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Original article

THE CHIMERIC ALT-VASTUS LATERALIS FREE FLAP IN RECONSTRUCTION OF ADVANCED BRONJ OF THE MAXILLA

Francesca Toia¹, Michele Cillino¹, Salvatore D'Arpa¹, Sara Di Lorenzo¹,
Fabio Santanelli di Pompeo², Adriana Cordova¹

Summary

Introduction

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a dangerous complication of bisphosphonates, a class of pharmaceutical agents used in numerous bone disorders.

No gold standard therapy exists, but recent literature suggests that, in advanced stages, the best results are achieved with aggressive debridement.

In this paper, we report our experience of treatment of stage 3 BRONJ of the maxilla with extensive surgical debridement and reconstruction with a chimeric ALT-Vastus lateralis flap.

Methods

Five selected patients with stage 3 BRONJ underwent partial maxillectomy with disease-free margins followed by immediate reconstruction with a chimeric ALT-Vastus lateralis free flap.

Results

Only two patients experienced minor complications. All other patients healed uneventfully within two weeks and donor site morbidity was minimal.

Conclusions

Our data suggest that aggressive debridement and reconstruction with a chimeric ALT-Vastus lateralis flap is an effective option for the treatment of stage III BRONJ of the maxilla.

Introduction

Bisphosphonate related osteonecrosis of the jaw (BRONJ) is defined as the presence of exposed bone in the oral cavity that does not regress within eight weeks in a patient who is currently, or has previously been, treated with bisphosphonates and who has not had radiotherapy to the craniofacial region¹.

Address of the authors:

¹Plastic and Reconstructive Surgery. Department of Surgical, Oncological and Oral Sciences. University of Palermo, Palermo, Italy.

²Plastic Surgery Unit. Sant'Andrea Hospital; "Sapienza" University of Rome, Rome, Italy.

Send correspondence to: Francesca Toia, francescatoia@gmail.com

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It is a relatively rare but potentially dangerous complication of treatment with bisphosphonates², a class of pharmaceutical agents used in numerous bone disorders, including osteoporosis, bone metastases, and multiple myeloma.

The exact pathogenetic mechanism of BRONJ has still to be established, but it is clear that infection, trauma and reduced vascularity play important roles^{3,4}. The most commonly reported initiating factor for BRONJ, in fact, is tooth extraction, although periodontal disease and damage caused by dentures have also been implicated^{5,6}.

Bisphosphonates inhibit bone turnover, stimulating osteoclastic apoptosis and constricting osteoblast-mediated osteoclastic activity and neoangiogenesis^{2,7-9}. Thus, the jaws are most frequently affected because of their high turnover.

BRONJ is usually staged according to the following classifications³:

- stage 1: asymptomatic bone exposure;
- stage 2: painful bone exposure due to concurrent infection at the level of the exposed bone;
- stage 3: complicated cases with extraoral fistulae and fractures.

Mawardi et al. defined "stage 0" or "non-exposed BRONJ" as an early stage without exposed bone¹⁰. This definition has also been incorporated among the AAOMS BRONJ diagnostic criteria³. Wilde et al.¹¹ distinguished advanced disease in stage 3 (exposed necrotic bone associated with pain, infection with swelling and abscesses, multiple intraoral fistulas, and extended osteolysis in the radiologic findings) and stage 4 (exposed necrotic bone associated with pain, infection with swelling and abscesses, pathologic fracture, naso-oral fistula, extraoral fistula, or osteolysis extending to the inferior border). Begogni et al.¹² proposed a different three stage classification as an alternative to the AAOMS classification:

- stage 1: focal (alveolar bone) osteosclerosis;
- stage 2: diffuse (alveolar and basal bone) osteosclerosis;
- stage 3: clinical and radiological signs of advanced and complicated disease.

They do not include a stage 0, with the

idea that BRONJ patients with exposed and non-exposed necrotic bone simply represent distinct clinical pictures within the same disease stage. Pain and purulent discharge are no longer used to distinguish between different disease stages, but only between asymptomatic (a) and symptomatic (b) forms of BRONJ. While there is no consensus yet on the gold standard therapy for BRONJ, recent literature suggests that, differently from early stages, in advanced stages the best results are achieved with aggressive debridement^{3,13-15} and subsequent reconstruction.

In this paper, we report our experience on the treatment of stage 3 BRONJ of the maxilla with extensive bone resection and reconstruction with a chimeric ALT-Vastus lateralis flap.

Methods

From 2008 to 2013, five patients with stage 3 BRONJ (figure 1) were surgically treated at a single center. Two were male and three were female. Mean age was 63 years old (range: 49-69). In all cases the osteonecrosis was localized in the maxilla. No patients had any history of head and neck malignancy or radiation therapy. Indications for bisphosphonates therapy were breast carcinoma in three cases, lung carcinoma in one case, and prostatic carcinoma in one case. Duration of therapy ranged from nine to 42 months (mean: 23) (table 1).

All patients received peri- and post-operative antibiotic treatment.

All patients underwent a partial maxillectomy with disease-free margins followed by immediate reconstruction with a chimeric ALT-Vastus lateralis free flap (figure 2). Resection was not limited to resection of the necrotic bone, but entailed aggressive debridement up to the visualization of healthy bleeding bone.

Mean follow up was 13 months (range: 6-24). Healing time, postoperative complications and BRONJ recurrence were assessed. Recipient and donor site outcomes were evaluated.

Results

All patients healed uneventfully within two weeks, with the exception of a

PATIENT	SEX/AGE	STAGE	INDICATION FOR BISPSPHONATES THERAPY	COMPLICATIONS
1	F/69	III	Breast cancer	None
2	F/65	III	Breast cancer	None
3	F/49	III	Breast cancer	Flap dehiscence
4	M/64	III	Lung cancer	None
5	M/68	III	Prostatic cancer	None

Table 1: Patients' data on BRONJ diagnosis and treatment



Figure 1: Preoperative view of a 65 years old female patient with a stage 3 BRONJ of the maxilla

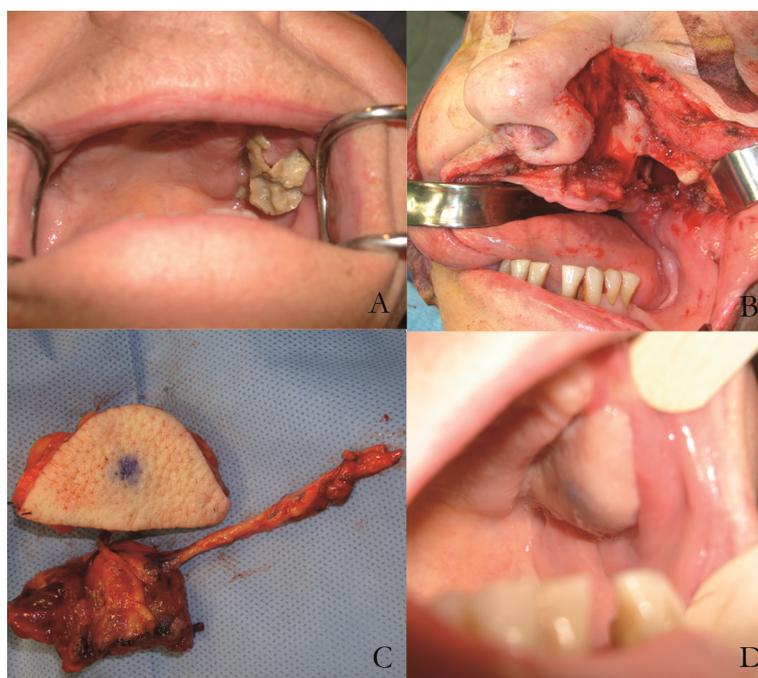


Figure 2: A. Preoperative view of a 64 years old male patient with a stage 3 BRONJ of the maxilla. B. An extensive surgical debridement was performed until healthy bleeding bone was visualized. C. A chimeric ALT-Vastus lateralis flap was harvested for reconstruction. D. Six months post-operative result.

wound dehiscence in one case (20%) that required revision surgery. All flaps survived completely. All patients resumed oral diet one week after last surgical procedure.

Diagnosis of BRONJ was histologically confirmed in all cases.

After a mean follow-up of 13 months, no clinical or radiographic evidence of recurrent BRONJ was evident in any patients. No patient complained about deficits in quadriceps strength affecting his/her daily life.

Discussion

Our case series shows that aggressive debridement and reconstruction with chimeric ALT-Vastus lateralis flap is an effective option for the treatment of patients with a stage III BRONJ of the maxilla.

Recent literature recommends conservative treatment for BRONJ in the early stages, and more aggressive treatment for advanced disease^{3,13-15}. Moreover, in a recent report Rupen et al. advocate that extensive surgery ensures better outcomes compared with conservative surgery, irrespective of the BRONJ stage, and not only in advanced stages¹⁶.

In our series, aggressive debridement was performed in all patients up to visualization of healthy bleeding bone. Cold instruments were used for this purpose, to avoid bone damage from the high temperature developed by high-energy drills and saws.

All patients received antibiotic treatment from one hour before surgery to 15 days post-operative, as we considered the bone infected by definition, given a stage III BRONJ diagnosis. In fact, several authors¹⁷⁻¹⁹ suggest a constant role of infection in the clinical course of this disease.

Many reconstructive options have been proposed following sequestrectomy, including local flaps, bone grafts and vascularized bone-free flaps^{13,20}. However, no treatment has been recognized as the gold standard so far.

Differently from other head and neck regions^{21,22}, traditional, perforator or propeller local flaps are not recommended, as they do not allow for the filling of the

dead space left by bone resection. Also, the mucosa surrounding the osteonecrosis area is often unstable and prone to ulcerations and infections.

The use of bone reconstruction is still debated^{4,13,20}. Bone grafts are biologically inert and do not supply the vascular support needed in a hypovascular bone. Recent reports on bone reconstruction with a fibula free flap are promising and suggest that it is a safe and effective procedure in BRONJ patients. Literature on this topic is still limited, and larger series are required to validate application on a large clinical scale^{20,23,24}. Despite being generally accepted that axial and appendicular bones are less susceptible to bisphosphonates, concerns still remain about the risk of transferring a bone that is not completely "healthy"²⁵, especially in cases of multiple mieloma. However, in spite of this, there are the successful reports of bone reconstruction in these patients that, despite rigid fixations do perform well^{12,20,23}. Also, the use of implants requires good coverage (local tissues are often inadequate for this purpose) and exposes the patient to a higher infection risk (on an already contaminated field)¹⁷⁻¹⁹.

For these reasons, we do recommend reconstruction with a distant well-vascularized, soft tissue flap. We believe that the chimeric ALT-Vastus lateralis flap is a valuable option for stage III BRONJ of the maxilla, as the muscle part of the flap provides a good vascular supply and enough tissue to fill the dead space, while the skin allows for intraoral resurfacing. Also, the versatility of ALT-Vastus lateralis flap in the head and neck region has already been demonstrated by several authors²⁶⁻³⁰. As for other head and neck defects, the mobility between skin and muscle allows for a customized three-dimensional reconstruction in patients affected by BRONJ.

The limit of this technique is that it does not follow the principle of a "like-with-like" reconstruction, and it fills a defect but does not restore functionality. This is why we do recommend the technique only for reconstruction of the maxilla, and not of the mandible, where the functional unrepaired deficit would be more

evident. Considering the uneventful healing, the early resumption of oral diet, and the absence of recurrent disease, we believe that the advantages of this therapeutic option justify the residual functional deficit in patients with a maxillary localization who are not candidates for prosthetic rehabilitation: patients in our series were weakened cancer patients with limited life expectancy, for which the main indications for surgery were pain and foul smelling discharge. For patients with mandibular localization, however, bone reconstruction should be considered more deeply, as significant mandibular deviation and difficulties with chewing arise if mandible stabilization/reconstruction is not performed.

Donor site morbidity is limited by the small amount of muscle usually required for reconstruction.

Altogether, our data suggest that aggressive debridement and reconstruction with a chimeric ALT-Vastus lateralis flap is an effective option for the treatment of stage III BRONJ of the maxilla. A limitation of our study is the small sample size; larger and comparative clinical studies are desirable to compare techniques and establish clinical guidelines.

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