

> J.L. CALVO-GUIRADO¹, A. BOQUETE-CASTRO², J. GUARDIA³, A. AGUILAR SALVATIERRA RAYA³, J.M. MARTÍNEZ GONZÁLEZ⁴, G. GÓMEZ-MORENO⁵

¹ Senior Lecturer of General Dentistry and Implantology, DDS, MS, PhD. Faculty of Medicine and Dentistry, University of Murcia, Murcia, Spain

² Postgraduate Student, Master in Integrated Dentistry and Implantology, DDS, Faculty of Medicine and Dentistry, University of Murcia, Murcia, Spain

³ Collaborator of Pharmacological Interactions in Dentistry, DDS, PhD. Faculty of Dentistry, University of Granada, Granada, Spain

⁴ Senior Lecturer of Oral Surgery, DDS, MS, PhD. University Complutense of Madrid, Madrid, Spain

⁵ Full Professor of Pharmacological Interactions in Dentistry, DDS, PhD. Faculty of Dentistry, University of Granada, Granada, Spain

Osteonecrosis of the jaw after dental implant placement. A case report

TO CITE THIS ARTICLE

Calvo-Guirado JL, Boquete-Castro A, Guardia J, Aguilar Salvatierra Raya A, Martínez González JM, Gómez-Moreno G. Osteonecrosis of the jaw after dental implant placement. A case report. *J Osseointegr* 2014;6(1):15-18.

ABSTRACT

Background In the past few years, the occurrence of an oral lesion, called osteonecrosis of the jaw, has increasingly been reported in patients undergoing treatment with systemic bisphosphonates (BPs); however, few papers dealing with oral bisphosphonates related osteonecrosis of the jaws (BRONJ) can be found in the literature. The purpose of the present case was to report an occurrence of BRONJ after implant insertion.

Case report Ten years ago, eight dental implants were inserted in the jaw of a 65-year-old female. After 5 years of treatment with alendronic acid, a breakdown of the oral mucosa covering the implants occurred with a purulent discharge in the left side of the jaw; periapical radiolucency was present around both distal implants. An en-block resection of the alveolar bone including the two implants was performed. Thirty-five hyperbaric sessions were taken and no signs of recurrence of the lesion were observed after a follow-up of 20 months. Before the new implant insertion, the patient had suspended the treatment with alendronic acid for 6 months. At the interface of one of the implants, a gap was observed between bone and implant. This bone was non vital, and many osteocyte lacunae were empty. Moreover, this bone appeared to be partially demineralized.

Conclusion There is certainly a temporal association between oral BPs use and development of BRONJ, but a correlation does not necessarily mean causation. In patients undergoing oral treatment, clinicians must be aware of the increased risk of implant failure.

KEYWORDS Alendronate; Bisphosphonates; Bisphosphonate-related osteonecrosis of the jaw (BRONJ); Dental implants.

INTRODUCTION

Oral bisphosphonates are commonly prescribed for patients with osteoporosis to arrest bone loss and preserve bone density. Nitrogen-containing bisphosphonates, such as alendronate, risedronate, ibandronate, and zoledronate, are agents that inhibit bone resorption (1, 2). Recent reports have shown a link between these medications and osteonecrosis of the jaw, which is a complication resulting in exposed non vital maxillary or mandibular bone (3, 4,5,6).

Attempts have recently been made to predict the development of bisphosphonate-related osteonecrosis of the jaw (BRONJ). Several prospective studies have investigated the predictive value of serum levels of C-terminal telopeptide of collagen I for the development of BRONJ. Despite measurement of serum levels of C-terminal telopeptide of collagen I is not a definitive predictor of BRONJ, it plays an important role in the risk assessment before oral surgery (4). Bisphosphonate-associated osteonecrosis is a complication that almost exclusively affects the jaw bones. As this complication has only been recognized within the past 10 years, management of patients with bisphosphonate-associated osteonecrosis is poorly defined. The clinical presentation of BRONJ often mimics that of other conditions, such as routine dental disease, osteoradionecrosis or avascular necrosis; therefore, diagnosis can be difficult. Physicians have to choose between continuing the bisphosphonate therapy (to reduce the risk of skeletal complications in patients with metastatic bone disease or osteoporosis) or discontinuing the drug (to possibly improve the odds for tissue healing) (7).

The incidence of BRONJ after oral surgery involving bone is greater among patients receiving frequent, high doses of intravenous bisphosphonates than among patients taking oral BPs (8). BRONJ seems resistant to conventional treatment approaches. Resection of the

necrotic bone followed by an adequate wound closure is a surgical technique that shows high success rates, so patients may benefit from this approach (9). Future research should focus on the pathobiological mechanisms involved in the development of BRONJ, which could help to explain why this complication affects only a small number of those who use bisphosphonates, and also suggest strategies for prevention and management (7).

CASE REPORT

A 65-year-old woman has been taking oral alendronic acid (Fosavance®, MS&D, Whitehousestation, USA) as a treatment of postmenopausal osteoporosis disease during the last 5 years. The dose of the bisphosphonate was one tablet of 70 mg once a week. The woman was non-smoker and had a good oral hygiene. No other risk factors for osteonecrosis were present.

In the first surgery, 10 years ago, eight SteriOss (Nobelbiocare, Göteborg, Sweden) implants were placed in the mandible in the positions 4.6, 4.5, 4.3, 4.2, 4.1, 3.1, 3.2, 3.3, 3.5, 3.6 and a screwed implant-supported prosthesis was realized.

After 5 years of oral bisphosphonates use, the patient referred punching pain, numbness and paresthesia. In an oral exploration, sequestrum formation was noted at the left side of mandible (Fig. 1). Radiolucency was

present around both left posterior implants (Fig. 2).

A resection of the alveolar bone including the two distal implants was performed under local anesthesia, with deep margins in an apparently healthy bone; the flaps were accurately sutured. The implants and the surrounding tissues were stored immediately after removal in 10% neutral buffered formalin. Microscopical analysis of the specimens was carried out (Fig. 3).

Osteonecrosis process continued advancing, so five of the eight initial implants were lost. Only implants in position 3.1, 3.6 and 4.6 survived (Fig. 4, 5).

The histopathological examination of the specimens revealed BRONJ. After the surgical resection of affected areas and the pharmacological treatment (Amoxiciline 500 mg/6h + Clorhexidine 0.12%) bone did not achieve the adequate level of regeneration; therefore, the patient underwent 6-months sessions of hyperbaric camera (Naval Hospital, Cartagena, Murcia, Spain). Sessions were daily, with a duration of an hour. Moreover, the patient underwent a strict clinical and radiological follow-up. After the evaluation period, bone remodeling of the defects was successful and no signs of recurrence of osteonecrosis were detectable.

On postoperative follow-up the wound was well healed and X-ray showed good periapical bone remodeling. Subsequently, four additional M4 Implants (MIS, Tel Aviv Israel) were inserted in the lower jaw (3.3, 3.2, 4.2, 4.3). Before implant insertion, the patient had



FIG. 1 Sequestrum formation in the mandible; intraoral aspect.



FIG. 2 Sequestrum formation in mandible; radiographic aspect.



FIG. 3 Tissues resected for microscopic evaluation.



FIG. 4 Loss of implant 3.6.



FIG. 5 Remaining implants.



FIG. 6 Final panoramic radiograph after BRONJ treatment and implant replacement.

suspended the oral bisphosphonate treatment for 6 months after indication of her specialist, and according to the approved protocol in use. No preexisting bone lesions were present at the preoperative panoramic radiography. After 4 months, implants osseointegration was successful and prosthetic rehabilitation was carried out (Fig. 6).

The histopathological examination was carried out. Microscopic analysis of the specimens revealed as follows.

- Fragment 1: the sample corresponded to trabecular bone. The main part of the sample was constituted by small pieces of bone presenting normal characteristics, but surrounded of several necrotic focuses with frequent images of "ghost trabecules" situated in the centre of wide friables and disorganized necrotic areas.
- Fragment 2: The other fragment corresponded to spongy bone with multiple necrotic areas of irregular disposition. Those areas were present in both samples, on the edges of them.

Diagnosis was the same for both samples: bone fragment with several necrotic areas, in other words, bone sequestration.

DISCUSSION

Bisphosphonates suppress bone resorption by interfering with osteoclast activity. Several of these agents have been shown to prevent fractures and increase bone mineral density in patients with osteoporosis. Long-term bisphosphonate therapy has been associated with osteonecrosis of the jaw and atypical femur fractures (10). Since 2003, there have been flurry of case reports and case series suggesting that bisphosphonate use may be associated with a condition called ONJ (osteonecrosis of the jaw) (11). Recent systematic reviews indicate that the use of bisphosphonates for osteoporosis is associated with an ONJ incidence of less than 1 in 100,000 patient-years of exposure (12, 13). ONJ appears to occur most often in patients with advanced cancer, particularly

in those with multiple myeloma or breast cancer, and specifically in those undergoing dental procedures (12, 14). The current definition of ONJ is based on clinical findings and includes nonhealing lesions with exposed bone, but without evidence of bone necrosis (12, 15).

Many pathogenic factors have been postulated to explain how bisphosphonates may play a role in ONJ. These include effects on blood supply, angiogenesis, excessive bone turnover in jaws leading to increased bisphosphonate uptake, excessive suppression by bisphosphonates of osteoclastic bone resorption, impaired mucosal healing, and use of other drugs (e.g., immunosuppressives and glucocorticoids) (16, 17).

Health care providers have been encouraged to advise their patients to practice good oral hygiene and have regular dental visits. If an invasive dental procedure is required, there is no evidence that discontinuation of bisphosphonate therapy improves dental outcomes, although many guidelines recommend some form of interruption (12, 18).

Ozone therapy had proven efficacy on improving the benefits of surgical and pharmacologic treatments, favoring the complete healing of the lesions with the disappearance of symptoms and even had brought cases of lesion progression down to zero. Thus, ozone therapy is a reliable option in treatment of ONJ; its benefits are remarkable and it improves significantly the outcomes of the surgical approach. Into the chamber, patients breath compressed air through oronasal mask, tube or endotraqueal intubation.

Bisphosphonates exert their therapeutic effects by reducing bone resorption, and this leads to a reduction in bone remodeling and turnover (19). The degree of reduction of bone turnover achieved by each bisphosphonate, as well as the duration of action appears to be associated with their mineral-binding affinity and skeletal retention. Bisphosphonates with higher mineral-binding affinity and potential retention, such as alendronate and zoledronate, are associated with greater reduction of bone turnover and have a longer duration of effect after treatment ending. Bisphosphonates with

lower mineral-binding affinity and retention, such as risedronate and etidronate, appear to reduce bone turnover less and this effect seems to be more readily reversible when therapy stops (2). A recent review of the available evidence on long-term efficacy and safety of osteoporosis treatments, indicated that it may be beneficial to continue osteoporosis therapy indefinitely in the majority of patients, with discontinuation of treatment in some specific cases, such as need of oral surgery.

CONCLUSION

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 recognize this clinical entity and fully explain all the benefits and risks of bisphosphonate therapy to their patients.

Conflict of interests

All materials used in this study were purchased by the main author and it is therefore free of any commercial or institutional interests.

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