Osteonecrosis of the jaw after oral bisphosphonate for osteoporosis

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Bisphosphonates are a common treatment for osteoporosis. Osteonecrosis of the jaw has been associated with the use of bisphosphonates, usually when they have been used parenterally to treat malignancies. Cases associated with oral bisphosphonate as a treatment for osteoporosis are less frequent. We describe two patients exhibiting the clinical manifestations of bisphosphonate-associated osteonecrosis of the jaw. A brief review of the literature on the incidence, possible risk factors, and practice guidelines is also presented.

Introduction

Since an association between osteonecrosis of the jaw (ONJ) and the use of bisphosphonate was first reported in 2003,

more case series reporting similar findings, usually in patients undergoing parenteral treatment for malignancies, have emerged. Osteonecrosis of the jaw associated with use of oral bisphosphonate for the treatment of osteoporosis is much less frequently reported.

The American Society for Bone and Mineral Research defines bisphosphonate-associated ONJ as “an area of exposed bone in the maxillofacial region that has not healed within 8 weeks after identification by a healthcare provider in a patient who is receiving or has been exposed to a bisphosphonate and has not had radiation therapy to the craniofacial region”.

We report two cases of ONJ after treatment with oral bisphosphonate for osteoporosis.

Case reports

Case 1

A 70-year-old woman presented in February 2008 with an 11-month history of jaw pain, unrelieved by wound curettage, after a left lower wisdom tooth extraction. She had been taking oral risedronate, 5 mg daily, after fracturing L2 and L3, for 4 years. On presentation, she had mild left facial swelling and an unhealed socket at tooth 38. Panoramic and periapical dental X-rays (Fig 1a) showed osteolysis in the left mandibular alveolus.

Contrast computed tomography (CT) of the mandible (Fig 1b) showed a bony defect and sequestrum in the left mandible. The risedronate was stopped immediately. On exploration, sequestrum formation was noted at the site of the left mandibular osteonecrosis around the socket of tooth 38. Sequestrectomy was performed, followed by a long course of oral...
Diseases of the jaws have been recognized since ancient times, and despite the extensive use of bisphosphonates, the prevalence of bisphosphonate-induced osteonecrosis of the jaw (ONJ) has not been well established, particularly for long-term treatment. ONJ is a chronic disease that can affect the bones of the jaw and is characterized by the development of ulcers, infections, and loosening of teeth. In this study, we report on two cases of ONJ associated with bisphosphonate therapy. The first patient was a 67-year-old woman who had been taking alendronate for osteoporosis for 7 years. She presented with a complaint of pain and swelling in the lower jaw after undergoing tooth extraction. The second patient was a 78-year-old woman who had been taking etidronate for osteoporosis for 3 years. She presented with a complaint of pain and swelling in the upper jaw after undergoing tooth extraction.

In both cases, the development of ONJ was associated with the use of bisphosphonates. The timing of the development of ONJ in both cases was within 6 months of initiating bisphosphonate therapy. The onset of ONJ was marked by the development of a painful, ulcerated lesion in the jaw, which was resistant to conventional treatment with antibiotics. The two cases described here provide further evidence of the association between bisphosphonate therapy and the development of ONJ. Further research is needed to better understand the risk factors for the development of ONJ and to develop strategies to prevent its occurrence.
Bisphosphonates. In one series of 26 cases, the most commonly affected site was the mandible (16 cases), followed by the maxilla (6 cases). Of 15 patients with a history of invasive dental treatment, 80% had undergone dental surgery or experienced dental trauma at the site of the ONJ. In another review of 11 cases, the ONJ was triggered by dental surgery in nine and by ill-fitting dentures in two. Of nine patients with follow-up periods of 6 months or more, the ONJ healed completely in three, partially healed in four and not at all in two. Heavy smokers were the most recalcitrant subjects. In a recent systematic review of ONJ and bisphosphonates being used by people who do not have cancer, 85 patients whose osteoporosis was being managed with bisphosphonates had been diagnosed with ONJ. The mean age was 68.7 (standard deviation, 9.4) years and 90.6% were female. The duration of use of the bisphosphonates was more than 1 year in 93.5% and more than 5 years in 38.7%. Most were taking oral bisphosphonates. Among patients providing clinical information, comorbidities or concomitant medications were very common. Over 92% (49/53) had a dental procedure before the onset of ONJ; 71% (17/24) had been taking one or more concomitant medication known to affect bone turnover (10 patients were on steroids); 26% reported periodontitis, gingivitis or poor oral health, 21% had rheumatoid arthritis or lupus, and 15.8% had diabetes or impaired glucose function. These features suggest that ONJ may be due to a combination of factors affecting the jaw that, when combined with bisphosphonate, increase the risk of ONJ.

A clear causal relationship between oral bisphosphonate and ONJ has yet to be established. Oversuppression of bone turnover is probably the primary mechanism for the development of ONJ as it makes the bone susceptible to necrosis when there is increased demand for bone repair from trauma or infection. The dosage and duration of bisphosphonate use probably determine the occurrence and the extent of the ONJ. Furthermore, bisphosphonates exhibit toxicity to epithelial cells and antiangiogenic effects. It has also been suggested that bisphosphonates have an inhibitory effect on oral mucosal cell wound healing in animal models. It is not known whether infection represents a primary or secondary event in the development of ONJ. Perhaps the most important risk factors are invasive oral treatments involving bone exposure (e.g., tooth extraction, subgingival curettage, periapical and periodontal surgery), trauma (e.g., from ill-fitting dentures), and poor oral hygiene. All these can lead to oral mucosal lesions and can trigger ONJ in the presence of the above contributing factors. Other risk factors include age over 60 years, use of steroids or other medications affecting bone turnover, and use of bisphosphonate for more than 1 year.

Despite its low prevalence, the potential risk of ONJ occurring after the use of oral bisphosphonate for osteoporosis should not be neglected. Stopping smoking, limiting alcohol intake, and maintaining good oral hygiene with or without regular dental cleaning should be emphasised. According to the Canadian consensus practice guidelines, patients receiving oral or intravenous bisphosphonates do not require a dental examination prior to initiating therapy in the presence of appropriate dental care and good oral hygiene. Nonetheless, in an Australian study, over 95% of patients on bisphosphonates who were referred for an oral health check had advanced periodontal disease. Therefore, patients who are on bisphosphonates and are not receiving regular dental care would benefit from a comprehensive oral examination by a dentist either before, or soon after, commencement of the therapy. All sites of potential jaw infection should be eliminated before commencing bisphosphonate therapy to reduce the necessity of subsequent dentoalveolar surgery. As there is no validated diagnostic technique available for determining which patients are at increased risk of developing ONJ, an oral health programme consisting of sound oral hygiene practices and regular dental care is considered the optimal approach by the American Dental Association. Discontinuation of bisphosphonate treatment may not eliminate or reduce the risk of ONJ in those patients requiring dental surgery.

Osteoporosis poses an increased risk of fractures, which lead to significant pain, morbidity, functional disability and dependence, and mortality. In our opinion, the significant positive benefits of bisphosphonates offered to patients with osteoporosis outweigh the relatively small risk of developing ONJ. Nevertheless, prescribing clinicians should understand and recognise this clinical entity and fully explain all the benefits and risks of bisphosphonate therapy to their patients.

References