

Immediate Onset of Osteoradionecrosis Post-radiotherapy in Postoperated Oral Squamous Cell Carcinoma Patient: A Case Report

KUNDAN SHIBJEE JHA¹, NITIN BHOLA², SANJANA WADEWALE³

(CC) BY-NC-ND

ABSTRACT

Osteoradionecrosis (ORN) of the jaws is a severe complication of radiotherapy for head and neck cancers and is characterised as hypovascular, hypocellular and hypoxic tissue. ORN is more commonly seen in the mandible and only occasionally in the maxilla and zygomatic bone. The present case describes atypical features of ORN that developed in the zygomatic bone in a relatively young patient after Intensity-Modulated Radiation Therapy (IMRT). A 42-year-old male with squamous cell carcinoma of the right buccal mucosa underwent IMRT (60 Gy in 30 fractions). Ten days after radiotherapy, he presented with extraoral wound dehiscence, purulent discharge and severe pain. Clinical examination revealed erythema and inflammation, with a 7.8 mm oro-cutaneous fistula near the maxillectomy site. Histopathology showed necrotic bone with bacterial invasion and culture identified Methicillin-Susceptible *Staphylococcus Aureus* (MSSA). Conservative management with antibiotics and local wound care was initiated because there was no evidence of severe necrosis or a pathologic fracture. Hyperbaric Oxygen Therapy (HBOT) was unavailable, but the patient responded well. Sequestrectomy was planned, illustrating that early-stage ORN can be managed conservatively when HBO is inaccessible. The present case highlights the need for personalised management plans and underscores close surveillance in the initial stages of ORN. The report discusses early diagnosis, culture-guided antibiotics and an individualised approach to treatment for patients with ORN.

Keywords: Maxillary disease, Post-oncosurgery, Post-radiotherapy complications, Radiotherapy-induced necrosis

CASE REPORT

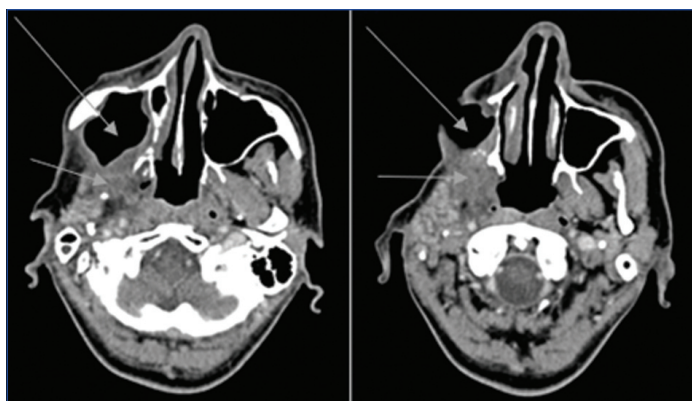
A 42-year-old male presented to the Department of Oral and Maxillofacial Surgery with extraoral wound dehiscence and purulent discharge 10 days after radiotherapy. He had a history of well-differentiated squamous cell carcinoma (Stage IVA) of the right buccal mucosa with extraoral fungation, managed surgically with composite resection of the lesion, neck dissection and reconstruction with a regional flap [Table/Fig-1]. The patient had hypertension for four years and diabetes mellitus for approximately three years and was a pan and kharra chewer for about 10 years prior to surgery. Adjuvant chemoradiotherapy was given postoperatively. The radiation dose was 60 Gy in 30 fractions over six weeks. On examination, there was wound dehiscence above the superior suture line of the extraoral flap accompanied by purulent discharge [Table/Fig-2]. The surrounding area appeared erythematous and inflamed. The patient also reported severe pain that was gradual in onset, dull and continuous in nature, with periods of sharp exacerbations. It progressively worsened and was exacerbated by mastication and exposure to cold food or air and was only partially relieved by analgesics. There is no history of dental extraction after radiotherapy. On Computed Tomography (CT) scan [Table/Fig-3], there was a 7.8 mm oro-cutaneous fistula adjacent to the maxillectomy area and a 14 mm flap-reconstruction area, with air in the right maxillary sinus region. After the operation, no structure was seen at the posterolateral wall of the right maxillary sinus. As expected after surgical resection of the tumour, no abnormal enhancing lesions were observed in the operative bed. Microbial culture showed *Staphylococcus aureus* (susceptible to vancomycin and linezolid) with no growth of other aerobic, anaerobic, or fungal cultures after 48-72 hours of incubation. Histopathological examination {Haematoxylin and Eosin (H&E)}, as shown in [Table/Fig-4], confirmed loss of viable osteocytes and empty lacunae in



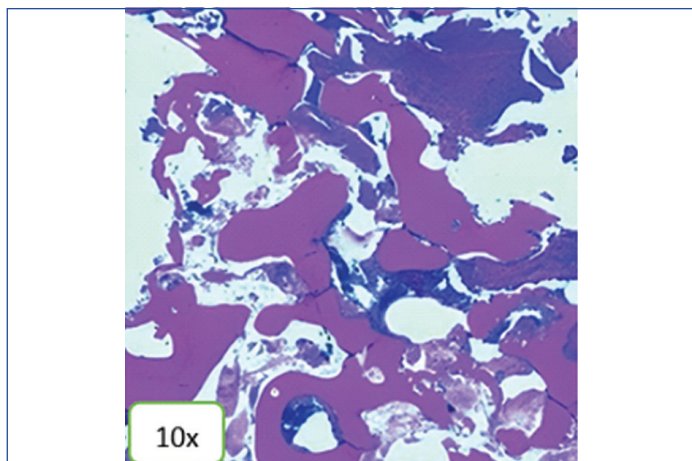
[Table/Fig-1]: Immediately before starting of radiotherapy



[Table/Fig-2]: One month post-radiotherapy.



[Table/Fig-3]: CT scan showing post-ORN changes with arrows denoting postoperative ORN changes.



[Table/Fig-4]: Histopathological image showing ORN (H&E, 10x).

the necrotic bone. The tumour stroma showed abundant collagen with marked neutrophilic and lymphocytic infiltration. There was bacterial adhesion to necrotic bone tissue with procoagulant effects. Adjacent bone showed remodelling with evidence of active osteoclastic resorption together with newly formed reactive bone. No malignancy was detected. For infection control, vancomycin 1 g i.v. every 12 hours was prescribed based on culture sensitivity reports. The patient showed gradual improvement [Table/Fig-5]. Sequestrectomy followed by reconstruction was planned for further management later, as ORN occurred immediately after radiotherapy and surgical intervention could not be performed at that time. Therefore, local wound care was continued for now.



[Table/Fig-5]: Four months post-radiotherapy.

DISCUSSION

The ORN is an area of exposed bone that has been irradiated and does not heal within 2-3 months, with no evidence of local malignancy. ORN remains a significant challenge in the management of head and neck cancer survivors. Contributing factors include high-

dose radiation and trauma. Historically, reported prevalence ranged from 0.4% to 56%, with incidence ranging from 5% to 15% [1,2]. Although its frequency has diminished, advancements in radiation therapy techniques—from conventional treatments to 3D Conformal Radiotherapy (3D CRT) and IMRT—coupled with improvements in dental preventive care, have significantly reduced its occurrence [3]. These technological and preventive improvements reduced prevalence from 11.8% before 1968 to 5.4% between 1968 and 1992 and to 3% after 1997 [3].

The ORN results from hypovascularity, hypocellularity and hypoxia in radiosensitive tissues, which cause vascular damage, ischaemia and impaired wound healing [4]. Meyer's theory, published in 1971 as the radiation trauma and infection theory, proposes that injury allows oral microbiota to invade the underlying irradiated bone. This theory helps explain the rationale for antibiotics combined with surgery in treating ORN. Predisposing factors for ORN include high radiation doses (typically exceeding 60 Gy), large radiation fields and single-field therapies that undermine bone structure. Radiation-related complications include delayed wound healing and, though less frequent, infection within irradiated fields; in combination with trauma from dental extractions and surgeries, these factors further complicate the situation and amplify the risk of microbial infections originating from the oral cavity. The wound may also fail to heal due to systemic issues such as diabetes, poor nutrition and social habits like smoking and alcohol consumption. In irradiated bone, the physiologically impaired state of hypoxia, hypovascularity and hypocellularity delays healing, leading to a chronic course of necrosis and infection. Clinically, ORN presents with pain, exposed or denuded bone, purulent discharge and a predisposition to fistulas [5]. Although symptoms often appear after completion of head and neck cancer treatment, the risk persists for life. Imaging may show ill-defined radiolucency without a sclerotic margin; sequestrum may be radiopaque and bone pathology can be subtle in later stages. Magnetic Resonance Imaging (MRI) may show low signal intensity with cortical destruction and can mimic recurrent tumors, while CT helps detect cortical interruptions and loss of trabecular bone (spongiosa) [5].

Several risk factors contribute to the development of ORN. The most significant is the radiation dose, particularly when exceeding 60 Gy. Additional factors include trauma or dental extractions in irradiated areas, poor oral hygiene, smoking, alcohol abuse, nutritional deficiencies, ill-fitting prostheses, preexisting dental infections and systemic conditions such as diabetes mellitus. The mandible is more commonly affected due to its relatively limited vascularity, although the maxilla is not exempt, especially with radiation above 60 Gy. Concurrent chemotherapy, absence of preradiation dental clearance and delayed management of post-radiation complications further elevate the risk [6].

Pathophysiology of ORN, based on Marx's hypoxic-hypocellular-hypovascular theory, comprises hypoxia-induced tissue injury, deranged collagen turnover and pre-existing chronic nonhealing wounds and forms the basis for HBOT [4]. The fibro-atrophic theory posits that fibrosis, driven by cytokines, replaces normal bone matrix, decreases vascularity and increases damage, impairing healing [4]. Knowledge of these mechanisms helps develop pharmacological and surgical treatments for advanced ORN, such as radical surgery and HBOT.

The patient presented with a 10-day history of extraoral wound breakdown, foul discharge, severe pain, erythema and inflammation. CT imaging revealed a 7.8 mm percutaneous fistula, a 14 mm flap reconstruction defect and an antral aspirate in the right maxillary sinus. Histopathology confirmed necrotic bone with empty osteocyte lacunae and reactive bone formation, while bacterial culture identified vancomycin- and linezolid-sensitive *Staphylococcus aureus*. These findings, along with the history of radiation therapy and surgery, confirmed ORN.

The management of ORN typically involves three primary modalities: conservative management, HBOT and surgical intervention [5]. The initial treatment option is often conservative, where the lesion's extent and the ORN stage are considered. Local wound care consists of irrigation with normal saline, along with analgesic and antibiotic coverage to alleviate pain and local inflammation [7]. Some drugs, such as pentoxifylline and tocopherol, are usually recommended to halt the fibro-atrophic process of ORN and to enhance tissue remodelling and inflammation [7]. Another non invasive ultrasound technique is available, administered at 1 W/cm², 3 MHz, pulsed 1:4 per day for 60 days (over 15 minutes), which induces neovascularity and neocellularity in ischaemic tissues, promoting tissue regeneration and healing [7]. Local wound debridement and sequestrectomy can be employed. Clodronate, a non aminobisphosphonate, inhibits chronic inflammation, osteoclast activity and fibroblast proliferation and is used in the PENTOCLO protocol (Pentoxifylline, Tocopherol and Clodronate) for non surgical treatment of resistant cases (pathological fractures) [7]. Bone Morphogenetic Protein 2 (BMP-2), an osteoinductive bone repair agent and Leukocyte- and Platelet-Rich Fibrin (L-PRF), a tissue-regenerative wound-healing agent, work synergistically to enhance Medication-related Osteonecrosis of the Jaw (MRONJ) healing, since both BMP-2 and L-PRF can heal MRONJ [8].

The HBO, notably the Wilford Hall Protocol by Marx, is effective for refractory ORN cases, enhancing vascularity and fibroblast proliferation to limit necrosis and reduce tissue excision [4]. The protocol includes Stage I: 30 initial treatments, with 10 additional if needed; Stage II: bone sequestration followed by 20 more sessions if healing is incomplete; and Stage III: surgical intervention (e.g., sequestrectomy or resection with or without reconstruction). In general, there is generally no indication for active surgical treatment of ORN unless pathological fracture, percutaneous fistulas, or extensive bone necrosis are present [5]. ORN surgical options include sequestrectomy, resection and reconstruction with Microvascular Free Flaps (MVFF), regional pedicle flaps, or autologous bone grafts at resection [9]. Given the better functional and aesthetic results compared with head and neck cancer reconstruction, mandibular defects are preferably reconstructed with MVFF, with similar survival and complication rates [10].

Patients with early ORN (<1 month post-radiotherapy) and no severe complications were managed conservatively, without surgery. Broad-spectrum antibiotics, nutritional and stress support and close monitoring were part of the treatment. Management involved maintaining the condition stable according to low-grade ORN guidelines, using non surgical interventions and monitoring for progression, as HBOT was unavailable. This fundamental goal of

management was to prevent the evolution of complications and to give the wound time to heal while retaining surgical interventions as a back-up when the patient's response to less invasive forms of therapy is unsatisfactory.

CONCLUSION(S)

The present case report discusses the difficulties in managing Oral Squamous Cell Carcinoma (OSCC), particularly its postoperative complication—ORN. Early detection and management of ORN can be facilitated at both preventive and therapeutic levels, playing a critical role in improving outcomes for these individuals. This emphasises the importance of effective pre- and post-treatment planning, including scheduling of surgery in relation to radiotherapy, in order to avoid difficulties caused by high-dose radiation exposure. In the end, the present case teaches a lesson about heightened awareness, comprehensive patient education and the ongoing need to adjust treatment regimens to find a balance between cancer management and quality of life.

REFERENCES

- [1] Moreno AC, Watson EE, Humbert-Vidan L, Peterson DE, van Dijk LV, Urbano TG, et al. International Expert-based consensus definition, classification criteria, and minimum data elements for osteoradionecrosis of the jaw: An interdisciplinary Modified Delphi study. *Int J Radiat Oncol*. 2025 Jan 16.
- [2] Topkan E, Kucuk A, Somay E, Yilmaz B, Pehlivan B, Selek U. Review of osteoradionecrosis of the jaw: Radiotherapy modality, technique, and dose as risk factors. *J Clin Med*. 2023;12(8):3025.
- [3] Owosho AA, Tsai CJ, Lee RS, Freymiller H, Kadempour A, Varthi S, et al. The prevalence and risk factors associated with osteoradionecrosis of the jaw in oral and oropharyngeal cancer patients treated with intensity-modulated radiation therapy (IMRT): The Memorial Sloan Kettering Cancer Center experience. *Oral Oncol*. 2017;64:44-51.
- [4] Marx RE. A new concept in the treatment of osteoradionecrosis. *J Oral Maxillofac Surg*. 1983;41(6):351-57.
- [5] Raj R, Nair AH, Krishnan NA, Balasubramanian D, Iyer S, Thankappan K. Advances and controversies in the management of osteoradionecrosis after head and neck cancer treatment: A narrative review. *J Maxillofac Oral Surg*. 2022;21(3):836-44.
- [6] Nabil S, Samman N. Incidence and prevention of osteoradionecrosis after dental extraction in irradiated patients: A systematic review. *Int J Oral Maxillofac Surg*. 2011;40(3):229-43.
- [7] McLeod NMH, Pratt CA, Mellor TK, Brennan PA. Pentoxifylline and tocopherol in the management of patients with osteoradionecrosis, the Portsmouth experience. *Br J Oral Maxillofac Surg*. 2012;50(1):41-44.
- [8] Park JH, Kim JW, Kim SJ. Does the addition of bone morphogenetic protein 2 to platelet-rich fibrin improve healing after treatment for medication-related osteonecrosis of the jaw? *J Oral Maxillofac Surg*. 2017;75(6):1176-84.
- [9] Rommel N, Kesting MR, Rohleder NH, Wolff KD, Weitz J. Surgical management of severe osteoradionecrosis of the mandibular bone by using double free flap reconstruction. *J Cranio-Maxillofac Surg*. 2018;46(1):148-54.
- [10] Hirsch DL, Bell RB, Dierks EJ, Potter JK, Potter BE. Analysis of microvascular free flaps for reconstruction of advanced mandibular osteoradionecrosis: A retrospective cohort study. *J Oral Maxillofac Surg*. 2008;66(12):2545-56.

PARTICULARS OF CONTRIBUTORS:

1. Postgraduate Student, Department of Oral and Maxillofacial Surgery, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
2. Professor and Head, Department of Oral and Maxillofacial Surgery, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
3. Assistant Professor, Department of Oral and Maxillofacial Surgery, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Kundan Shibjee Jha,
701, Geetanjali Jewel, Plot No. 130, Sector 19, Kharghar,
Navi Mumbai-410210, Maharashtra, India.
E-mail: mr.jhakundan@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jan 18, 2025
- Manual Googling: May 13, 2025
- iThenticate Software: May 15, 2025 (6%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

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: Jan 15, 2025

Date of Peer Review: Mar 15, 2025

Date of Acceptance: May 17, 2025

Date of Publishing: Oct 01, 2025