 30-dives, bony resection and/or reconstruction, followed by soft-tissue coverage. An additional ten dives are also administered [1,3].

Extraction socket usually heals completely within one month. However, dental extraction after radiotherapy is the most common precipitating factor of ORN [17]. Incidence of ORN is also three times higher in dentate individuals than in edentulous ones, mainly because of post-extraction trauma [8]. All indicated tooth-extractions should be performed at least two weeks before commencement of radiotherapy to prevent ORN [18]. In patients who require dental extractions after four months of radiotherapy should be treated with HBOT. Twenty dives before extraction and ten dives after extraction are recommended [19].

The present case is that of a mandibular ORN from body-to-body region following teeth extraction. It can be considered as a severe case of ORN due to the symptoms, bone features and extraoral fistula. Sequestrectomy and curettage was performed and the patient was referred for HBOT.

CONCLUSION(S)

The ORN can cause unbearable pain, pathological fracture, sequestrum formation and/or oro-cutaneous fistula. Prompt diagnosis and treatment is mandatory to manage this pernicious complication of radiotherapy and improve quality of life. Prevention of ORN is based on the preventive extractions of decayed or periodontally compromised teeth before radiotherapy.

REFERENCES

[1] Nadella KR, Kodali RM, Guttikonda LK, Jonnalagadda A. Osteoradionecrosis of the jaws: Clinico-therapeutic management: A literature review and update. J Maxillofac Oral Surg. 2015;14(4):891-901. Doi: 10.1007/s12663-015-0762-9. Epub 2015 Mar 10. PMID: 26604460; PMCID: PMC4648774.

[2] Rathy R, Sunil S, Nivia M. Osteoradionecrosis of mandible: Case report with review of literature. Contemp Clin Dent. 2013;4(2):251-53. Doi: 10.4103/0976-237X.114882. PMID: 24015021; PMCID: PMC3757894.

[3] Marx RE. Osteoradionecrosis: A new concept of its pathophysiology. J Oral Maxillofac Surg. 1983;41(5):283-88. Doi: 10.1016/0278-2391(83)90294-x. PMID: 6572704.

[4] Lang K, Held T, Meixner E, Tonndorf-Martini E, Ristow O, Moratin J, et al. Frequency of osteoradionecrosis of the lower jaw after radiotherapy of oral cancer patients correlated with dosimetric parameters and other risk factors. Head Face Med. 2022;18(1):7. Doi: 10.1186/s13005-022-00311-8. PMID: 35219324; PMCID: PMC8881856.

[5] Perrier M, Moeller P. [Osteoradionecrosis. A review of the literature]. Schweiz Monatsschr Zahnmed. 1994;104(3):271-77. [Article in French]. PMID: 8165448.

[6] Iqbal Z, Kyzas P. Analysis of the critical dose of radiation therapy in the incidence of osteoradionecrosis in head and neck cancer patients: A case series. BDJ Open. 2020;6:18. Doi: 10.1038/s41405-020-00044-3. PMID: 33042578; PMCID: PMC7515872.

[7] Pereira IF, Firmino RT, Meira HC, Vasconcelos BCE, Noronha VRAS, Santos VR. Osteoradionecrosis prevalence and associated factors: A ten years retrospective study. Med Oral Patol Oral Cir Bucal. 2018;23(6):e633-e638. Doi: 10.4317/medoral.22310. PMID: 30341256; PMCID: PMC6260996.

[8] Lyons A, Ghazali N. Osteoradionecrosis of the jaws: Current understanding of its pathophysiology and treatment. Br J Oral Maxillofac Surg. 2008;46(8):653-60. Doi: 10.1016/j.bjoms.2008.04.006. Epub 2008 Jun 17. PMID: 18562055.

[9] Støre G, Evensen J, Larheim TA. Osteoradionecrosis of the mandible. Comparison of the effects of external beam irradiation and brachytherapy. Dentomaxillofac Radiol. 2001;30(2):114-19. Doi: 10.1038/sj/dmfr/4600591. PMID: 11313733

[10] Chronopoulos A, Zarra T, Ehrenfeld M, Otto S. Osteoradionecrosis of the jaws: Definition, epidemiology, staging and clinical and radiological findings. A concise review. Int Dent J. 2018;68(1):22-30. English. Doi: 10.1111/idj.12318. Epub 2017 Jun 25. PMID: 28649774; PMCID: PMC9378891.

[11] Guttenberg SA. Osteoradionecrosis of the jaw. Am J Surg. 1974;127(3):326-32. Available from: https://doi.org/10.1016/0002-9610(74)90042-7.

[12] Kahenasa N, Sung EC, Nabili V, Kelly J, Garrett N, Nishimura I. Resolution of pain and complete healing of mandibular osteoradionecrosis using pentoxifylline and tocopherol: A case report. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012;113(4):e18-23. Doi: 10.1016/j.oooo.2011.10.014. PMID: 22668439.

[13] Peleg M, Lopez EA. The treatment of osteoradionecrosis of the mandible: The case for hyperbaric oxygen and bone graft reconstruction. J Oral Maxillofac Surg. 2006;64(6):956-60. Doi: 10.1016/j.joms.2006.02.017. PMID: 16713813.

[14] Moraes PC, Thomaz LA, Silva MBF, Junqueira JLC, Teixeira RG. Successful in a conservative treatment of osteoradionecrosis of the jaw: A case report and review of literature. Rev Gaúch Odontol. 2016;64(2):212-18. Doi: 10.1590/1981-86372016002000143190.

[15] Dorsaf T, Ons HME, Yosri AM, Lamia O. Conservative approach of a severe case of osteoradionecrosis of the mandible- Case report. Int J Drug Res Dental Sci. 2020;2(3):45-54.

[16] Jenwitheesuk K, Mahakkanukrauh A, Punjaruk W, Jenwitheesuk K, Chowchuen B, Jinaporntham S, et al. Efficacy of adjunctive hyperbaric oxygen therapy in osteoradionecrosis. Biores Open Access. 2018;7(1):145-49. Doi: 10.1089/biores.2018.0019. PMID: 30310729; PMCID: PMC6178923.

[17] Lajolo C, Rupe C, Gioco G, Troiano G, Patini R, Petruzzi M, et al. Osteoradionecrosis of the jaws due to teeth extractions during and after radiotherapy: A systematic review. Cancers (Basel). 2021;13(22):5798. Available from: https://doi.org/10.3390/cancers13225798.

[18] Devi S, Singh N. Dental care during and after radiotherapy in head and neck cancer. Natl J Maxillofac Surg. 2014;5(2):117-25. Doi: 10.4103/0975-5950.154812. PMID: 25937720; PMCID: PMC4405951.

[19] 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. Doi: 10.1634/theoncologist.2016-0298. Epub 2017 Feb 16. Erratum in: Oncologist. 2017;22(11):1413. Doi: 10.1634/theoncologist.2016-0298erratum. PMID: 28209748; PMCID: PMC5344641.

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Oral and Maxillofacial Surgery, Rural Dental College, PIMS-DU, Loni, Ahmednagar, Maharashtra, India.
2. Professor, Department of Oral and Maxillofacial Surgery, Rural Dental College, PIMS-DU, Loni, Ahmednagar, Maharashtra, India.
3. Professor and Head, Department of Oral and Maxillofacial Surgery, Rural Dental College, PIMS-DU, Loni, Ahmednagar, Maharashtra, India.
4. Professor, Department of Oral and Maxillofacial Surgery, Rural Dental College, PIMS-DU, Loni, Ahmednagar, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Pulkit Khandelwal,
Associate Professor, Department of Oral and Maxillofacial Surgery, Rural Dental College, PIMS-DU, Loni, Ahmednagar-413736, Maharashtra, India.
E-mail: khandelwal.pulkit22@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: May 31, 2024
- Manual Googling: Jun 24, 2024
- iThenticate Software: Aug 06, 2024 (14%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **May 30, 2024**
Date of Peer Review: **Jun 21, 2024**
Date of Acceptance: **Aug 07, 2024**
Date of Publishing: **Sep 01, 2024**