Unhealed tooth extraction wound in a breast cancer patient

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Available online: 9 May 2014

**Case presentation**

In July 2013, a 65-year-old white woman presented with pain and exposed bone in the right mandible after tooth extraction 3 weeks previously. She was a known case of metastatic breast cancer, hypertension and osteoporosis, and completed chemotherapy: capecitabine and adjuvant radiotherapy in 2012. Her medications included tamoxifen, Karvezide® (irbesartan/hydrochlorothiazide), metoprolol, denosumab, pantoprazol, calcium and vitamin D supplements, hydromorphone, and sultamicillin. She never received bisphosphonates (BP).

On oral examination, an area of exposed bone was 4 cm long in the right mandible without infection and tumor metastasis. The surrounding mucosa was erythematous and tender to palpation. The bone surface was irregular but firmly attached with no clinical evidence of sequestration (figure 1). A panoramic radiograph showed normal postextraction sockets without bony sequestration or destruction (figure 2).

**What is your diagnosis?**

Denosumab-associated osteonecrosis of the jaw (DAONJ).
**Discussion**

Diagnosis of osteonecrosis of the jaw (ONJ) requires two characteristics: exposed, necrotic bone in the maxillofacial region, which exists for \( \geq 8 \) weeks, with/without pain, infection, or previous trauma; and no history of irradiation of the involved bone [1].

Most patients receive BP and develop ONJ after dental extraction or trauma, but spontaneous cases are also possible. ONJ may be linked to altered bone remodeling, angiogenesis inhibition, chronic microtrauma, drug toxicity to soft tissue, bacterial infection (e.g. *Actinomyces*), oral biofilm formation and malfunction of the local immune system. However, the most prominent hypothesis relates ONJ with inhibition of osteoclast function and differentiation [1–3].

Denosumab is a human receptor activator for nuclear factor kappa-B ligand (RANKL) monoclonal antibody. RANKL has 2 main functions:
- promoting fusion of preosteoclasts into osteoclasts;
- involving in activation and function of mature osteoclasts. It works together with osteoprotegerin (OPG) to maintain a healthy bone resorption balance.

The more RANKL/OPG ratio is, the more bone will be resorbed. Denosumab blocks binding of RANKL to RANK; thereby, it inhibits mobility and chemotaxis of monocytes/macrophages, as well as formation, activity and survival of osteoclasts. This drug is currently available for treatment of osteoporosis, and primary and metastatic bone cancers. Studies show that denosumab decreases osteoclast numbers, serum bone turnover markers, and tumor-induced osteolysis, and subsequently increases bone mass and density [1–4].

DAONJ has been sporadically reported in the literature. Its pathogenesis remains unclear [1,4]. In animal models, suppression of bone remodeling critically develops DAONJ [2]. Incidence of DAONJ ranges from 1.3% to 2.5% of patients receiving denosumab (dose-dependent) [4]. However, some patients also have other risks, such as receiving chemotherapy or anti-angiogenic therapy, prior BP therapy or tooth extraction, poor oral hygiene and dental appliance. These factors increase risk of DAONJ [3]. For details on the disease pathogenesis, we refer the interested readers to other reviews [4,5].

Patients receiving denosumab and BP require the same dental health measures: an oral examination and appropriate preventive dentistry before initiating the medicament, maintaining good oral hygiene and avoiding invasive dental procedures whenever possible [1,3,4]. Although incidence of DAONJ is similar to (or probably higher than) ONJ from BP [3], the effects of denosumab on bone turnover are more rapidly reversible than the effects of BP. Moreover, DAONJ may resolve more quickly with a drug holiday than ONJ related to BP [4].

Our patient underwent osteoplasty/ostectomy with local flap closure under local anesthesia. The postoperative course was uneventful, and she was hospitalized for 10 days for intravenous antibiotics and wound care. She has received close follow-up. At the time of this writing, she has been free of disease for 9 months.

**Disclosure of interest** The authors declare that they have no conflicts of interest concerning this article.

**References**


