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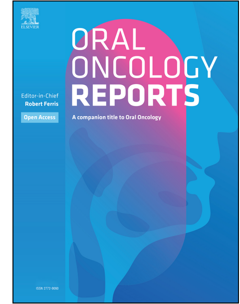

Atypical presentation of medication-related osteonecrosis of the jaw in a young male patient undergoing chemotherapy for acute lymphoblastic leukemia

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Title: Atypical Presentation of Medication-Related Osteonecrosis of the Jaw in a Young Male Patient Undergoing Chemotherapy for Acute Lymphoblastic Leukemia

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Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Letter to the editor

Title: Atypical Presentation of Medication-Related Osteonecrosis of the Jaw in a Young Male Patient Undergoing Chemotherapy for Acute Lymphoblastic Leukemia

Abstract
This case report aims to highlight the importance of close oral monitoring before and during chemotherapy in patients with B-cell acute lymphoblastic leukemia (B-ALL) to prevent medication-related osteonecrosis of the jaw (MRONJ). A 22-year-old male patient diagnosed with B-ALL who developed MRONJ during chemotherapy, despite not receiving bisphosphonates or denosumab, was presented. The patient's medical history, treatment regimen, clinical examination findings, and treatment outcomes were reported. The patient developed maxillofacial cellulitis during chemotherapy, leading to a diagnosis of stage 3 MRONJ. Conservative treatment was initiated, resulting in the reversion of the disease to stage 1 and stabilization of the progression. The patient achieved remission and underwent prophylactic cranial radiotherapy. This case report presents a unique case of MRONJ in a young patient without prior use of antiresorptive agents or denosumab. It highlights the need for close oral monitoring in patients with B-ALL before and during chemotherapy, as MRONJ can develop in the absence of these medications.

Keywords: Acute lymphoblastic leukemia, Chemotherapy drugs, Medication related osteonecrosis of the jaw

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Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is an adverse event characterized by progressive destruction and necrosis of the mandibular and/or maxillary bone, without prior radiation therapy [1]. Although it is rare in the general population, it is commonly encountered in clinical settings when considering the frequency of medication use. MRONJ is more frequently observed in women, older individuals, and in the mandible. Antiresorptive medications (such as bisphosphonates and denosumab) and antiangiogenic drugs (such as anti-VEGF, TKIs, and mTOR inhibitors) are the most commonly implicated medications in the development of MRONJ due to their effects on bone metabolism [2]. Preventive dental treatments prior to initiating medication can reduce the incidence of MRONJ [3].

B-cell acute lymphoblastic leukemia (B-ALL) is the most common cancer in children and has a multifactorial etiology [4]. Its treatment typically involves high-dose chemotherapy and, in some cases, allogeneic stem cell transplantation [5]. In recent years, monoclonal antibodies and targeted therapies have been considered promising advancements in the management of B-ALL [6].

This case report presents a 22-year-old male patient diagnosed with B-ALL who developed MRONJ during chemotherapy, despite not receiving bisphosphonates or denosumab. The aim of this report is to highlight the importance of close oral monitoring before and during chemotherapy in patients with B-ALL.

Case Report

Informed consent was obtained from the patient for presentation of this case report. The participant in this case report is a 22-year-old male patient who presented with complaints of leg pain. He had no known allergies and had no history of smoking or alcohol use. The patient was referred to a medical center in 2022, where a pathology sample was taken for diagnosis of acute leukemia. The pathology report confirmed B-ALL, and the patient initiated chemotherapy treatment.

The patient received 4 cycles of HyperCVAD chemotherapy, which consisted of the following drugs and dosages: Cyclophosphamide (total dose: 2750mg), dexamethasone (total dose: 280mg), doxorubicin (total dose: 90mg), vincristine (total dose: 4mg), methotrexate (total dose: 1874mg), calcium folinate (total dose: 30mg), cytarabine (total dose: 10900mg), and mesna (total dose: 9700mg).

During the course of chemotherapy, the patient developed maxillofacial cellulitis, leading to a referral to the Oral and Maxillofacial Surgery Clinic. Upon clinical examination, a 2 cm diameter exposed bone was observed in the posterior region of the left maxilla, at the level of the palatal bone. Aa MRI revealed that the lesion extended into the maxillary sinus, accompanied by oro-antral communication. Based on the classification system developed by Ruggiero et al., the patient was diagnosed with stage 3 MRONJ [7] and was placed under 15-day follow-up (Figure 1).

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The initial treatment for the patient's acute infection was initiated with antibiotics (amoxicillin and clavulanate 1g, one tablet every 12 hours for 21 days) and chlorhexidine 0.2% mouthwash (every 12 hours). After eigth months, the exposed bone tissue had expanded to a diameter of 4 cm, severe mobility of the posterior maxillary teeth was observed, and a spontaneous demarcation line was observed around the necrotic bone. The patient continued to use chlorhexidine mouthwash for the entire three-month period (Figure 1).

After six months, the patient did not report any complaints, and he was classified as stage 1 MRONJ. Control bone marrow aspiration showed remission, and the patient underwent prophylactic cranial radiotherapy. Autologous peripheral stem cell transplantation was performed, and the patient continued to be monitored for complete remission.

Discussion

This case report describes a unique case of medication-related osteonecrosis of the jaw (MRONJ) in a young patient without prior use of bisphosphonates or denosumab. The patient's age, rapid progression of the disease after the initiation of chemotherapy, remission with conservative treatment, and reversion to stage 1 make this case distinct. The development of MRONJ in this patient can be attributed to the risk factor of immunosuppression due to the use of corticosteroids and multiple drugs.

To our knowledge, this is the youngest B-ALL patient case of MRONJ without the use of antiresorptive agents or denosumab in the literature. Although studies on the risk of MRONJ in the adult population are more extensive [8], there have been no reported case reports concerning the pediatric population [9]. Consequently, making clinical decisions regarding these patients is challenging due to limited information on the incidence in the young population. A systematic review that included children and young adults reported no cases of necrosis associated with bisphosphonates between 2003 and 2018 [10]. This case report is consistent with previous gender-based epidemiological studies (55% male), but not with age-based epidemiological studies (mean age = 61).

The medications used in the treatment of B-cell acute lymphoblastic leukemia (B-ALL) in this case include cyclophosphamide, dexamethasone, doxorubicin, vincristine, methotrexate, calcium folinate, cytarabine, and mesna. While each of these medications can have side effects such as bone marrow suppression, immunosuppression, and tissue damage, there is no strong evidence in the current literature to suggest that these agents directly increase the risk of MRONJ [11]. Corticosteroids and methotrexate impede bone healing, with the former suppressing bone remodeling and angiogenesis, and the latter inhibiting osteoblastic activity. Both elevate the risk of infection and necrosis [12]. This treatment regimen can generally decrease the patient's overall immune competence, potentially creating a susceptible environment for secondary infections and complications.

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The decision to employ conservative treatment in this case was successful in reverting the disease from stage 3 to stage 1 and stabilizing the progression of the disease after the removal of necrotic bone. Conservative treatment options for MRONJ typically include oral hygiene measures, antibiotics, analgesics, and local debridement [13]. In this case, the use of conservative treatment proved to be effective in managing the disease and preventing further complications.

Conclusion

In conclusion, MRONJ remains a complex healthcare challenge, affecting an increasingly diverse demographic and elicited by various medications. This report affirms that MRONJ can occur without antiresorptive agents. Given the absence of standardized treatment protocols, pre-medication dental evaluations are crucial for all patients at risk. Further research is needed to understand MRONJ risk in younger individuals undergoing chemotherapy.

Acknowledgment

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Figure Legends

Figure 1. Composite image showcasing different diagnostic modalities of the patient. (A) Preoperative axial slice MRI of the patient. (B) Preoperative panoramic radiograph. (C) Image displaying the sequestrated necrotic bone.

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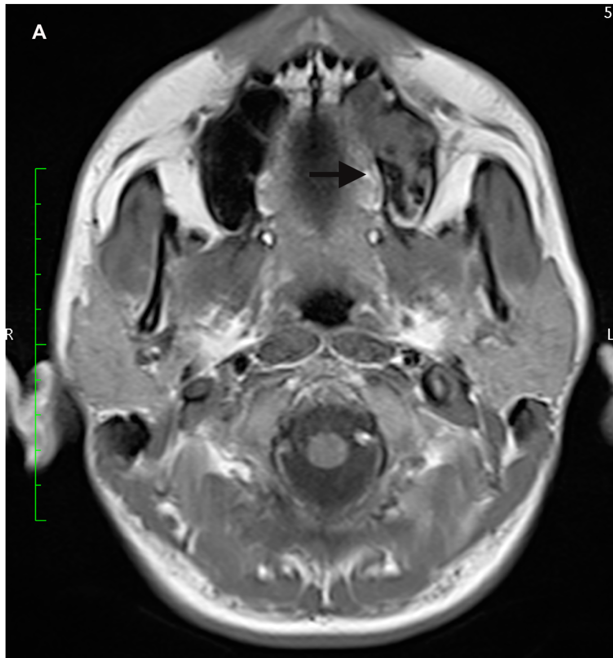

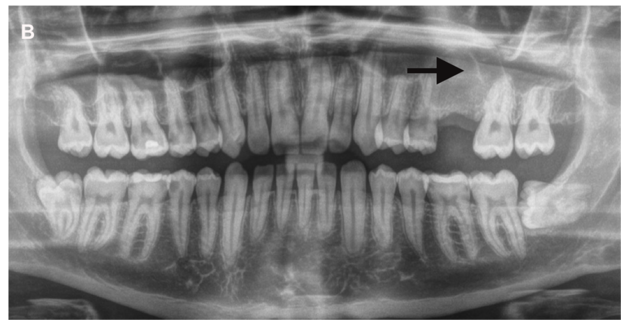

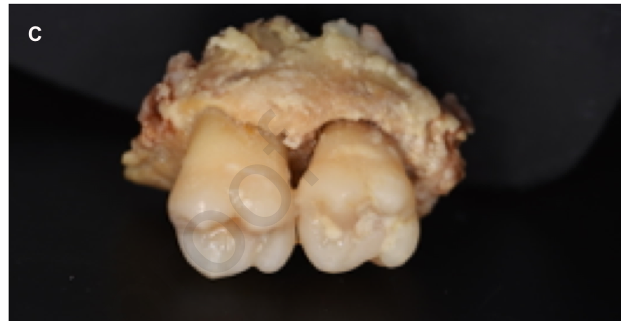

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- Presents a rare case of MRONJ in a young B-ALL patient without exposure to bisphosphonates or denosumab.
- Emphasizes the rapid progression and remission of MRONJ under conservative treatment in a pediatric leukemia patient.
- Highlights the necessity for dental evaluation prior to initiating medications with potential effects on bone metabolism across all age groups.

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Declaration of interests

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