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Non-Surgical Treatment of Medication-Related Osteonecrosis of the Jaw with Essential Oils: A Case Report

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Abstract

Medication-related osteonecrosis of the jaw (MRONJ) is a severe adverse reaction associated with antiresorptive therapy, where non-surgical treatment remains limited. We report the case of a 70-year-old female patient with breast cancer and bone metastases, who developed stage 2 MRONJ after treatment with denosumab. Due to contraindications for surgical intervention, a conservative, integrative therapeutic approach was adopted, using the topical application of a specific combination of essential oils (EOsZG). Notably, 260 days after initiating this therapy, the patient spontaneously expelled a 2 cm necrotic bone sequestrum, marking a critical turning point that demonstrated a favorable response, leading to rapid symptom resolution and progressive soft-tissue healing. In conclusion, local treatment with essential oils may facilitate sequestrum demarcation and spontaneous separation. The therapeutic effects are likely driven by the antimicrobial activity of EOsZG, their penetrative capacity of necrotic tissue, enhancement of local microcirculation and accelerated debris removal via leukocyte activation between necrotic and healthy tissue. This case suggests topical essential oil therapy is a viable, effective non-surgical strategy that results in significant improvement in MRONJ.

Keywords

MRONJ, Oncology Patient, Non-Surgical Treatment, Essential Oils

1. Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is a serious, adverse drug reaction that is most commonly observed in oncological patients having received

antiresorptive therapies such as denosumab [1]-[3]. Its incidence has increased with the widespread use of denosumab as a potent bone-modifying agent in cancer-related skeletal diseases [1]. Denosumab (marketed as Xgeva for oncologic indication) is a fully human monoclonal antibody that inhibits osteoclast formation and function, therefore reducing bone resorption and increasing bone mineral density [4]. However, its suppression of bone remodeling may result in impaired mucosal healing and predispose patients to osteonecrosis, particularly after invasive dental procedures. The mandible is more frequently affected than the maxilla, perhaps due to its relatively lower vascularity and higher remodeling rate in terms of masticatory forces [5]. Management of MRONJ in patients who have received high-dose denosumab (120 mg) remains challenging, particularly with regard to wound healing and infection control [1]. The condition often follows a prolonged clinical course, with no universally accepted protocol of treatment having yet been established. Current management strategies are primarily supportive, focusing on symptom control, infection management and clinical monitoring. The present report describes a case of denosumab-induced osteonecrosis of the mandible, with particular emphasis on the rationale for adopting a conservative treatment with essential oils.

2. Case Presentation

It should be noted that the patient has provided informed consent in writing for the publication of this case report. Briefly, the patient was diagnosed with breast cancer four years ago. Initial diagnostic PET/CT imaging showed mildly increased metabolic activity in the skeletal system, specifically in the region of pre-existing sclerotic lesions at the right costovertebral junction, involving the 11th rib and the 8th thoracic vertebra. In addition, mildly increased metabolic activity was observed in a sclerotic lesion on the proximal right humerus. The patient reported a previous traumatic event involving the right shoulder. In this context, metastatic involvement of the bones remained inconclusive and therefore high-dose denosumab therapy was not sufficiently precise. Concerning treatment, the patient underwent four cycles of chemotherapy according to a docetaxel-based protocol, resulting in a complete metabolic response as demonstrated by PET/CT imaging. Following completion of chemotherapy, target therapy with abemaciclib and letrozole, along with the osteomodulator denosumab, was initiated. After 36 months of denosumab treatment, the patient was diagnosed with medication-related osteonecrosis of the jaw (MRONJ), stage 2 (**Figure 1**), and denosumab therapy was discontinued. On the most recent evaluation, after five routine follow-up PET/CT scans, the patient remains in remission with a complete metabolic response. She is a non-smoker, and her only comorbidity is thalassemia minor.

Figure 1 presents the timeline following the diagnosis of stage 2 MRONJ and the initiation of treatment with essential oils. Based on the anamnesis, the patient's complaints consisted of swelling, pain and the presence of a gingival fistula.

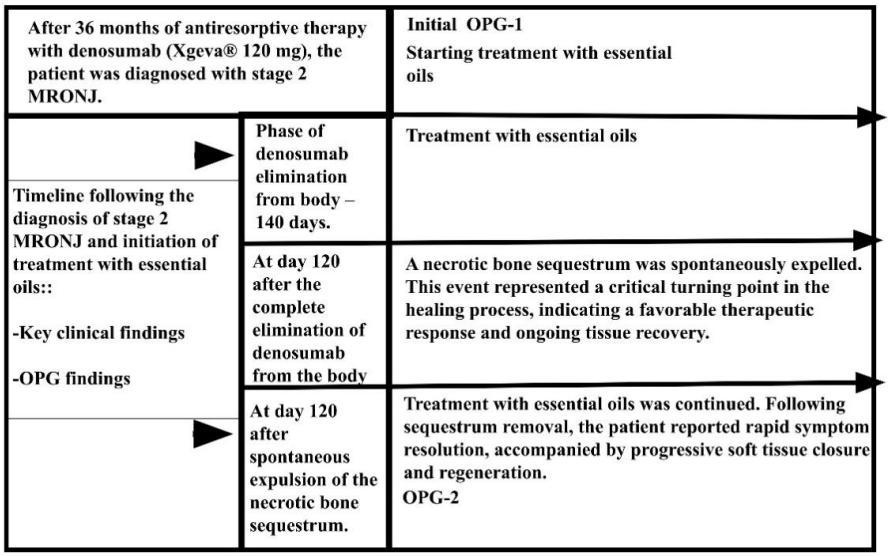

Figure 1. Timeline of the present case. After 36 months of antiresorptive therapy with denosumab (Xgeva® 120 mg), the patient was diagnosed with stage 2 MRONJ according to the criteria of the American Association of Oral and Maxillofacial Surgeons [6]. Timeline illustrates the clinical course following the diagnosis and initiation of treatment with essential oils, including key clinical and OPG findings.

Following a clinical examination by a dentist and evaluation of the initial orthopantomogram (OPG-1, **Figure 2(A)**), the following findings were observed: (i) on objective examination, a fistula was identified in the left premolar region of the mandible, corresponding to the projection of tooth 33. No suppuration or bone exposure was observed in the maxilla or in other regions of the mandible. The parotid glands and cervical lymph nodes revealed no palpable pathological masses. The submandibular region was unremarkable. (ii) Based on the OPG-1 findings (**Figure 2(A)**), the mandible was confirmed to be edentulous.

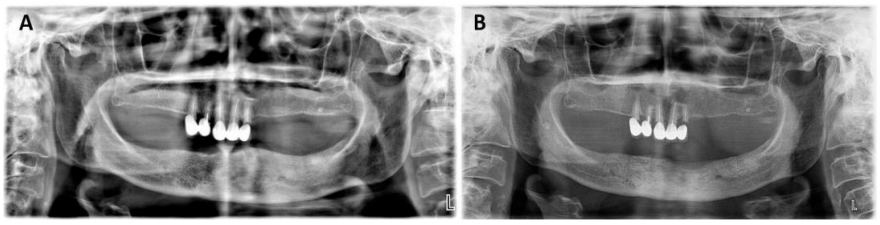

Figure 2. OPGs obtained before and after treatment with essential oils. (A) at the time the patient was diagnosed with stage 2 MRONJ; (B) after sequestrum removal and treatment with essential oils.

Evidence of a previous extraction socket was observed at the site of tooth 33, which had been extracted three months earlier. Osteonecrosis had developed in the region of the extracted tooth. The condition was classified as stage 2 MRONJ. The patient was offered surgical intervention after complete elimination of denosumab from the body (approx. 140 days). However, the treating oncologist expressed the opinion that surgical treatment was contraindicated in this case. Con-

sequently, during this period, the patient initiated treatment with essential oils, following a strictly designed protocol. The treatment course and its effects can be conditionally divided into two stages: (i) the period prior to the complete elimination of denosumab from the body, and (ii) the period following its elimination. During the initial phase, the patient continued to report gingival discomfort and irritation. She described the sensation as "sand stuck in [her] gums" and reported a persistent urge to manipulate the affected area with cotton swabs. These symptoms were associated with the gradual release of small necrotic materials. On clinical examination by a craniofacial surgeon, signs of gingival irritation, erythematous and ulcerated mucosa were observed in areas where necrotic fragments protruded or perforated through the gingiva. During the second period (ii), following the complete elimination of denosumab and specifically 120 days later, the patient spontaneously shed a necrotic bone fragment (sequestrum) measuring approximately 2 cm (Figure 3).

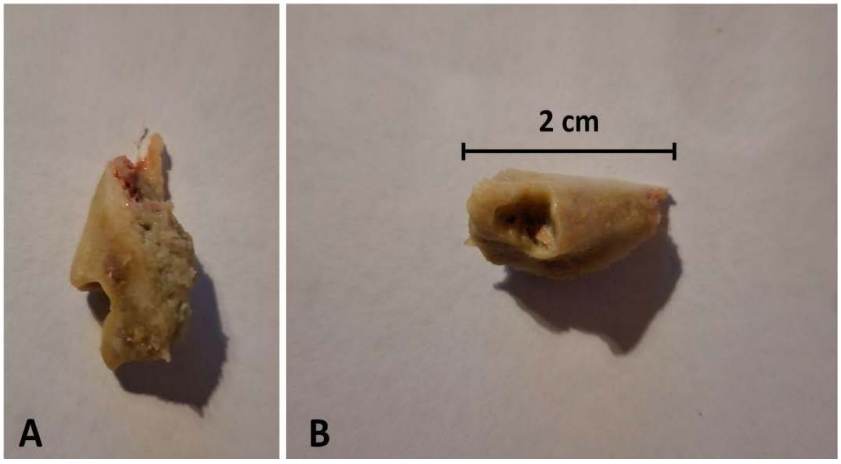

Figure 3. Photographs of the necrotic bone sequestrum in two positions (A and B), which was spontaneously expelled following treatment with essential oils.

This event represented a critical turning point in the healing process, indicating a favorable therapeutic response and ongoing tissue repair. The spontaneous shedding of the sequestrum reflects the body's inherent capacity to eliminate devitalized bone tissue. Following its expulsion, the patient reported rapid resolution of symptoms, accompanied by progressive soft-tissue closure and regeneration.

The OPG-2 findings (Figure 2(B)) indicate bone remodeling and gradual regression of the osteonecrotic changes following sequestrum separation, consistent with a favorable healing course after conservative local treatment. Imaging findings demonstrated reduction of the previously identified osteolytic area, partial restoration of the trabecular bone architecture, and smoothing with sclerosis of the bony margins in the affected region. No evidence of new sequestration was found.

Essential oils are increasingly being investigated in dentistry as adjuncts to conventional therapies for gingival inflammation and infection, due to their antimi-

crobial and anti-inflammatory properties [7]. They also demonstrate considerable potential for development as therapeutic agents for a variety of oral diseases [8]. In this respect, our attention was focused on their potential application in MRONJ cases. In this one, a local treatment of the patient's gingiva was performed using combinations of essential oils, collectively referred to as EOsZG. This formulation was developed following a multimodal pharmacological approach aimed at microbial control, modulation of local inflammation and promotion of tissue repair. The essential oils were diluted in a carrier oil base consisting of *Simmondsia chinensis* and *Prunus amygladus dulcis* to a final concentration of approximately 5% - 10% (v/v), with adjustments made according to local tolerability. Details about composition of EOsZG are provided in **Table 1**. The structured distribution of functional groups balances antimicrobial efficacy with tissue compatibility and may facilitate sequestrum demarcation, microbial control, and subsequent healing in MRONJ. Particular attention was paid to optimize the dose and local tolerability. Phenol-rich and ketone-containing components were maintained at carefully controlled low concentrations to minimize risk of cytotoxicity. Prior to clinical application, the formulation was tested for local tolerability and no adverse reactions—such as increased pain, ulceration, or chemical irritation—were observed during treatment.

Table 1. Composition of essential oils prepared for the patient.

Functional groups	Essential oils	Concentrations	Activity
Phenol-rich essential oils	*Cinnamonum verum*, *Syzygium aromaticum*	at low concentrations ≤ 1% each; total 1% - 2%	To ensure potent antimicrobial activity while minimizing mucosal irritation.
Anti-infective and tissue-penetrating oils	*Leptospermum scoparium*, *Lavandula stoechas*	forming the core of the formulation 2% - 3%	To contribute to broad-spectrum antimicrobial effects and diffusion into poorly vascularized tissues.
Circulation-modulating components	*Mentha piperita*, *Citrus limon*	1% - 2%	Supporting local microcirculation and enhancing tissue permeability
Regenerative and immunomodulatory oils	*Commiphora myrrha*, *Salvia officinalis*	1% - 2%	Included to support tissue repair and modulation of local inflammation.

The use of essential oils here strikes an optimal balance between antimicrobial efficacy and potential mucosal irritation. In this case, careful titration of the dose allowed effective microbial control while preserving tissue integrity. Favorable clinical results indicate that, under controlled conditions, the therapeutic benefits may outweigh the potential risks.

The essential oils were applied topically by smearing the affected area of the gum, 3 times daily, following a 5-day on-and-2-day off schedule. The patient was controlled periodically by the dentist for tolerability of essential oils and side effects.

In addition, the essential oils combination (EOsZG) was evaluated *in vitro* for

antimicrobial activity against reference strains of *Candida albicans* and *Staphylococcus aureus*, using the standard Kirby-Bauer disk diffusion method [9], which is widely used to evaluate the inhibitory potential of antimicrobial agents against bacterial and fungal microorganisms. The results demonstrated pronounced antimicrobial effects, as evidenced by the formation of clear inhibition zones around the impregnated disks (**Figure 4**).

Antimicrobial activity was assessed using sterile commercial filter paper disks (6 mm diameter) impregnated with EOsZG and applied according to the Kirby-Bauer disk diffusion susceptibility testing protocol.

The study used reference strains of *Staphylococcus aureus* 749 and *Candida albicans* 74, obtained from the National Bank for Industrial Microorganisms and Cell Cultures (Sofia, Bulgaria). The assay was performed in triplicate. The mean inhibition zone diameter for *S. aureus* was 18 mm (±0.5 mm), while that for *C. albicans* was 30 mm (±0.5 mm). No statistically significant differences were observed among the replicate measurements, indicating good reproducibility of the results.

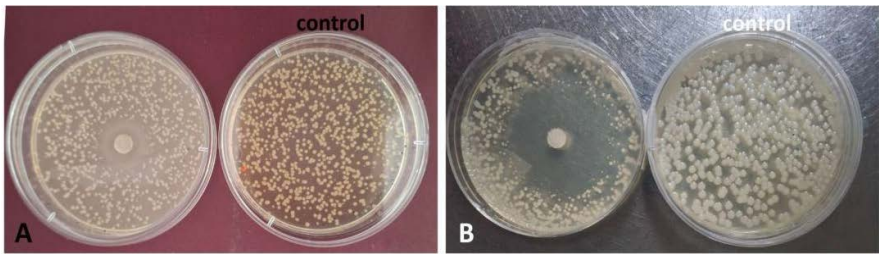

Figure 4. Antimicrobial activity of the essential oil combination assessed by the disk diffusion method against *Staphylococcus aureus* (A) and *Candida albicans* (B).

It should also be noted that the patient did not take antibiotics and antifungals. Essential oils were used along with standard conservative care, including daily rinsing with antiseptic infusions of natural origin, such as chamomile and cornelian cherry leaf decoction.

3. Discussion

The case presented here deserves attention as a report of a patient with MRONJ and its successful management using conservative therapy based on essential oils, although such treatment is not yet known as an alternative approach. Standard management in such cases typically includes antiseptic measures (antimicrobial rinses, systemic antibiotics and antifungal agents), gentle debridement, and ongoing monitoring [10] [11]. To discuss the therapeutic effects of essential oils, a thorough understanding of the pathophysiology of denosumab-induced MRONJ is necessary. By preventing the activation of RANK receptors on the surface of osteoclast precursors, denosumab effectively inhibits osteoclast formation and function, reduces bone resorption and increases bone mineral density [1]. Briefly, denosumab disrupts normal bone metabolism in patients with MRONJ. Its potent

inhibition of bone remodeling may compromise mucosal healing and lead to subsequent bone necrosis, particularly following invasive dental procedures involving the mandible [12] [13]. In cases of osteonecrosis of the jaw, sequestrum formation, defined as a fragment of avital (necrotic) bone, typically results from focal bone necrosis associated with ischemia or systemic factors such as medication use [14]. The body recognizes the non-vital bone as a foreign material and forms a layer of granulation tissue to separate the necrotic bone from the surrounding viable bone. While a sequestrum is present, osteonecrosis generally remains in an active, chronic inflammatory state. In the present case however, topical treatment with the essential oil combination (EOsZG) may have assisted and potentially facilitated the demarcation ("release") of the sequestrum, followed by its spontaneous expulsion. Unlike antibiotics and antifungals, used alone, the essential oils used in this case may provide protective antimicrobial activity against both bacterial and fungal infections simultaneously. Additionally, essential oils have the advantage of penetrating necrotic tissue more effectively and deeper than conventional antimicrobial agents, potentially improving local blood circulation and facilitating the removal of cellular debris and liquefied necrotic material.

The demarcation of necrotic from healthy tissue in osteonecrosis of the jaw represents a complex immune-mediated process. A central role in this process is played by specific leukocyte populations that prepare the necrotic bone for sequestration and removal. Neutrophils contribute through enzymatic tissue degradation and the formation of leukocyte barriers, while macrophages are responsible for detritus clearance and regulation of the inflammatory response. Osteoclasts participate in the separation of necrotic from viable bone through bone resorption. In MRONJ, the normal function of these cells, particularly osteoclasts, is impaired, which compromises the natural demarcation process [15]-[17]. In this context, the EOsZG combination may also exert a local immunostimulatory effect by enhancing leukocyte activity involved in the differentiation of necrotic and healthy tissue in osteonecrosis of the mandible. Furthermore, this combination may promote the formation of granulation tissue during the healing process. In conclusion, this case report illustrates that topical treatment with essential oils was associated with marked improvement and healing of MRONJ over a relatively short duration.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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