Case Report

Dental implants in oral rehabilitation after denosumab and bisphosphonate-related osteonecrosis of the jaw in a young patient: an unusual case

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Abstract – Patients often request oral rehabilitation after surgical resection. Here, a 19-year-old patient developed medication-related osteonecrosis of the jaw after treatment with antiresorptive therapy. After the surgical treatment for osteonecrosis, dental implants were discussed. While there is a known risk of provoking secondary osteonecrosis of the jaw in such cases, other factors should also be taken into account. This case report highlights the importance of close monitoring for patients with a history of medication that incurs a risk osteonecrosis, and the feasibility of dental implants on the surgical site in some conditions. Decisions relative to implant placement were made based on the patient’s specific history, their present situation, and the potential options that were available.

Introduction

Giant cell tumors (GCT) of bones affect bones but also spread to the soft tissues. GCT represents about 5% of primary bone tumors and develops most often in younger patients 20 to 40 yr of age. This condition is aggressive due to its osteolytic properties and the proliferation of giant cells. It is classified as intermediate grade tumors in the WHO 2020 classification [1,2]. Surgical treatment is generally associated with antiresorptive therapy such as denosumab to minimize the risk of recurrence.

Medication-related osteonecrosis of the jaw (MRONJ) is a potentially devastating condition with disabling functional consequences. The prevalence and incidence rates are difficult to estimate because of the reporting bias for this condition, but several meta-analyses have attempted to manage these biases [3,4]. The prevalence can be estimated at between 1% and 15% in cancer patients treated with bisphosphonate (BPP) or denosumab, while the rate is only 0.01% for patients who have non-malignant conditions such as osteoporosis.

When damaged bone is exposed to germs, there is a risk that healing will be delayed. The risk of morbidity and mortality is high in such cases, and there is an uncertain therapeutic arsenal, because official guidelines have not been established. MRONJ severity is classified by the American Association of Oral and Maxillofacial Surgeons (modified in 2022) from stage 0 to 3 [5].

This case report presents a patient with MRONJ. It is of interest because of the patient’s young age, 19-year-old when osteonecrosis was developed, the associated complications and the therapies performed (curettage and dental rehabilitation). After discussion with the patient, rehabilitation with implant initiated 1 yr after the surgical resection. In individuals treated with BPP or denosumab or post-MRONJ, the use of implants must be carefully assessed before placement. This is a topic that is not yet well described in the literature. Only 2 clinical cases in older osteoporosis patients [6,7] have described post-curettage implant placement in MRONJ after intravenous bisphosphonate.

Finally, we placed 2 implants on the site that had been operated on for osteonecrosis. The implants were perfectly Osseo integrated. There was no recurrence of osteoradionecrosis and the mucosal healing was sufficient to support the implants and be impermeable at 2 yr follow-up.
Case report

A 20-year-old patient was referred to the odontology department of our hospital for a history of progressive left maxillary swelling since a year. The symptoms were initially attributed to a dental abscess, so her dentist performed a root canal treatment of the first left premolar.

The patient’s medical history was notable for a GCT with an aneurysmal cyst on a pathological fracture of the right femoral neck, detected at age 12. Surgical treatment was associated with an anti-resorptive treatment (denosumab) until she was 18 yr old, administered monthly, to prevent recurrence. Subsequently, at the end of denosumab, the patient developed hypercalcemia of malignancy. It was treated with intravenous (IV) BPP (Zometa 4 mg).

The clinical examination in our unit revealed, terminal mobility of the first left premolar with pathological migration, swollen, purulent discharge from the sulcus of the first left premolar. Radiological investigations by orthopantomogram and cone beam-CT (CBCT) showed an osteolytic lesion, with a clearly individualized maxillary bone sequestrum, including the left lateral incisive to the first molar (Fig. 1). The clinical and radiological examination, associated with the patient’s history, suggested MRONJ, which likely began at the age of 19. The biopsy confirmed the diagnosis. Curative treatment consisted of left maxillary sequestrectomy with extraction of the left canine, the premolar and first molar. The curettage was complicated by oro-antral communication, which was closed with an advanced flap. A platelet-rich fibrin (PRF) membrane was placed on the deep plane between the communication and the flap to promote healing of the mucus membrane. A resorbable collagen membrane (BioGide®) was placed to isolate the bone during healing and avoid excessive invagination of the soft tissue, which can complicate the healing process and the future prosthetic rehabilitation (Fig. 2). This young patient requested a long-term fixed prosthetic solution, but she was offered a provisional removable partial denture until re-evaluation.

Eighteen months after curettage of the osteonecrosis and 3 yr after the end of denosumab and zoledronic acid, following a collegial decision, we initiated oral rehabilitation, in order to fulfil our patient’s desire for permanent implants. In view of the general context and the fact that implants were being offered outside the usual therapeutic framework, an indication for the placement of two implants was retained, avoiding bone graft as much as possible. Preoperative CBCT evaluation revealed satisfactory bone healing with overall favorable available bone volume but with vertical loss and a cupuliform depression at Fig. 1. CBCT. Medication-related osteonecrosis of the maxillary, localized to the left maxillary bone.
the crest (Fig. 3). The operation consisted of the placement of two implants, one to replace the left canine and one to replace the left first molar (NobelActive 4.3*10 mm and 5.0*8.5 mm) (Fig. 4). Implantation was achieved on very sparse bone, type 4 according to the Lekholm and Zarb classification. The post-implant course was favorable with no complications or recurrence of osteonecrosis and satisfactory healing. Implants were exposed and healing abutments placed, followed by prostheses (Figs. 5 and 6). The 2 yr clinical and radiological follow-up was uneventful.

Discussion

While it is both recommended and necessary to conduct an oral evaluation before prescribing an antiresorptive treatment, there was no evidence that a dental examination was performed in this patient before the start of denosumab or bisphosphonates. The initial symptoms were treated as a dental infection with an endodontic treatment and then as periodontal disease. Clinical manifestations of MRONJ can include pain, localized edema, secondary infection, dental mobility, and bone exposure [8]. In the literature, the probability of a young patient developing MRONJ is extremely low. A recent systematic review of the literature demonstrated the absence of such recorded cases of MRONJ [9]. Of the more than 600 children treated with BPs in this review, none developed osteonecrosis. However, it should be noted, that the study did not include case reports. A systematic review from 2021 of any type of antiresorptive therapy, including denosumab, in young people still found no cases of MRONJ [10].

It would be interesting to study cases of MRONJ occurring in patients with the same condition undergoing the same treatment. The fact that giant cell tumors are uncommon makes the probability of MRONJ particularly rare. A prospective study [11] of 97 patients with GCT treated with denosumab found no cases of osteonecrosis of the jaw. In 2017 and in 2019, MRONJ cases were described in individuals receiving denosumab. In the first one, the authors describe 6 out of 97 patients treated between 2006 and 2015 (6.1%) developed osteonecrosis of the jaw [12]. The origin of MRONJ is also multifactorial, with the presence of confounding factors. In a 2019 cohort [13] with 16 treated with denosumab for an osteonecrosis incidence of 2.8% (7/250 patients) was reported, in all age groups. Only 5% of patients were adolescents. The outcome was found to be dose and duration dependent.

In summary, the occurrence of maxillary bone necrosis in a 19-year-old patient treated with denosumab and bisphosphate (single dose) is highly uncommon.

Implant placement in patients with a history of antiresorptive therapy is much debated in the current literature, particularly related to the occurrence of osteonecrosis and the prognosis of the implant.

International recommendations [5] do not provide cut-guidelines. It is accepted that the risk of osteonecrosis of the jaw after using oral bisphosphonates for a benign condition is low, so implant placement is not contraindicated. For malignant diseases treated with IV bisphosphonates over the long term, implant placement is contraindicated. However, there are no established recommendations for short-term IV bisphosphonates therapy (single or limited injections). For denosumab, the risk of osteonecrosis is dose- and duration-dependent [5, 14]. The AAOMS takes the same precautions as for BPs. For nonmalignant disease, drug holidays are controversial and should be evaluated individually [5]. The rarity of MRONJ makes it difficult to establish a safe drug holiday.

The incidence of MRONJ is low (between 0.001% and 0.1%) for benign disorders with oral administration, but increases to 1 to 10% in malignant disorder [5, 6, 15]. Concerning implant therapy, the benefit/risk ratio must be weighed. For our patient, for decision-making, we took into account her young age and excellent oral hygiene, the fact that she was non-smoking, in remission for GCT (intermediate grade, locally aggressive), and the antiresorptive therapy stopped since 3 yr.

Literature reviews that discuss implants after treated MRONJ have been published. However, after elimination of duplicates and case reports, we identified a small number of cases with both MRONJ and dental implants make it difficult to come to a firm conclusion.

A systematic review from 2021 [16] assessed implant failure and the appearance of osteonecrosis of the jaw in patients with a history of BPs or denosumab treatment. Concerning implant success, there was no significant difference between cases (3074) and controls (8605) [16]. In terms of osteonecrosis, the mean incidence of MRONJ was 12.3% (2841 implants in 830 patients, 102 cases of MRONJ), depending on dose and duration treatment.

In the randomized study by Watts et al. [17], 1 out of 212 patients who received Denosumab developed an osteonecrosis. This patient was treated with extractions, sinus lift and the simultaneous placement of two implants, without stopping denosumab. The literature suggests that there is a risk of developing osteonecrosis following dental implants, but it does not seem to be increased for patients treated with BPs or denosumab for a benign condition.
Here, the residual bone height after curettage was low, but horizontal volume was preserved. In a healthy patient with no relevant disease history, we would have done pre-implant bone grafting in order to level the crestal bone and to provide an ideal setting for the placement of implants. In a patient such as ours, it is difficult to predict how the bone will react to the implant, notably due to the intake of IV BPP and the theoretical risk of recurrence of MRONJ. We found a compromise by placing two implants for an implant-supported bridge, without modifying the bone. This required only a single surgery, thus reducing the risk of osteonecrosis and hazards related to wound healing.

Fig. 3. CBCT related to dental implant planning.

Fig. 4. Orthopantomogram. Implants surgery — replace the left canine and the left first molar.

Fig. 5. Placement of healing abutment associated to a non-invasive vestibuloplasty.
**Conclusion**

The rather unique situation of the patient presented here required careful consideration due to the factors that were favorable to her desire for implants (i.e., time elapsed since curettage of MRONJ, optimal oral hygiene and regular follow-up, non-smoking...). The chosen treatment has been successful so far. Follow-up has been implemented. MRONJ can result in tooth loss and complex removable prosthesis. After curettage for osteonecrosis, oral rehabilitation with a removable prosthetic is recommended to preserving the impacted site, functional goal and improving quality of life, but implants are possible in some cases, as shown in this report.

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**Data availability statement**

The datas will be made available upon request.

**Author contribution statement**

**N. Salabert**: Conception and design of the article, acquisition of data, drafting the article; **L. Loison-Robert**: acquisition, analysis and interpretation of data; **V. Ahossi**: supervision, final approval; **D. Hoarau**: Conception and design of the article, acquisition, analysis and interpretation of data, review & editing the article, visualization.

**Ethics approval**

This article follows the International Standards for Authors published by the Committee on Publication Ethics (COPE). This case report does not involve any deviations during treatment, ethical approval was not required through a specific protocol.

**Informed consent**

The experiments were undertaken with an understanding of the diagnosis, a decision on the treatments and their risks. The patient also understood and accepted publication of the article in a journal. The physical elements in the photos make it impossible to identify the person. Informed consent was obtained verbally before participation.

**References**


