

Short communication

Management of an aggressive giant cell granuloma of the mandible with denosumab: a case report

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Available online 21 June 2019

Abstract

The management of giant cell granulomas is challenging, and aggressive lesions have a high tendency to recur after enucleation alone. Based on assumptions regarding cell type and receptors, multiple pharmacological adjuncts have been used to manage them. We describe the use of denosumab, which was successfully used as a single method of treatment, suggesting that it may be a viable alternative or adjunct to operation on giant cell granulomas of the jaws.

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Keywords: Giant Cell Granuloma; Denosumab; Monoclonal Antibodies; Osteoclasts; RANKL; neo-ossification; Medication related osteonecrosis

Introduction

Giant cell granulomas account for 7% of all benign tumours of the jaws. Chuong et al¹ described them as “aggressive” and “non-aggressive” based on clinical and radiographic findings. This distinction is clinically relevant because aggressive lesions carry an appreciably higher tendency to recur after enucleation alone.

The traditional treatment of giant cell granulomas has been surgical removal, but recurrence rates of 11% - 49% after operation alone have been reported. A number of pharmacological alternatives or adjuncts to operation have been proposed.

The neoplastic cells in these lesions express high concentrations of RANK ligand (RANKL) and activate RANK-positive osteoclasts such as giant cells and their precursors.² RANKL is expressed on the surface of osteoblasts and stromal cells, binds to RANK on the surface

of osteoclasts, and so encourages osteoclast differentiation and proliferation.^{3,4}

Denosumab (Prolia[®], Amgen Ltd, Xgeva[®], Amgen Ltd), a human monoclonal antibody, inhibits RANKL, to prevent RANK-RANKL interactions, which results in less differentiation of osteoclasts, and ultimately reduces bony resorption that is associated with giant cell granuloma. Thomas et al, in a large open-label phase 2 study reported that 30/35 patients with giant cell tumours of bone responded well to denosumab,⁵ and more recently, it has been used to manage giant cell granulomas of the jaws.⁶ We describe its use to manage a mandibular lesion.

Case report

A 51-year-old woman presented with an 8-month history of a painful, rapidly-expanding lesion in the left mandible. She had no associated sensory nerve deficit, and intraorally, there was a firm bony swelling (Figs. 1–3). The histopathological analysis from an incisional biopsy examination

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Fig. 1. Intraoral photograph showing buccolingual expansion.

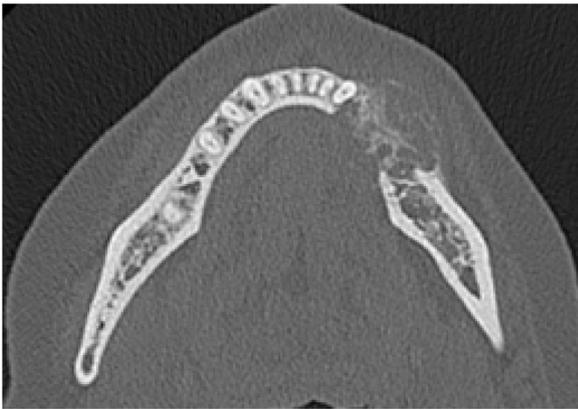


Fig. 2. Computed tomogram before treatment.



Fig. 3. Computed tomogram taken immediately after cessation of treatment with denosumab.

was consistent with a diagnosis of giant cell granuloma. Hyperparathyroidism was excluded on the basis of normal concentrations of serum calcium and parathyroid hormone. Given that both the clinical and radiographic features of the lesion were consistent with an aggressive giant cell granuloma, and owing to the fact that the patient was keen to avoid deleterious surgery, a decision was made to manage the lesion with denosumab. In total, she received three monthly doses of 120 mg, combined with daily supplementation of Vitamin D (400 IU) and calcium (500 mg). During this time, she com-

plained of tiredness and pain in her upper thigh, but had no other side effects of note. A computed tomogram taken at that time showed satisfactory bony infill and this, along with increasing tiredness, and a lack of symptoms associated with the mandibular lesion, led to cessation of the denosumab.

To facilitate future prosthetic rehabilitation, she returned to theatre 6 weeks later (18 weeks after the treatment with denosumab had been begun) to recontour the bone, and a biopsy examination showed neo-ossification but no evidence for residual granuloma. An orthopantomogram that had been taken 4 months after cessation of denosumab showed continued bony infill. To date, the length of follow-up is 6 months and there has been no radiographic or clinical evidence of recurrence.

Discussion

The management of aggressive giant cell granulomas is challenging. Originally developed for the management of osteoporosis, and suppression of bony turnover in patients with cancer, denosumab specifically inhibits RANKL, and so inhibits osteoclast-mediated destruction of bone.⁷ The key components of RANKL signalling have been found in giant cell granulomas of the jaws.⁸

Unlike bisphosphonates, which have a potential half-life of up to 10 years, the inhibition of osteoclast-mediated bony resorption by denosumab is a result of reversible binding to RANKL. The effects of denosumab, therefore, which does not bind to bone, could disappear within 6 months of cessation of the drug.⁹ Nevertheless, the potential for medication-related osteonecrosis remains.

Conclusion

The management of giant cell granulomas of the jaws remains challenging. Aggressive lesions have a reported high recurrence after operation. We wanted to highlight the potential for denosumab to be an alternative or adjunct to other methods in their management. It may limit the need for deleterious surgical procedures or indeed eliminate the need for surgical intervention altogether, as happened in our case.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patient's permission

Ethics approval not applicable. Consent was obtained.

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