

tomograph indicated a widened periodontal ligament (PDL) space distal to 47, a recognised early radiographic feature of MRONJ (Fig. 2).<sup>1</sup>

Initial management included a course of broad spectrum antibiotics (co-amoxiclav 625 mg TDS), effective analgesia and the use of long-handled angled interdental brushes (TePe) with chlorhexidine gel to help control the infection and inflammation. At her two-week review, the pain and bleeding had reduced and the communication to bone via the periodontium remained. Maintenance on doxycycline 100 mg OD was commenced. Intra-oral radiography six months after the initial presentation indicated increased PDL space of the second and third molars and early sequestrum formation (Fig. 3).



Fig. 1 Intra-oral photograph indicating subtle oedema between second and third molars

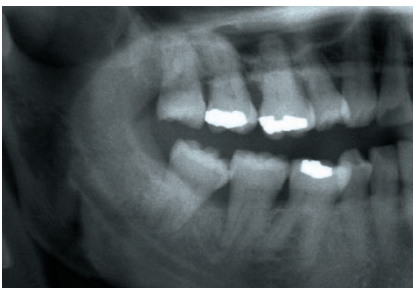


Fig. 2 Section of DPT showing marked widening of the periodontal ligament space suggestive of a vertical defect to the distal of the vital second molar

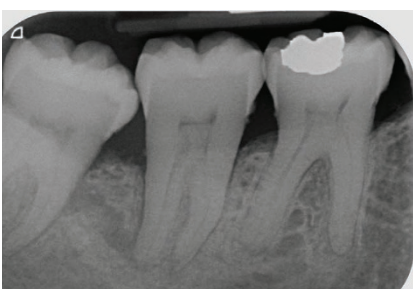


Fig. 3 Periapical radiograph of lower right second and third molars indicating increased PDL space on second and third molars, early sequestrum formation and diffuse sclerosis in the area

Previous similar presentations to our unit had been managed in different ways, including the use of subgingival ultrasonic scaling for assumed periodontal disease and occasionally root canal therapy. This case was identified early after referral due to the concentration of cases of MRONJ seen in this dedicated unit, enabling our clinicians to gain insight in to the different ways MRONJ can present.

In our experience, the risk factors which indicate a probable diagnosis of MRONJ rather than periodontal disease include:

- A patient at high risk of MRONJ - almost exclusively oncology patients who have received many months of intravenous or subcutaneous anti-resorptive therapy, such as denosumab
- Severe pain, which is not usually associated with chronic periodontal disease
- Oedematous soft tissues with loss of attachment which on detailed examination extends to the alveolar bone.

Increasing numbers of people now survive cancer, often now considered a chronic condition, who increasingly present to GDPs, including those who receive frequent anti-resorptive or anti-angiogenic medications. While the differences in clinical periodontal appearance are subtle, it is the detailed history which should raise flags for GDPs, on whom one relies so heavily for providing routine dental care for these at-risk patients.

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### Cause of osteonecrosis

Sir, denosumab, a human monoclonal antibody that binds and inhibits RANKL, a mediator required for the formation, functioning and survival of osteoclasts, is one of the medications that causes medication related osteonecrosis of the jaw (MRONJ).

A 77-year-old female patient who entered menopause at age 35 with total hysterectomy who had used alendronat and zoledronic acid for five years and one year respectively, attended our outpatient clinic in February 2017. DXA results of the patient were as follows: L1-4:-3.5, L2-4:3.7, Femur neck:-0.9, Femur total:-1.1. The patient was started on

denosumab therapy. Three months prior, the patient had full-full dentures, then two months after injection she started to experience pain in the right posterior mandible and therefore consulted an oral, dental and maxillofacial surgeon. Radiological findings were unremarkable according to the bone density measurements made by digital volumetric tomography at first grade of disease, so she was diagnosed with MRONJ clinically and prescribed an antibiotic and mouthwash then directed to our outpatient clinic in June 2017. Denosumab administration to the patient was suspended until the completion of her intraoral treatment. In August 2017, a 1 cm bone fragment in the right mandible broke off, which was found to be compatible with osteonecrosis of the jaw after it was examined pathologically. The patient reported that her pain ended with the rupture of the fragment. A review in September 2017 the region in which the necrosed bone fragment of the patient broke off was observed to have re-epithelised.

As the patient used two different antiresorptive medications the medication that caused MRONJ could not be clarified. The half-life of denosumab is 26 days, whereas that of bisphosphonates (BP) varies between 10-12 years. In contrast to BP, denosumab seems not to accumulate in the bones; therefore, many authors have stated that denosumab-related MRONJ is less aggressive and can be treated with a more conservative therapeutic approach.<sup>1</sup>

In our case, the rupture of the necrotic bone fragment two months after the observation of necrosed alveolar bone, rapid regression of the symptoms with the rupture of fragment and re-epithelisation of that area within one month led us to believe that the osteonecrosis was related to denosumab. With future technological and medical advancements, we hope to know for sure which drug is the cause of osteonecrosis and whether it is caused by synergistic effect.

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