BMC Oral Health

RESEARCH

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Identification and management of recurrent oral squamous cell carcinoma in the clinical presentation of osteoradionecrosis: a single-center case series for treatment experience sharing

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Abstract

Introduction Radiotherapy is an integral component of the comprehensive and sequential treatment approach for advanced oral squamous cell carcinoma (OSCC). One of the significant complications associated with radiotherapy is osteoradionecrosis (ORN), which most frequently affects the mandible. Differentiating between osteoradionecrosis (ORN) and recurrent oral squamous cell carcinoma (ORSCC) can be challenging when relying solely on clinical and radiologic characteristics. The diagnosis becomes even more difficult when bone necrosis of jaw presents as the first clinical symptom.

Objectives This study aims to present the clinical manifestations and treatment processes of patients at our institution who have developed bone necrosis of jaw after radiotherapy and subsequently diagnosed with recurrent oral squamous cell carcinoma (ORSCC).

Case presentation We have collected six patients with recurrent oral squamous cell carcinoma (ORSCC) who developed bone necrosis of jaw after radiotherapy. These patients subsequently underwent surgical repair and reconstruction and were eventually diagnosed with ORSCC. We present a case series reviewing their basic characteristics, radiological reports, surgical treatment, and pathological diagnosis. All six patients initially presented with oral or facial pain and were diagnosed with osteoradionecrosis (ORN) through imaging studies. All patients underwent surgical treatment, with free flaps used to repair postoperative defects. Among them, five patients

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were diagnosed with tumor recurrence through preoperative or intraoperative frozen biopsy, and one patient was confirmed with recurrence in the osseous resection through postoperative examination.

Conclusion Identified ORSCC in the suspected ORN of the jaw following radiotherapy is relatively rare, yet it poses identification challenges and can significantly impact treatment decisions. Consequently, surgeons must remain vigilant and ensure clear pathological diagnoses for suspicious patients, either before or during surgery.

Keywords Oral squamous cell carcinoma (OSCC), Osteoradionecrosis (ORN), Recurrent oral squamous cell carcinoma (ORSCC), Reparative and reconstructive surgery, Free flap

Introduction

Radiation therapy is a crucial component in the comprehensive treatment of head and neck malignancies; however, radiation-induced osteonecrosis (ORN) remains a significant complication associated with this treatment [1, 2]. ORN is commonly defined as bone necrosis that occurs due to tissue damage and infection secondary to radiation injury affecting bone tissue and its vasculature following radiation exposure [3, 4]. ORN is typically characterized by bone lesions that fail to heal within 3 to 6 months and occur without any signs of tumor recurrence [5–7]. At present, the pathogenesis of ORN remains not fully understood. Research suggests that radiation, trauma, and infection are the three primary contributing factors. After radiation damage, the jaw experiences reduced oxygen levels, a diminished cell count, decreased blood vessel density, and impaired repair and anti-infection capabilities [3, 5, 8, 9]. Consequently, when the jawbone sustains further injury or infection, the healing process becomes challenging, potentially leading to the development of ORN [10]. High-risk factors for ORN include the radiation dose, the area of exposure, the patient's periodontal health, traumatic procedures performed in the oral cavity, and poor overall physical condition [1, 3, 11–14]. ORN typically occurs 6 to 12 months following radiotherapy, although some patients may experience an earlier or later onset [9].

In clinical practice, conservative treatment is generally used for early-stage ORN, as doctors are often concerned that changes in the surgical area following radiotherapy might impede wound healing. These methods include hyperbaric oxygen therapy, local debridement of necrotic bone, systemic administration of antibiotics, and oral rinses. In advanced cases, such as those with skin fistulas, severe jawbone destruction, or pathological fractures, complete resection of the affected jawbone and surrounding necrotic soft tissue is necessary, followed by simultaneous soft and hard tissue reconstruction.

However, recurrence of oral squamous cell carcinoma (ORSCC) may share several clinical symptoms and signs with ORN, such as oral pain, skin fistulas and severe jawbone destruction. When ORSCC with osteonecrosis clinical presentation is diagnosed, early and complete resection of the affected area, including both the jawbone and soft tissues, is crucial, followed by combined soft and hard tissue repair and reconstruction.

Unfortunately, distinguishing between ORN with ORSCC is often challenging when ORSCC patients presented bone necrosis of jaw presents as the first clinical symptom. A physical examination may reveal ulcerated tissue and exposed bone [15]; However, some patients present only with soft tissue necrosis, making it difficult to detect necrotic bone. Clinical presentation alone is insufficient to accurately differentiate between ORN and tumor recurrence. Although imaging can assist in evaluating the presence of necrotic bone or pathological fractures, it cannot definitively rule out the possibility of tumor recurrence. Both conditions may appear as soft tissue proliferation or enhancement on imaging, which complicates clinical differentiation [16, 17]. Misdiagnosing ORSCC as ORN will inevitably delay the appropriate treatment for the patient.

Considering that clinical cases of ORN combined with ORSCC are relatively rare and literature on the topic is limited, many clinicians may not be sufficiently aware of this condition. Through this case series study, we summarized the clinical manifestations, treatment processes, and outcomes of six ORSCC patients with osteonecrosis clinical presentation who were treated in the Department of Oral and Maxillofacial Surgery at the Hospital of Stomatology, Wuhan University, from 2018 to 2023. By sharing the clinical experiences from this study, we aim to provide valuable insights for clinicians managing in these complex cases.

Case series presentation

Basic information

This study included six ORSCC patients with firstly clinical suspicion for ORN who received treatment in the Department of Oral and Maxillofacial Surgery at the Hospital of Stomatology, Wuhan University, from 2018 to 2023. This Case series study was reviewed and approved by the Institutional Medical Ethics Committee of School and Hospital of Stomatology, Wuhan University (WDKQ2024-B25). The requirement for written consent to participate was waived due to the case series study design. Written consent for publication of the details of their medical data was obtained from the patient in this

Table 1 Patient characteristics

Characteristics	#1	#2	#3	#4	#5	#6
Age	48	58	48	47	69	53
Gender	Male	Female	Male	Male	Male	Male
Cancer site	Gingiva	Buccal mucosa	Tongue	Buccal mucosa	Floor of mouth	Buccal mucosa
TNM stage	T2N1M0	T2N1M0	T2N1M0	T2N1M0	T2N1M0	T2N3bM0
AJCC stage	III	III	III	III	III	IVB
Smoking history	Y (20 packs per day)	N	N	Y (15 packs per day)	Y (25packs per day)	Y (20 packs per day)
Active smoking	N	N	N	N	Y	Y
Chewing tobacco	N	N	N	N	Y	N
Significant alcohol use	N	N	N	Y	N	Y
Radiation dose (Gry/Fr)	44/22	44/22	60/30	56/28	64/32	64/32
Systemic therapy	Y	Y	N	N	Y	N
Reconstruction	RF	RF	ALT	RF	N	RF

Abbreviations: RF, radial forearm flap; ALT, anterolateral thigh flap; Y, yes; N, no Fr, frequency

Table 2 Osteonecrosis related clinical presentation of the patients

Signs	#1	#2	#3	#4	#5	#6
Oral pain	Y	Y	Y	Y	Y	Y
Trismus	N	Y	Y	N	Y	Y
Exposed bone	Y	N	Y	N	Y	N
Xerostomia	Y	Y	Y	Y	Y	Y
Mucositis/ ulceration	Y	N	Y	N	Y	Y
Fistula	Y	N	Y	N	Y	N
Tooth loss	Y	Y	Y	Y	Y	Y
Tooth decay	Y	N	Y	N	N	Y
Tooth loosening	N	Y	Y	Y	N	Y
Cacosmia	Y	N	Y	N	Y	Y
Oral hygiene	poor	general	poor	general	poor	poor

Abbreviations: Y, yes; N, no

study. The age distribution of the study participants was as follows: the average age was 53.8 years, with three patients aged between 40 and 50, two patients aged between 50 and 60, and one patient over 60. The group consisted of five male patients and one female patient. Regarding lifestyle factors, four patients had a history of smoking, two of whom had quit; one patient had a history of alcohol consumption, and two patients had a history of betel nut chewing. Specifically, two patients had a history of heavy alcohol consumption. All patients' primary tumors were located in the oral cavity with squamous cell carcinoma as the pathological type. The distribution of primary tumor sites was as follows: three patients with buccal cancer (ICD-10: C06.001), one patient with tongue cancer (ICD-10: C02.900), one patient with floor-of-mouth cancer (ICD-10: C04.900), and one patient with mandibular gingival cancer (ICD-10: C03.100). All patients underwent neck lymph node dissection during their initial surgery and received radical surgery for oral cancer; Five patients required free flap reconstruction and one patient used a local flap. Of the free flaps, one patient received a forearm flap and four patients received anterolateral thigh flaps, all of which survived. Clinical staging (AJCC) indicated that five patients were in stage III and one patient in stage IVB. Postoperatively, all six patients received radiotherapy with the radiation field involving the mandible, and an average radiation dose of 55 Gy was administered. Additionally, three patients received concurrent chemotherapy during radiotherapy. The basic information of these patients is depicted in Table 1.

Clinical signs

After completing radiotherapy and during the follow-up phase, all six patients sought medical attention due to oral or facial pain. Four patients experienced varying degrees of trismus (limited mouth opening), and five patients presented with oral ulcers of differing severity. Three patients exhibited bone exposure in the oral or facial regions, accompanied by symptoms such as fistulas, discharge, foul odor, and poor oral hygiene. All patients experienced some degree of dry mouth (xerostomia) and tooth loss; some also showed signs of tooth loosening and dental caries. The clinical signs of these patients are depicted in Table 2.

Table 3 Radiologic CT findings in the patients

Radiologic features	#1	#2	#3	#4	#5	#6
Soft tissue thickening	Y	N	Y	Y	Y	Y
Osteolysis/ bony erosion	Y	N	Y	Y	Y	Y
Trabecular disorganization	Y	Y	Y	Y	Y	Y
Bony sclerosis	N	Y	N	Y	N	N
Pathologic fracture	N	N	Y	N	Y	N
Osteomyelitic sequesetration	N	N	N	N	Y	N

Abbreviations: Y, yes; N, no

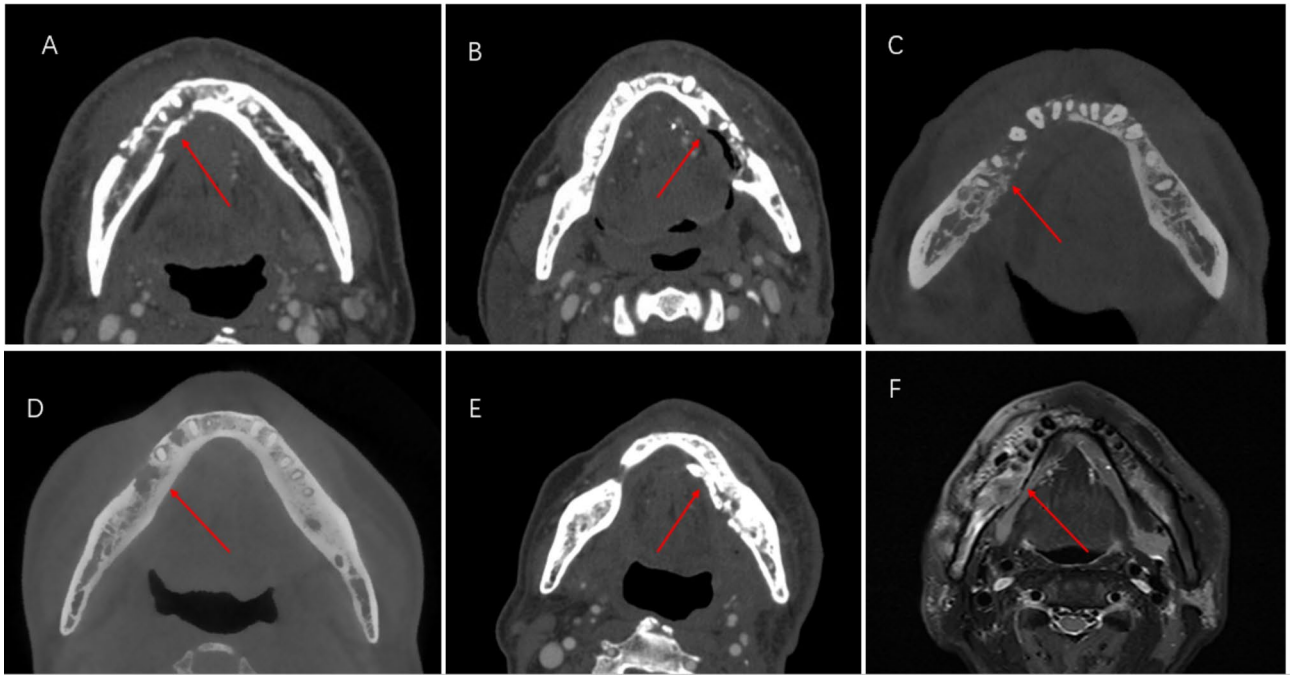

Fig. 1 Imaging examinations of these six patients. (**A**), patient 1. (**B**), patient 2. (**C**), patient 3. (**D**), patient 4. (**E**), patient 5. (**F**), patient 6

Imaging findings

In all six patients, changes in the trabecular structure of the mandible were observed. Five patients exhibited varying degrees of soft tissue thickening, edema, and moth-eaten bone invasion in the affected areas. One patient, who had titanium plate fixation during the initial surgery, developed nonunion of the bone following radiotherapy. Another patient experienced the formation of necrotic bone, which was accompanied by a pathological fracture. The imaging features of these patients are depicted in Table 3. The imaging findings of these patients are depicted in Fig. 1.

Treatment methods

Among the six patients, five were diagnosed with ORSCC by biopsies before surgical treatment or intraoperative frozen-section analysis. Five patients underwent soft tissue reconstruction: four utilized anterolateral thigh flaps, and one used a forearm flap. One patient received a fibula flap reconstruction. The treatment plans for these patients are depicted in Table 4. As a representative display, Patient #6 with recurrent squamous cell carcinoma of the right cheek, complicated by osteonecrosis, underwent resection of the lesion. The oral and facial soft and hard tissue defects were reconstructed using an anterolateral thigh free flap, as depicted in Fig. 2. Patient #4 who diagnosed with recurrent squamous cell carcinoma of the right cheek by intraoperative frozen-section analysis, underwent resection of the soft and hard lesion. The oral and facial soft and hard tissue defects were reconstructed using a fibula flap, as depicted in Fig. 3.

In the group of four patients who underwent anterolateral thigh flap reconstruction, one experienced vascular complication due to arterial occlusion, leading to flap necrosis. This patient subsequently underwent pectoralis major flap closure surgery, but developed a postoperative Pseudomonas aeruginosa infection. The other five patients showed good flap recovery with no significant signs of infection. In two out of the six patients, the ipsilateral vessels were of poor quality due to high radiation

Table 4 Treatment protocol

Therapeutic regimen	#1	#2	#3	#4	#5	#6
Salvage reconstruction	Y	Y	Y	Y	Y	Y
Flap type	ALT	RF	ALT	FF	ALT	ALT
Artery	LA	LA	Contralateral FA	LA	Contralateral FA	ECA/LA
Vein	EJV	EJV/FV	Contralateral FV	EJV/IJV	Contralateral EJV/AJV	EJV/IJV
Vascular crisis	N	N	Y	N	N	N
Postoperative infection	N	N	Y	N	N	N

Abbreviations: RF, radial forearm flap; ALT, anterolateral thigh flap; FF, fibular flap; LA, lingual artery; FA, facial artery; ECA, external carotid artery; EJV, external jugular vein; FV, facial vein; IJV, internal jugular vein; AJV, anterior jugular vein; Y, yes; N, no

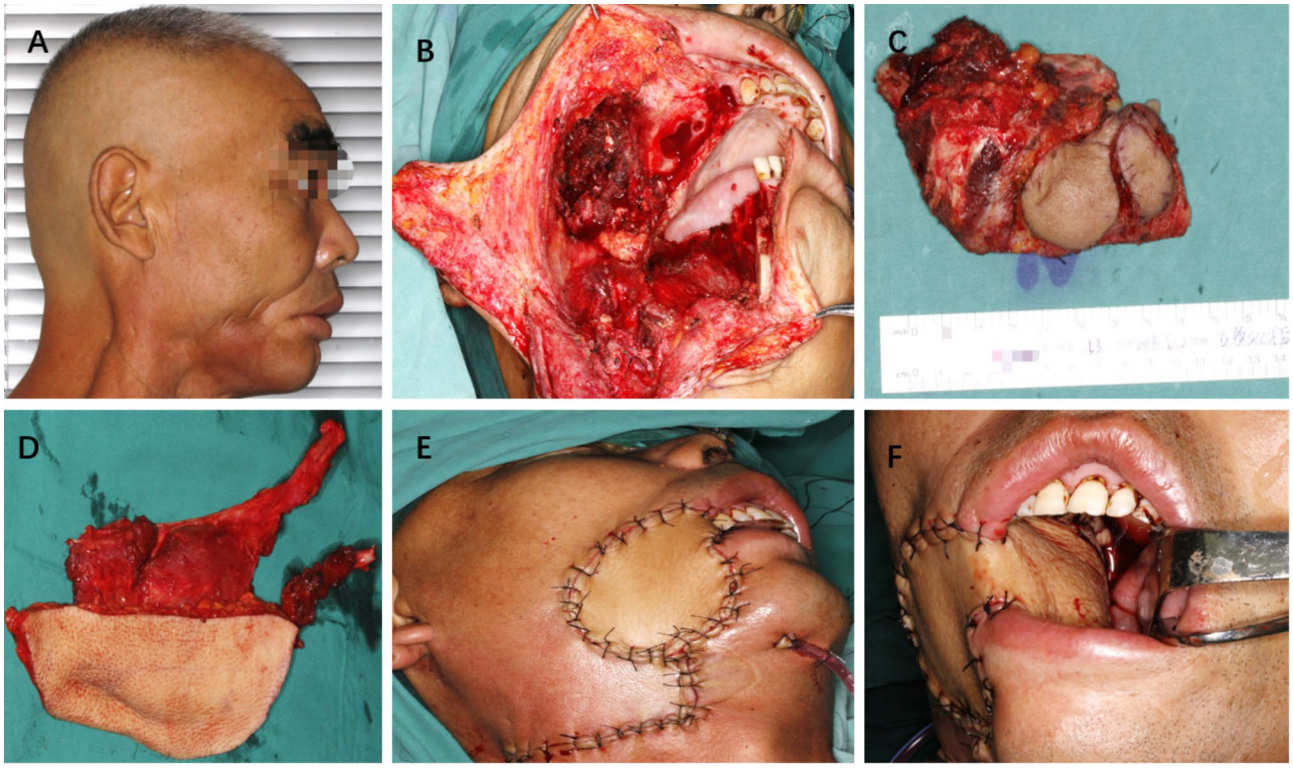

Fig. 2 Recurrent squamous cell carcinoma of the right cheek, complicated by radiation-induced osteonecrosis, underwent resection of the lesion. The oral and facial soft and hard tissue defects were reconstructed using an anterolateral thigh free flap. **A**: Preoperative condition of the patient's face; **B**: Condition of the oral cavity and face after lesion resection; **C**: Resected lesion; **D**: Harvested anterolateral thigh flap; **E-F**: Post-reconstruction appearance of the external face and oral cavity

doses, necessitating the use of contralateral vessels for reconstruction. For the remaining four patients, ipsilateral vessels were used for neck reconstruction.

Histopathology report

After surgical treatment, all six patients were confirmed with a recurrence of oral cancer at various sites by pathological diagnosis. Patient #1's recurrence was in the right mandibular gingiva (ICD-10: C03.100), diagnosed as squamous cell carcinoma. Patient #2's recurrence was in the left buccal mucosa (ICD-10: C06.001), diagnosed as squamous cell carcinoma and partial ossification of the left mandible surrounded by bacteria, with osteoclasts absent in the bone lacunae, indicative of radiation osteomyelitis. Patient #3's recurrence was in the right mandibular gingiva (ICD-10: C03.100), diagnosed as Grade III squamous cell carcinoma. Patient #4's recurrence was in the right buccal (ICD-10: C06.001) and right mandibular gingival regions (ICD-10: C03.100), diagnosed as moderately differentiated squamous cell carcinoma that infiltrated and destroyed the jawbone. Patient #5's recurrence was in the left lower mandibular gingiva (ICD-10: C03.100), diagnosed as Grade II squamous cell carcinoma. Patient #6's recurrence was in the right buccal mucosa (ICD-10: C06.001), diagnosed as high to moderately differentiated squamous cell carcinoma with infiltration into the striated muscle.

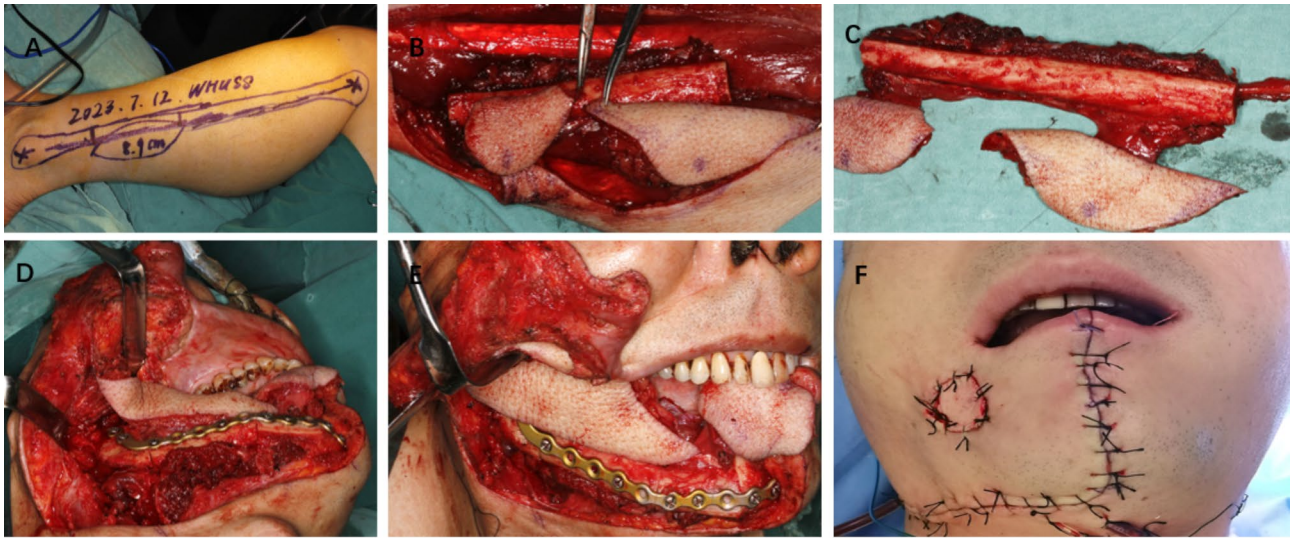

Fig. 3 Recurrent squamous cell carcinoma of the right cheek, complicated by radiation-induced osteonecrosis, underwent resection of the lesion. The oral and facial soft and hard tissue defects were reconstructed using a fibula flap. **A**: Marking diagram for the left fibula harvest; **B-C**: Harvesting the double skin paddle free fibula flap; **D-E**: Restoration of mandibular continuity and contour after shaping the free fibula; **F**: Post-reconstruction external facial appearance

Follow-up

All patients were successfully discharged. The median follow-up time for patients who were disease free as of their last follow-up was 33.6 months. The Patient #3 and Patient #5 experienced recurrences again at 3 months and 14 months, respectively. The Patient #1, #2, #4 and #6 were disease free at last follow-up were followed for 78 months, 38 months, 18 months and 17 months respectively.

Discussion

ORN is a severe complication following radiotherapy for head and neck tumors, with an incidence rate of 5–15% [12, 18]. ORN shares many clinical and radiological similarities with ORSCC and secondary primary malignancies, presenting significant challenges for clinical diagnosis and treatment. According to the literature, if similar symptoms arise within six months post-radiotherapy, there should be strong consideration of ORSCC or secondary primary malignancies. In this report, all six patients presented symptoms more than six months after radiotherapy, with all experiencing pain, foul odor, and exposed bone. Although these are typical symptoms of ORN, ORSCC was also discovered in these patients, suggesting that the common symptoms of ORN might mask or mimic signs of malignancy. Therefore, when diagnosing ORN, the possibility of concurrent ORSCC or secondary primary malignancies must be taken into account.

Clinically, distinguishing ORN from ORSCC or secondary primary malignancies based solely on symptoms is challenging. Radiologically, the presence of distinct solid or cystic masses is often regarded as a hallmark of ORSCC or secondary primary tumors [16]. When evaluating tumor recurrence, the presence of discrete masses provides important diagnostic clues. In cases of ORN, soft tissue thickening is usually associated with inflammation and edema in the surrounding muscle tissue [19–21]. In contrast, over 50% of patients with recurrent malignancies present with asymmetrical discrete masses, which are exceedingly rare in ORN and occur in only 2% of cases. Nearly half of the patients with recurrent malignant tumors exhibit cystic masses, whereas such findings are present in only 10% of ORN cases. This suggests that, in patients suspected of having ORN, the presence of cystic components should not be immediately assumed to be an abscess caused by osteomyelitis. Instead, the possibility of tumor recurrence should be considered [16]. However, our case report suggests that the soft tissue manifestations are not entirely consistent, and there is overlap in the presentation of ORN and ORSCC or secondary primary malignant tumors [22]. Literature reviews suggest that both conditions may be accompanied by soft tissue thickening, bone destruction, and bone sclerosis on CT scans [23, 24]. Some studies highlight that the most effective imaging feature to differentiate ORN from tumor recurrence is the presence of bone sclerosis [16]. Although some scholars argue that SCC is more likely to cause bone destruction rather than sclerosis, while ORN is more often associated with bone sclerosis [25, 26], in this report, all three patients exhibited bone sclerosis, which made it more challenging to distinguish between ORN and ORSCC based solely on this feature.

Literature suggests that CT and MRI can aid in the diagnosis of ORN; however, both imaging techniques have limitations when it comes to distinguishing active tumors from post-radiation tissue changes [27, 28]. Due to the small sample size and potential biases in this study, the generalizability of the conclusions is limited. Clinically, the differentiation between the two conditions ultimately relies on pathological diagnosis [29]. According to the literature, for patients clinically diagnosed with ORN alone, a biopsy prior to ORN resection is not recommended, as the small biopsy sample may be insufficient to detect malignancy unless the patient presents with clear clinical symptoms. In this report, one patient (#4) underwent preoperative evaluations that could not definitively determine the coexistence of both conditions. A pathological examination of the soft tissue within the external jawbone failed to yield a conclusive result. Following the complete resection of the affected ORN specimen, intraoperative frozen-section analysis of the surrounding soft tissue revealed the recurrence of malignancy. Then, a vascularized fibular flap was planned for reconstruction. Another patient (#5) was preoperatively diagnosed with radiation-induced osteonecrosis accompanied by a pathological fracture, extensive skin ulceration, exposed bone, and severe local soft tissue infection. Considering the patient's age, financial situation, and the severity of the infection, a free anterolateral thigh flap was chosen to repair the defect. Postoperatively, a small recurrence of malignancy was detected in the soft tissue within the osseous resection. In clinical practice, pathological examinations of ORN cases generally focus on representative samples rather than the entire specimen, which may lead to missed diagnoses of malignancies. Although our center has included only a small number of cases of ORSCC with ORN related clinical manifestation, we believe these cases will serve as helpful references for future research on distinguishing ORN with ORSCC or secondary primary malignancies.

Conclusion

In conclusion, this case series study suggests that malignant tumors may be present in specimens resected from patients clinically diagnosed with ORN. Therefore, clinicians should take into account the possibility of malignancy when diagnosing ORN. Moreover, this study also shared the challenges encountered in clinical practice and the selection of surgical options for patients, and provided a helpful reference for future clinical work.

Author contributions

S.-L Zhang: drafted the manuscript, contributed to data acquisition. S.-R Ma: drafted the manuscript. L. Mao: contributed to data acquisition. J.-C LI: contributed to conception and design, data acquisition and analysis, drafted and critically revised the manuscript; Z.-L Yu: contributed to data acquisition; drafted the manuscript. J. Jia: contributed to conception and design, data acquisition and analysis, drafted and critically revised the manuscript.

Funding

This work was supported by Guidance Project of the Scientific Research Program of the Hubei Provincial Department of Education (B2023109) and Beijing Xisike Clinical Oncology Research Foundation (Y-HR2022MS-0452).

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This case series study was reviewed and approved by the Institutional Medical Ethics Committee of School and Hospital of Stomatology, Wuhan University (WDKQ2024-B25). All studies were conducted in accordance with the Declaration of Helsinki. The requirement for written consent to participate was waived due to the case series study design, which was approved by the Institutional Medical Ethics Committee of School and Hospital of Stomatology, Wuhan University (WDKQ2024-B25).

Consent for publication

Informed written consent for publication of the details of their medical data was obtained from the patient in this study.

Competing interests

The authors declare no competing interests.

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Received: 23 September 2024 / Accepted: 3 February 2025
Published online: 13 February 2025

References

1. Lee IJ, Koom WS, Lee CG, Kim YB, Yoo SW, Keum KC, Kim GE, Choi EC, Cha IH. Risk factors and dose-effect relationship for mandibular osteoradionecrosis in oral and oropharyngeal cancer patients. Int J Radiat Oncol Biol Phys. 2009;75(4):1084–91.
2. Yang D, Zhou F, Fu X, Hou J, Lin L, Huang Q, Yeh CH. Symptom distress and interference among cancer patients with osteoradionecrosis of jaw: a cross-sectional study. Int J Nurs Sci. 2019;6(3):278–82.
3. Bras J, de Jonge HK, van Merkesteyn JP. Osteoradionecrosis of the mandible: pathogenesis. Am J Otolaryngol. 1990;11(4):244–50.
4. Chang CT, Liu SP, Muo CH, Liao YF, Chiu KM, Tsai CH, Huang YF. The impact of dental therapy timelines and irradiation dosages on osteoradionecrosis in oral cancer patients: a population-based cohort study. Oral Oncol. 2022;128:105827.
5. Marx RE. A new concept in the treatment of osteoradionecrosis. J oral Maxillofacial Surgery: Official J Am Association Oral Maxillofacial Surg. 1983;41(6):351–7.
6. Tsai CJ, Hofstede TM, Sturgis EM, Garden AS, Lindberg ME, Wei Q, Tucker SL, Dong L. Osteoradionecrosis and radiation dose to the mandible in patients with oropharyngeal cancer. Int J Radiat Oncol Biol Phys. 2013;85(2):415–20.
7. 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.
8. Pingarrón ML, Arias Gallo J, González Martín-Moro J, Palacios Weiss E, Burgueño García M. Rhytidectomy approach for surgical treatment of branchial cyst. Oral Maxillofacial Surg. 2010;14(1):1–2.
9. 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.

10. Støre G, Eribe ER, Olsen I. DNA-DNA hybridization demonstrates multiple bacteria in osteoradionecrosis. Int J Oral Maxillofac Surg. 2005;34(2):193–6.
11. Dose-volume correlates. Of mandibular osteoradionecrosis in Oropharynx cancer patients receiving intensity-modulated radiotherapy: results from a case-matched comparison. Radiotherapy Oncology: J Eur Soc Therapeutic Radiol Oncol. 2017;124(2):232–9.
12. Reuther T, Schuster T, Mende U, Kübler A. Osteoradionecrosis of the jaws as a side effect of radiotherapy of head and neck tumour patients–a report of a thirty year retrospective review. Int J Oral Maxillofac Surg. 2003;32(3):289–95.
13. Baldi D, Izzotti A, Bonica P, Pera P, Pulliero A. Degenerative periodontal-diseases and oral osteonecrosis: the role of gene-environment interactions. Mutat Res. 2009;667(1–2):118–31.
14. 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.
15. Wong ATT, Lai SY, Gunn GB, Beadle BM, Fuller CD, Barrow MP, Hofstede TM, Chambers MS, Sturgis EM, Mohamed ASR, et al. Symptom burden and dysphagia associated with osteoradionecrosis in long-term oropharynx cancer survivors: a cohort analysis. Oral Oncol. 2017;66:75–80.
16. Alhilali L, Reynolds AR, Fakhran S. Osteoradionecrosis after radiation therapy for head and neck cancer: differentiation from recurrent disease with CT and PET/CT imaging. AJNR Am J Neuroradiol. 2014;35(7):1405–11.
17. Liu SH, Chang JT, Ng SH, Chan SC, Yen TC. False positive fluorine-18 fluorodeoxy-D-glucose positron emission tomography finding caused by osteoradionecrosis in a nasopharyngeal carcinoma patient. Br J Radiol. 2004;77(915):257–60.
18. Moring MM, Mast H, Wolvius EB, Verduijn GM, Petit SF, Sijtsema ND, Jonker BP, Nout RA, Heemsbergen WD. Osteoradionecrosis after postoperative radiotherapy for oral cavity cancer: a retrospective cohort study. Oral Oncol. 2022;133:106056.
19. Chong J, Hinckley LK, Ginsberg LE. Masticator space abnormalities associated with mandibular osteoradionecrosis: MR and CT findings in five patients. AJNR Am J Neuroradiol. 2000;21(1):175–8.
20. King AD, Griffith JF, Abrigo JM, Leung SF, Yau FK, Tse GM, Ahuja AT. Osteoradionecrosis of the upper cervical spine: MR imaging following radiotherapy for nasopharyngeal carcinoma. Eur J Radiol. 2010;73(3):629–35.
21. Ng SH, Liu HM, Ko SF, Hao SP, Chong VF. Posttreatment imaging of the nasopharynx. Eur J Radiol. 2002;44(2):82–95.
22. Tufano-Sugarman AM, Wang KY, Kohn N, Ghaly M, Parashar B, Frank D, Kamdar D, Pereira L, Fantasia J, Seetharamu N. Osteoradionecrosis versus Cancer recurrence: an unresolved clinical dilemma. its Relat Specialties. 2023;85(1):28–35. ORL; journal for oto-rhino-laryngology.
23. Owosho AA, Tsai CJ, Lee RS, Freymiller H, Kadempour A, Varthis S, Sax AZ, Rosen EB, Yom SK, Randazzo J, 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.
24. Lambade PN, Lambade D, Goel M. Osteoradionecrosis of the mandible: a review. Oral Maxillofacial Surg. 2013;17(4):243–9.
25. Glastonbury CM, Parker EE, Hoang JK. The postradiation neck: evaluating response to treatment and recognizing complications. AJR Am J Roentgenol. 2010;195(2):W164–171.
26. Store G, Larheim TA. Mandibular osteoradionecrosis: a comparison of computed tomography with panoramic radiography. Dento Maxillo Fac Radiol. 1999;28(5):295–300.
27. Bisdas S, Chambron Pinho N, Smolarz A, Sader R, Vogl TJ, Mack MG. Biphosphonate-induced osteonecrosis of the jaws: CT and MRI spectrum of findings in 32 patients. Clin Radiol. 2008;63(1):71–7.
28. Cheng NM, Lin CY, Liao CT, Tsan DL, Ng SH, Yen TC. The added values of (18) F-FDG PET/CT in differentiating cancer recurrence and osteoradionecrosis of mandible in patients with treated oral squamous cell carcinoma. EJNMMI Res. 2023;13(1):25.
29. Marwan H, Green JM 3rd, Tursun R, Marx RE. Recurrent malignancy in Osteoradionecrosis Specimen. J oral Maxillofacial Surgery: Official J Am Association Oral Maxillofacial Surg. 2016;74(11):2312–6.

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