Medication related osteonecrosis of the jaws (MRONJ): Diagnosis and treatment

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‘Autoreconstruction’ of the mandible: report of a case

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ABSTRACT

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) was first mentioned in the literature in 2003. Since then, several reports have been published referring to this disease. The etiology of BRONJ still remains unclear. The treatment of BRONJ also remains a topic of discussion between those who are in favor of a conservative treatment and those who are convinced that surgical treatment gives the best results. In this case report, a patient is presented with BRONJ in the mandible which has been treated surgically in combination with antibiotic treatment. During surgery it appeared that a large part of the jaw was sequestrated full-thickness with, at the same time, formation of a substantial amount of subperiosteal bone that was formed around the BRONJ, supporting the sequestrated part of the mandible and, after sequestrectomy, serving as a neo-mandible. This case shows the capacity of the jawbone despite bisphosphonate use to regenerate itself.

INTRODUCTION

Bisphosphonate related osteonecrosis of the jaw was first mentioned in the literature in 2003[1]. Since then several reports and research have been published referring to this disease. In the literature authors are divided about the treatment. Some suggest to stay as conservative as possible, for surgical intervenience could worsen the disease leading to loss of (parts of) the jaw[2,3]. Other authors plead for a prompt surgical approach to stop the disease from extending in the jaw thus preventing loss of continuity[4-6].

Subperiosteal bone is formed as a response to injury caused by an inflammation, trauma to the bone, cancer or chronic irritation of the periosteum. It takes at least a few weeks before subperiosteal bone apposition is visible on an X-ray. Usually subperiosteal bone consists of a thin layer and is being resorbed in the normal bone turnover whenever the original stimulus has gone. Only in the relatively rare proliferative periostitis[7-9] or Garré's osteomyelitis, larger quantities of subperiosteal bone are found[10]. In older literature however, cases of phosphorus necrosis of the jaw with abundant formation of subperiosteal bone are formed. Thus, apart from the chronicity of the osteomyelitis seen in BRONJ, possibly the use of bisphosphonates plays a role in acquiring a large quantity of subperiosteal bone.

So far, it has never been seen or reported, that BRONJ may lead to sequestration of a large part of the jaw with at the same time a presence of a substantial amount of subperiosteal bone that was formed around the BRONJ, supporting the sequestrated part of the mandible and after sequestrectomy, serving as a neo-mandible.

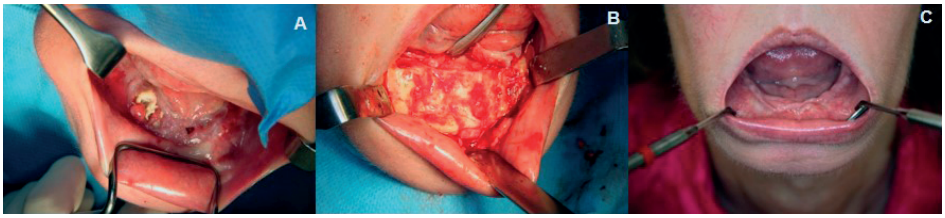
To our knowledge this case report is the first in literature to report about this phenomenon.

CASE REPORT

A 55 year old woman with metastasized breastcancer for more than three years and multiple intraoral fistulas since 6 months was referred to the department of Oral and Maxillofacial Surgery of the Leiden University Medical Center. The medical history further showed deep vein thrombosis, appendectomy, hypercholesterolemia and hepatitis. The patient used Bactroban, Paracetamol/Codein, Zoladex, Innohep and Tamoxiphen. The patient also used Pamidronate for 27 months with a dose of 90mg per month and Alendronate for 37 months orally with a dose of 70mg per week. Before surgery both anti-resorptive agents were stopped for one month, after surgery they were not continued. The patient smoked 10-20 sigarettes a day, did not use alcohol, stopped using drugs (marihuana, heroin) 32 years before. The patient did not receive radiotherapy in the head or neck region in the past.

At presentation pain, intraoral fistulas (fig 1A) and a extraoral fistula in the submental region were found. Two months before she had extractions of all her teeth in general anaesthesia elsewhere, because of caries and periodontitis, a productive submental fistula and pain. Afterwards she had antimicrobial treatment of 10 days Augmentin 625 (amoxicillin and clavulanic acid) and Perioaid mouth rinse. Despite the extractions the pain and the fistulas persisted.

Figure 1 Photographs before, during and after surgery



A= multiple intraoral fistula and denuded bone
B= subperiosteal bone before closure of the surgical wound
C= intraoral view 6 weeks after surgery with closed mucosa

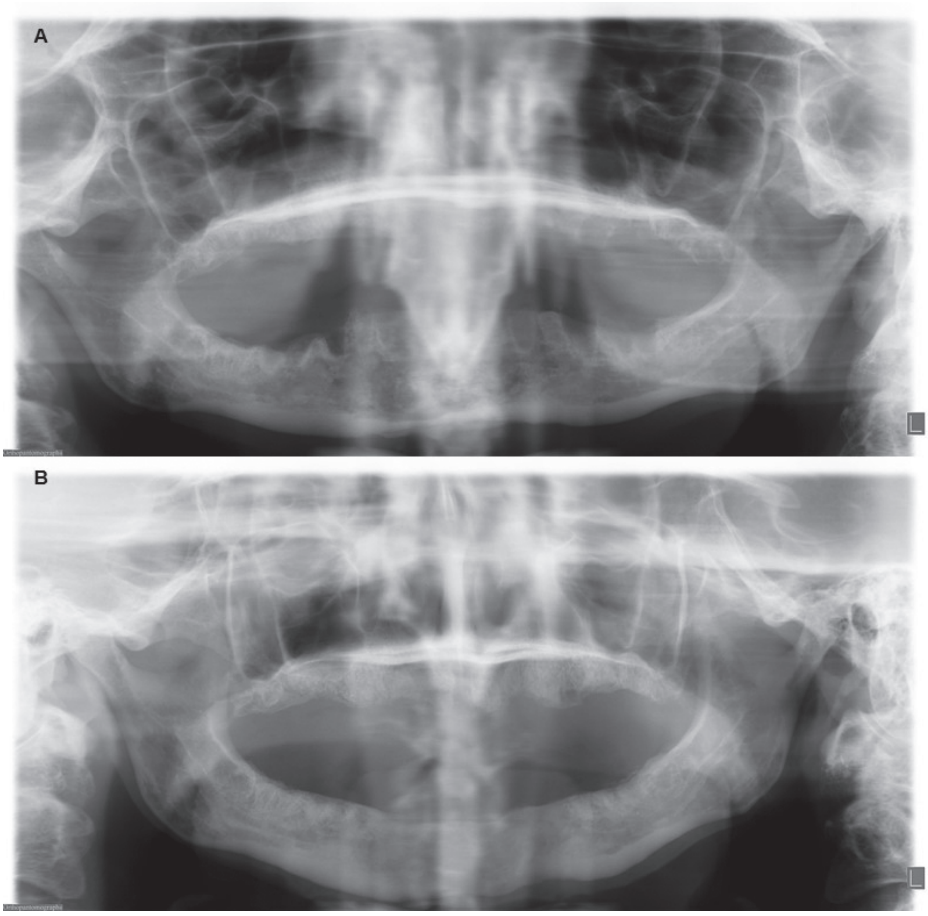
The panoramic radiograph showed osteolysis of the ventral part of the mandible (Fig 2). The CT scan (fig 3A) showed massive osteolysis and sequestration of the ventral part of the mandible from region 34 to 45 matching an osteomyelitis and BRONJ. The continuity of the mandible seemed intact just because of subperiostal bone formation (fig 3A).

A diagnosis of bisphosphonate related osteonecrosis of the jaw was made.

The patient was treated according to a protocol reported earlier by Alons[4] with a sequestrectomy in general anesthesia in combination with intravenous antibiotics. During surgery the original mandible from region 34 to 45 appeared to be completely necrotised and sequestrated. The mental nerve could not be identified on the right side, on the left side it could be identified. When the sequestrae were removed a large quantity of subperiostal bone was found around the defect especially at the former lingual border of the mandible. This subperiosteal bone seemed vital and perfused. After partial removal its buccal shape was lowered and rounded off. Finally the subperiosteal bone was shaped in order to make primary closure without dead space possible and seemed to have sufficient thickness to provide continuity of the mandible (fig 1B). The wound was closed primarily in layers[4]. The patient received anti-microbial treatment according to protocol (Penicillin G (6 x 1 million EH) and Metronidazole (3 x 500 mg) were administered for five days intravenously followed by Amoxicillin orally 3 x 500 mg for three weeks and Metronidazole 3 x 500 mg for three weeks.)

Histologic examination of the bone showed non-vital bone, signs of chronic inflammation and the extensive presence of microorganisms. Streptococcus constellatus, a mixed-cell infiltrate and Actinomyces were seen; there were no signs of metastases of the breast cancer in the mandible.

Figure 2 Radiologic findings before surgery and 9 months after surgery



A: Panoramic radiograph with extensive osteolysis, extending from the region of 46 to 34 up to the inferior border in the region of the symphyse
B: Panoramic radiograph 9 months post-operatively with healed, smooth edges of the mandibular corps

The patient's recovery was good without further complaints, intraoral dehiscences or fistulas (fig 1C). During follow-up no pathological fracture of the subperiosteal bone occurred. The panoramic radiograph showed continuity of the mandible and a cortex like structure. The CT scan 6 weeks after surgery showed a lingual neo-cortex of the mandible without any signs of resorption (fig 3B). At follow-up after 9 months the patient was still free of complaints.

DISCUSSION

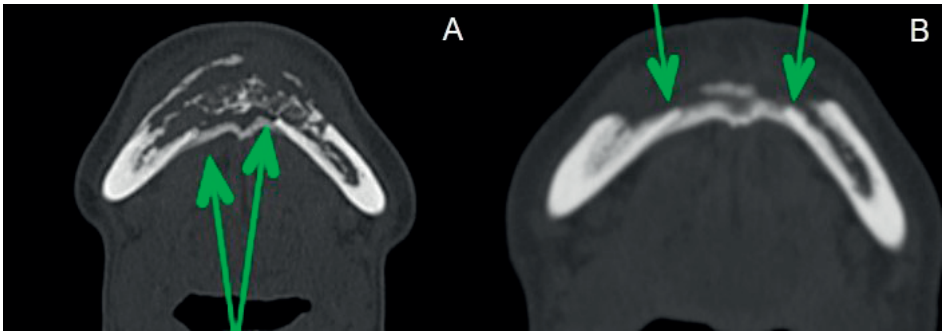
Bisphosphonates are built in in bone tissue and are released after cessation of therapy over a prolonged time. Therefore, bisphosphonates stay effective for years. Since bisphosphonates inhibit the osteoclasts, bone resorption is decreased, hence in this case probably also the subperiosteal bone resorption.

The reason of the subperiosteal bone growing to this volume is probably because of the long duration of chronic irritation of the periosteum caused by the former dentition with multiple inflammatory foci and the longterm use of bisphosphonates. However, subperiosteal bone is supposed to be resorbed entirely in the normal bone remodeling process. But in this case it did not. A possible explanation for this could be due to the bisphosphonates, which decrease (subperiosteal) bone resorption. In normal patients these amounts of subperiosteal bone formation would not have been reached due to the normal bone remodeling process and normal (subperiosteal) bone resorption. In our opinion there is not necessarily more subperiosteal bone formation in BRONJ patients compared to normal patients, but rather a decreased bone resorption due to bisphosphonates.

The pre and post-op CT scan confirmed this finding that the continuity of the original lingual cortex of the region from 34 to 45 was gone and replaced by subperiosteal bone (fig 3B).

The CT scan also showed that the subperiostal bone developed a cortex-like structure (fig 3B). The distinction between the former cortex of the mandible and the cortex of the neo mandible was visible on the CT scan (fig 3B). Where the first CT scan made at presentation clearly shows a distinction between the subperiosteal bone and the lingual cortex, the second CT scan made several weeks after presentation appears to have no such clear dinstinction anymore. It seems as if a new cortex has been formed.

Figure 3 Comparison CT scans before (A) and 3 months after surgery (B)



A= lingual subperiosteal bone can be seen and seems to connect both parts of the mandible
B= the difference between the cortex of the mandible and the subperiosteal bone is decreasing

It appears that this phenomenon is not entirely new. Older literature going back to the mid nineteenth century already showed subperiosteal bone formation in phossy jaw-patients during and after surgery[11,12]. Workers in matches industry were at risk for developing the phossy jaw caused by the inhalation of phosphorus vapours in the factories. These phosphorus vapours had a similar effect on the jawbone as bisphosphonates do[13,16]. Several written case reports of the phossy jaw patients are comparable in clinical features with the current BRONJ with in several cases abundant subperiosteal bone formation[11,12,17]. In this case the subperiosteal bone mass appeared sufficient to retain mandibular continuity during a follow up of more than 9 months.

CONCLUSION

This report of a case of BRONJ of the mandible with excessive subperiosteal bone formation shows a practical and patient friendly use of the excessive amount of this subperiosteal bone in BRONJ.

REFERENCES

1. Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic. J Oral Maxillofac Surg; 61:1115-1117, 2003
2. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws. J Oral Maxillofac Surg; 65:369-376, 2007
3. Ruggiero SL, Dodson TB, Assael LA Landesberg R, Marx RE, Mehrotra B; American Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws--2009 update. J Oral Maxillofac Surg 2009; 67: 2-12.
4. Alons K, Kuijpers SC, de Jong E, van Merkesteyn JP. Treating low- and medium-potency bisphosphonate-related osteonecrosis of the jaws with a protocol for the treatment of chronic suppurative osteomyelitis: report of 7 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009; 107:e1-e7.
5. Williamson RA. Surgical management of bisphosphonate induced osteonecrosis of the jaws. Int J Oral Maxillofac Surg 2010; 39:251-255.
6. Wilde F, Heufelder M, Winter K, Hendricks J, Frerich B, Schramm A, Hemprich A. The role of surgical therapy in the management of intravenous bisphosphonates-related osteonecrosis of the jaw. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010.
7. Tong AC, Ng IO, Yeung KM. Osteomyelitis with proliferative periostitis: an unusual case. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006; 102:e14-e19.
8. Belli E, Matteini C, Andreano T. Sclerosing osteomyelitis of Garre periostitis ossificans. J Craniofac Surg 2002; 13:765-768.
9. Wood RE, Nortje CJ, Grotepass F, Schmidt S, Harris AM. Periostitis ossificans versus Garre's osteomyelitis. Part I. What did Garre really say? Oral Surg Oral Med Oral Pathol 1988; 65:773-777.
10. Wood NK, Goaz PW. Differential diagnosis of oral & maxillofacial lesions. [5th edition], 488-492. 1997. St Louis, Mosby.
11. Savory WS. A Case of Necrosis of the Jaw and other bones from fumes of phosphorus. Med Chir Trans 1874;57:187-191
12. Hughes JPW, Baron R, Buckland DH, Cooke MA, Craig JD, Duffield DP, Grosart AW, Parkes PWJ, Porter A. Phosphorus necrosis of the jaw: a present-day study. Brit. J. industr. Med.; 19:83-99, 1962
13. Marx RE. Uncovering the Cause of "Phossy Jaw"Circa 1858-1906: Oral and Maxillofacial Surgery Closed Case Files-Case Closed. J Oral Maxillofac Surg 2008; 66:2356-2363
14. Hellstein JW and Marek CL. Bisphosphonate Osteochemonecrosis (Bis-Phossy Jaw): Is this Phossy Ja of the 21st Century? J Oral Maxillofac Surg 2005; 63:682-689
15. Abu-Id MH, Warnke PH, Gottschalk J, Springer I, Wiltfang J, Acil Y, Russo PAJ, Kreusch T. "Bis-phossy jaws"- High and low risk factors for bisphosphonate-induced osteonecrosis of the jaw. J Craniomaxillofac Surg 2008; 36:95-103
16. Whalen JP, O'Donohue N, Krook L, Nunez EA. Pathogenesis of Abnormal Remodeling of Bones: Effects of Yellow Phosphorus in the Growing Rat. Anat. Rec. 1973; 177:15-22
17. Wright WC. Case of Salivation and diseased jaw from the fumes of phosphorus. Medical Times 1846; 15 (377):224-225