MEDICINAL MISHAP

Osteonecrosis of the jaw and denosumab

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Case

The patient was an 87-year-old female with hypothyroidism, cardiovascular disease and gastro-oesophageal reflux disease. Her regular treatments were thyroxine, apixaban and esomeprazole. She had also been diagnosed as having osteoporosis and had received one injection of denosumab.

The left mandibular premolars were decayed so the patient was referred to an oral and maxillofacial surgeon for extraction of teeth 34 and 35. This extraction was performed seven months after her denosumab injection. Bone turnover measured by serum C-terminal telopeptide was 176 pg/mL, which is within the range for postmenopausal women. Initial healing had occurred when the patient was reviewed one week after surgery.

The woman presented again 11 weeks after the extractions with pain, swelling and exposed bone. She had been given another injection of denosumab 10 days after the extraction.

Medication-related osteonecrosis of the jaw was diagnosed. This was treated conservatively with chlorhexidine mouth rinses, analgesics and a short course of cephalosporin for the soft tissue infection. The C-terminal telopeptide was low at 116 pg/mL.

Symptoms persisted for six months after the last denosumab injection. X-rays showed a sequestrum (Fig.). As the C-terminal telopeptide was by then returning to normal (230 pg/mL), the sequestrum was removed under local anaesthesia and the wound primarily closed. One month later, when the area was healed, the denosumab was recommenced.

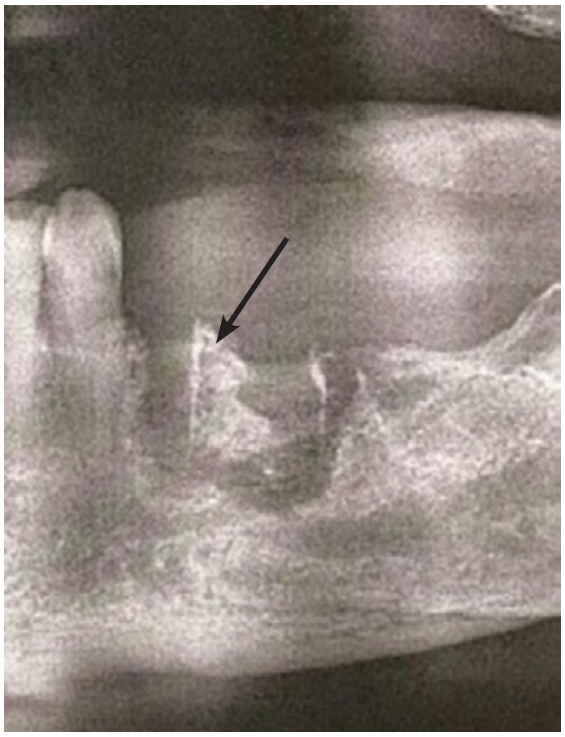
Comment

Despite having no clear guidelines to favour denosumab, it has substantially replaced the oral bisphosphonates as the first-line treatment for osteoporosis in Australia.[1] Denosumab is effective when given as a six-monthly 60 mg subcutaneous injection and has few adverse reactions. The main concern medically is that, if denosumab is discontinued or the injection is substantially delayed, there is a risk of vertebral fracture. This means effectively that, once started, the patient must remain on denosumab or another antiresorptive drug for the rest of their life.

Medication-related osteonecrosis of the jaw is a well-documented severe complication of dental extractions in patients on the oral bisphosphonates. It has been assumed that the risk with denosumab is similar to that with bisphosphonates.[2] This is incorrect. In the 2022 update of its position paper, the American Association of Oral and Maxillofacial Surgeons has stated that the risk is a magnitude higher for denosumab than the oral bisphosphonates.[3] The risk is 0.3%.

Minimising the risks of these two serious complications requires opposing actions. To avoid vertebral fractures denosumab should not be delayed, whereas to avoid medication-related osteonecrosis of the jaw, time is needed for a return to the normal bone turnover to allow wound healing.

Fig. **Stage 2 medication-related osteonecrosis of the jaw**



Note sequestrum

 This article is peer-reviewed

Conclusion and recommendations

Medication-related osteonecrosis of the jaw can occur following oral surgery if denosumab is recommenced before bony healing of the socket. If there is uncertainty about bone turnover, it should be measured at the time of the extraction.[3]

The Box shows evidence-based recommendations drawn from a prospective trial of 546 patients taking denosumab for osteoporosis, who had 1082 dental extractions, and another study of 13 patients who developed osteonecrosis.[4,5] Besides dental extractions, another risk group is patients with dental implants that sometimes lose integration during antiresorptive treatment. ≺

Conflicts of interest: none declared

Box Recommendations for dental care in patients treated with denosumab[4,5]

Risk factors

Factors include being female, aged over 70 years, having comorbidities, and taking antiresorptive drugs for over four years.

Communication

Prescribers, dentists and patients should communicate with each other.

Determination

Determine dental health, the need for extractions, and presence of implants. Dentist to consider alternative treatment.

Timing

Wait until six months after last injection for extractions.

Measure fasted C-terminal telopeptide if not sure of bone turnover.

Delay next dose of denosumab for one month after extraction until bone healing has occurred.

Avoid excessive delay or discontinuation of denosumab.

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