Journal of Cranio-Maxillo-Facial Surgery 46 (2018) 534–537

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Denosumab as a potential treatment alternative for patients suffering from diffuse sclerosing osteomyelitis of the mandible—A rapid communication

Sven Otto [a, *], Egon Burian [a], Matthias Troeltzsch [a], Gabriele Kaeppler [b], Michael Ehrenfeld [a]

[a] Department of Oral- and Maxillofacial Surgery (Head: Prof. M. Ehrenfeld), Ludwig-Maximilians-University, Munich, Germany
[b] Department of Oral Radiology (Head: Prof. G. Kaeppler), Ludwig-Maximilians-University, Munich, Germany

ARTICLE INFO

Article history:
Paper received 14 June 2017
Accepted 9 October 2017
Available online 16 October 2017

Keywords:
Denosumab
Diffuse sclerosing osteomyelitis
Jaw osteonecrosis
MRONJ
Antiresorptive treatment
Osteoclast

ABSTRACT

Purpose: Diffuse sclerosing osteomyelitis (DSO) is a rare disease of the jaw bone. Its treatment is challenging. Different medical and surgical treatment protocols have been proposed; however, none of these treatment protocols produce reliable results. Recently, ibandronate administration has been attempted as a treatment alternative in acute cases of DSO. Due to the similar antiresorptive effect, we sought to explore the application of the human monoclonal antibody to the receptor activator of nuclear factor kappaB ligand (RANKL), denosumab, in the treatment of DSO.

Materials and methods: One female patient with histologically verified DSO received subcutaneous injections of denosumab (Prolia® 60 mg). The further course of the disease was followed clinically and by radiography and scintigraphy.

Results: In this case, the use of denosumab displayed promising results in aiding pain relief and reducing inflammatory activity.

Conclusion: We suggest that antiresorptive treatment with denosumab can be considered as an alternative treatment for patients suffering from DSO. However further studies, with respect to clarifying the mechanisms of action and defining the necessary medication dose as well as application intervals, have to be conducted.

© 2017 Published by Elsevier Ltd on behalf of European Association for Cranio-Maxillo-Facial Surgery.

1. Introduction

Diffuse sclerosing osteomyelitis (DSO) is a rare disease clinically characterized by recurrent and severe facial pain, swelling, and trismus. Radiographic examinations can show osteolysis and sclerosis of the mandible depending on the stage of the disease (Fig. 1). As the disease progresses, bone sclerosis becomes a more prominent characteristic (Montonen et al., 2001; Yoshii et al., 2001).

The management of DSO is very challenging. Long-lasting improvement and relief of symptoms have yet to be attained in a stable manner (Kuijpers et al., 2011). Conservative treatment options include long-term analgesic medication, antibiotics, corticosteroids, and hyperbaric oxygen, and proceed to more invasive surgical treatment protocols including corticotomies and even extensive resections (Mari et al., 2014; Suei et al., 1997; Montonen et al., 1993; Van Merkesteyn et al., 1988; Jacobsson and Hollender, 1980). In this report, we present a novel approach to further improve and facilitate the medical therapy of DSO in the mandible. Currently, none of the above-mentioned treatment protocols have led to predictable and satisfactory outcome results (Kuijpers et al., 2011; Van Merkesteyn et al., 1998; Groot et al., 1992).

A recent study conducted by Otto et al. showed promising results for the use of ibandronate in acute cases of DSO (Otto et al., 2015a,b). Ibandronate is a highly potent nitrogen-containing bisphosphonate. After intravenous administration, the plasma half-life of ibandronate is 10–60 h (Barret et al., 2004). After that, approximately 50% of the dose administered binds to the hydroxyapatite of bone, including the jaw bone from where it is

* Corresponding author. Department of Oral- and Maxillofacial Surgery, Ludwig-Maximilians-University Lindwurmstraße 2a, Munich 80337, Germany. Fax: +49 89 4400 54746.
E-mail addresses: Sven.Otto@med.uni-muenchen.de, Otto_Sven@web.de (S. Otto).

https://doi.org/10.1016/j.jcms.2017.10.011
1010-5182/© 2017 Published by Elsevier Ltd on behalf of European Association for Cranio-Maxillo-Facial Surgery.

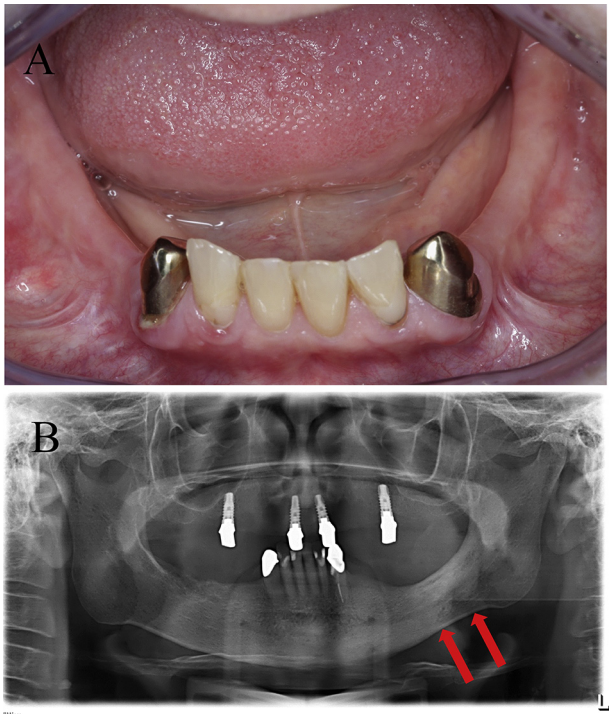

Fig. 1. (A) Clinical situation before treatment: normal mucosal tissue in the left mandible (region 33 to 37) with no signs of infection or fistula formation. (B) A panoramic radiograph showing high grade of sclerosis in the left mandibular corpus.

released by osteoclasts, leading to subsequent apoptosis of the respective osteoclast. The half-life in bone is very long (~10 years) (Barret et al., 2004; Bartl and von Tresckow, 2014).

Denosumab has some favourable characteristics compared to ibandronate, especially regarding half-life (~26 days) and controllability of effects as well as side effects such as impairment of renal function.

Denosumab is a human monoclonal antibody to the receptor activator of nuclear factor kappaB ligand (RANKL). By binding RANKL, denosumab blocks the interaction of RANKL and the RANK receptor on osteoclasts, thereby inhibiting osteoclast maturation and activation (Cummings et al., 2009). As a consequence, bone resorption is decreased. RANKL inhibitors are administered to manage diseases such as osteoporosis and metastatic bone disease (Stopeck et al., 2010; Cummings et al., 2009). RANKL inhibitor therapy is associated with decreased fracture rates, decreased bone metastasis, and few major side effects (Papapoulos et al., 2012; Smith et al., 2012).

However, as seen with other antiresorptive therapy, negative side effects of denosumab have been reported. Several cases of jaw bone necrosis have occurred, especially following treatment with denosumab in oncological dosing schemes, and further research is necessary to analyze the risk of jaw-bone necrosis due to RANKL inhibitors with both oncological treatment and osteoporosis management (Saad et al., 2012; Aghaloo et al., 2010; Taylor et al., 2009).

Despite the different mechanisms of action between bisphosphonates and denosumab, the final physiologic effect is quite similar. Both inhibit the function of osteoclasts, decrease bone resorption, and at high doses may terminate sclerotic recession (Otto et al., 2014, 2016; Bartl and von Tresckow, 2014).

Thus we aim to address this technical note to demonstrating the feasibility of denosumab application for patients with DSO of the jaw bone based on the example of one treatment approach.

2. Materials and methods

A 64-year old woman presented with severe pain in her left mandible since 5 years. Predominantly the left mandibular corpus and ramus were affected. The case had previously been diagnosed as diffuse sclerosing osteomyelitis of the mandible based on the combination of anamnestic information (recurrent severe episodes of pain, swelling and trismus), absence of fistula formation or suppuration in clinical examination, the tendency of localized increasing sclerotic bone formation in the panoramic radiograph, which was subsequently verified by histology, and no bacterial colonisation in microbiological testing.

There were no hints of other diseases of the jaw bone. Bacterial osteomyelitis was excluded as the mucosal barrier was intact; there was no bone exposure, no fistula formation, no pus exudation, no response to antibiotic treatment (amoxicillin/clavulanic acid 875/125 orally twice per day), and there were no indications of bacterial colonisation on pathological and microbiological investigations of bone specimens. There was also no hint of the presence of SAPHO syndrome (no synovitis, no acne papulopustulosa or hyperostosis) or chronic recurrent multifocal osteomyelitis (no multifocal occurrence, no fever, no uveitis, no inflammatory bowel disease, and atypical age of onset) apart from the recurrent severe pain and swelling. However, it should be noted that at present there is no generally accepted definition and nomenclature for osteomyelitis, diffuse sclerosing osteomyelitis (DSO), or chronic recurrent osteomyelitis (CRMO), and SAPHO syndrome is not completely clear throughout the literature.

Furthermore the patient was diagnosed with manifest postmenopausal osteoporosis. In the past, the diffuse sclerosing osteomyelitis the patient has already been successfully treated once with a single shot intravenous administrations of 6 mg ibandronate. The severe pain of the left decreased from visual analogue scale (VAS) 6–8 within 48 h after infusion to VAS 1. The patient had only very mild complaints (VAS 0–1) and had no episodes of severe pain in the mandible for around 1.5 years. However, 1 year after the single-shot administration of ibandronate (6 mg intravenously), following intensive discussions and written informed consent, the patient had received dental implants under antibiotic prophylaxis (amoxicillin/clavulanic acid 875/125 1-0-1 twice per day orally for 2 days prior to implant insertion and 5 days thereafter). The postoperative course, implant uncovering, and prosthetic rehabilitation were uneventful. However the patient was afraid of further necessity for dento-alveolar surgery under antiresorptive drugs. So when the pain, swelling and trismus recurred 2 years after the ibandronate infusion and 1 year after placement of dental implants she asked for a potential alternative with a shorter half-life so as to enable potential interventions on the newly placed implants. After intensive discussions of the treatment options, written informed consent, and evaluation of the disease activity using scintigraphy, which showed increased tracer uptake in the left mandible (Fig. 2), the decision was made to perform a subcutaneous injection with denosumab (Prolia® 60 mg).

Routine blood testing was performed especially to rule out impairments of renal function and low levels of 25-OH-vitamin-D3. The level of pain due to DSO of the mandible was determined every day for 10 days prior to treatment using a visual analogue scale (VAS). The patient was treated with subcutaneous denosumab application, and the pain level was recorded every day for 20 days post treatment, again using a VAS. All types of complications as well as symptoms related to the disease were recorded. The patient was followed up regularly for re-evaluation. After 6 months, the subcutaneous injection was repeated due to the re-onset of symptoms of DSO, and especially because of rising pain levels.

Download English Version:

https://daneshyari.com/en/article/8698821

Download Persian Version:

https://daneshyari.com/article/8698821

Daneshyari.com