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Successful long-term mandibular reconstruction and rehabilitation using non-vascularised autologous bone graft and recombinant human BMP-7 with subsequent endosseous implant in a patient with bisphosphonate-related osteonecrosis of the jaw

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Abstract

We describe a case of extensive osteonecrosis of the mandible after a dental extraction in a 71-year-old woman who was taking alendronic acid (Fosamax®, Merck) for osteoporosis. Bone damaged by bisphosphonate-related osteonecrosis of the jaw (BRONJ), also now known as medication-related osteonecrosis of the jaw (MRONJ), can be regenerated and filled with endosseous implants using non-vascularised autologous grafts.

Keywords: Bisphosphonates; BRONJ; MRONJ; Mandibular reconstruction; Bone morphogenic proteins; BMPs; Endosseous implants

Introduction

Bisphosphonates work because they inhibit osteoclasts. This reduces bony resorption but also disrupts normal remodelling. Resorption of old extracellular matrix induces osteoblasts to form new bone, but after bisphosphonates have been given intravenously or orally, they are liberated only when the bone into which they were deposited is resorbed. The half-life of bisphosphonates in bone can be in excess of 10 years,[1] and their effect extends far beyond the duration of treatment. Alendronic acid taken orally may continue to have an influence for more than 5 years after treatment has finished.[2]

A recent paper from the American Association of Oral and Maxillofacial Surgeons (AAOMS) suggests that bisphosphonate-related osteonecrosis of the jaw (BRONJ) should now be named medication-related osteonecrosis of the jaw (MRONJ). This is defined as an area of exposed bone in the maxillofacial region, or bone that can be probed through a fistula (either intraoral or extraoral and which has persisted for more than 8 weeks) in a patient who is currently taking or has previously taken antiresorptive or antiangiogenic medication, and has not had radiotherapy to the jaw.[3] The risk of osteonecrosis of the jaw after the extraction of teeth among patients who have taken bisphosphonates orally is estimated to be 0.5%, compared with between 1.6% and 14.8% when they had the medication intravenously.[3] A recent national study concluded that the risk can be considered

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"rare", as it occurs between only 1/10 000 and 1/1000 postmenopausal women who are taking bisphosphonates orally for osteoporosis.[4]

Any dentoalveolar procedure must be considered carefully in these patients: most obviously the extraction of teeth, but also periodontal and endodontic operations. What is relatively unknown, is how the jaw of a patient taking bisphosphonates, particularly those with BRONJ, will respond to bone grafts from a distant autologous site, and how this newly-grafted bone will react to implantation. We describe a case in which both were possible.

The AAOMS classification of MRONJ is largely the same as that of BRONJ. It is divided into 3 stages of severity, and appropriate management has been advised for each. Operation is still reserved for stage 3 MRONJ alone, for example, for exposed and necrotic bone or fistulas that probe into bone with evidence of infection, and one or more of the following: pathological fractures, extraoral fistulas, oroantral or nasal communications, extension of the exposed necrotic bone beyond the region of alveolar bone, or osteolysis that extends to the inferior border of the mandible or floor of the sinus.[3] However, operation can trigger progression. One prospective study into the effectiveness of resection of the jaw in patients with cancer and MRONJ showed a recurrence rate of 9.4% 6 months after the operation.[5] Resection of the jaw also poses the challenge of reconstruction and rehabilitation.

Several patients have had mandibular defects caused by MRONJ reconstructed successfully with fibular free flaps and osseointegrated implants.[6] Autologous non-vascularised bone grafts, on the other hand, are more likely to fail and because of this, reconstruction with a flap is more usual. When we operated in April 2009, we knew of no other reports of reconstruction with autologous non-vascularised bone and bone morphogenetic protein (BMP) complex with subsequent insertion of an endosseous implant into the regenerated bone.

Case report

A 71-year-old woman of Indian origin was referred for investigation of an extraction socket that had not healed almost a year after removal of a second molar on the lower right side. Her medical history included rheumatoid arthritis and osteoporosis for which she had been taking alendronic acid (Fosamax®, Merck) orally every week for several years. Examination, an orthopantogram, and a bone biopsy confirmed the diagnosis of MRONJ. She was given analgesics and asked to follow a strict regimen of oral hygiene. The bisphosphonate was replaced with strontium ranelate.

Four months later, she complained of a swollen face and severe pain in the right body of the mandible. There was a localised collection of pus adjacent to the right lower border of the mandible, which could be expressed from the extraction socket intraorally as well as from an extraoral sinus. The abscess was incised and drained under local anaesthetic and she was given a course of doxycycline.

Two months later, radiological examination showed a pathological fracture of the right body of the mandible (Fig. 1), and she had a partial mandibulectomy to remove the necrotic tissue adjacent to the fracture. The remaining bony defect after resection was about 36 mm long. A titanium reconstruction plate (Synthes® Compact 2.0 LOCK Mandible, Oberdorf, Switzerland) was inserted and the discharging cutaneous sinus was formally excised and closed (Fig. 2). Three weeks after the operation the intraoral wounds had healed well, and there was no evidence of discharge from the sinus.

We considered inserting a graft to aid bony regeneration because reconstruction plates used on their own will eventually fail. After full assessment and discussion of all possible treatments, the patient consented to have a bone graft from the iliac crest with the additional use of recombinant human (rh) protein BMP-7 (known in the United States as osteogenic protein (OP)-1).

Seven months after the initial procedure, the reconstruction plate and defect were opened up. Two cubic centimetres of mostly cancellous bone was harvested from the left iliac crest. The harvested cortical bone was first fixed to the mandible with 1.3 mm (Synthes®, USA) screws. The cancellous bone was then mixed with rhBMP-7 3.5 mg (Osigraft® Howmedica International) and Type I collagen, and applied to the defects in and around the reconstruction plate. Haemostasis was achieved and the wounds were closed. Radiological examination 4 months later showed considerable growth of new bone (Fig. 3). We then made a removable denture, but the patient could not tolerate it. After a detailed discussion of the risks of implantation into the bone, a single titanium implant 9.5 mm long and 3.5 mm wide (Ankylos®, DENTSPLY Implants, Mölndal, Sweden,) was placed into the regenerated bone about a year after the graft. To keep the partial lower cobalt chrome denture in place, a precision abutment was attached to the osseointegrated implant about 8 months later (Figs. 4 and 5).

Enough bone was regenerated and there was full osseointegration of the implant. Five years after the bone graft and 4 years after the implant, both were still securely in place and functioning well (Fig. 6).

Discussion

Although there has been much discussion about the reconstruction of mandibular defects after disease and trauma, little is known about mandibular reconstruction in patients with MRONJ, possibly because incidences are relatively low and resection is reserved for stage-3 disease.

There have been several reports on the use of vascularised free fibular flaps in which there was either minimal or no recurrence of MRONJ.[7–9] Ferrari et al,[6] described one patient who had restoration of a mandibular defect with a fibular