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Use of morphogenetic protein associated with xenogeneic graft for atrophic maxilla reconstruction: case report

Utilização de proteína morfogenética associada ao enxerto xenógeno para reconstrução de maxila atrófica: relato de caso

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ABSTRACT

With the loss of dental elements and subsequent bone resorption, the rehabilitation process in an atrophic maxilla becomes a challenge for professionals. Alternatives such as autogenous, xenogeneic and allogeneic grafts, as well as alloplastic biomaterials, have been used for bone volume gain. The technique of lifting the maxillary sinus to the posterior region of the maxilla is well described in the literature and does not present major complications. Morphogenetic proteins (BMPs) appear as adjuvants in this technique and can replace grafts or be combined with them. The objective of this study was to present the use of different materials for the reconstruction of the atrophic maxilla in order to give back to a patient the bone contour and volume she had lost. The reported case shows the employment of recombinant human bone morphogenetic protein 2 (rhBMP-2), associated with a particulate xenogeneic graft. The atrophic maxilla was reconstructed, and the indications, contraindications and possible limitations of the technique were discussed. It is possible to conclude that the technique used was satisfactory; the patient evolved well and is awaiting installation of an implant-supported prosthesis.

Keywords: BMP. Bone graft. Maxillary sinus.

RESUMO

Com a perda dos elementos dentários e posterior reabsorção óssea, o processo de reabilitação em uma maxila atrófica torna-se um desafio para o profissional. Alternativas como o enxerto autógeno, xenógeno, alógeno e biomateriais aloplásticos têm sido usados com o propósito de ganhar volume ósseo. A técnica de levantamento do seio maxilar para região posterior da maxila está bem descrita na literatura e não apresenta grandes complicações. As proteínas morfogenéticas (BMP) surgem como adjuvantes nessa técnica e podem substituir os enxertos ou estarem juntas a eles. O objetivo do trabalho foi apresentar o emprego de diferentes materiais para reconstrução da maxila atrófica com a finalidade de devolver ao paciente o contorno e volume do osso perdido. O caso relatado demonstra o emprego da proteína óssea morfogenética recombinante humana 2 (rhBMP-2), associada ao enxerto xenógeno particulado. Foi realizada a reconstrução da maxila atrófica, discutido suas indicações, contraindicações e possíveis limitações da técnica. É possível concluir que a técnica utilizada foi satisfatória, a paciente evoluiu bem e aguarda instalação da prótese implanto-suportada.

Palavras-chave: BMP. Enxerto ósseo. Seio maxilar.

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INTRODUCTION

Defects of the maxillomandibular complex caused by infection, trauma, neoplastic processes or severe atrophy by edentulism can bring serious psychosocial problems to patients, since they are directly related to facial aesthetics and function. Particularly in cases associated with severe maxillary atrophy, issues such as insufficient prosthetic retention, loss of soft tissue support, and decreased vertical dimension greatly limit the prognosis for conventional rehabilitation through mucosa-supported prostheses (Lopes, Vajgel, Oliveira, Santana, & Wassall, 2012).

The posterior region of the maxilla is considered the most problematic when it comes to rehabilitation with osseointegrated implants. This difficulty is due to several factors, such as reduced quantity of bone, pneumatization of the maxillary sinus after loss of dental elements, and low bone density (Santos, Cardoso, Pinheiro, Machado & Merly, 2017). In this context, maxillary sinus lift surgery has been considered a safe treatment modality with a low rate of complications (Silva et al., 2016).

Boyne and James (1980) published, as a clinical study, the maxillary sinus lift that was first described by Tatum. In the described technique, access to the maxillary sinus was through the bone crest. Various graft materials have been used in sinus lift surgery, including autogenous, xenogeneic and allogeneic bones, as well as alloplastic biomaterials (Rodolfo et al., 2017).

Autogenous bone is the gold standard for grafting, but due to surgical morbidity and the inherent disadvantages of the technique, the use of allogeneic and xenogeneic grafts is being increasingly indicated. The main advantage of autogenous bone is its potential for integration into the receptor site through the mechanisms of osteogenesis, osteoinduction and osteoconduction. The allogeneic graft, in its turn, presents osteoconductive and osteoinductive characteristics, due to the presence of the family of morphogenetic proteins, preserved even after freezing. Proteins that are responsible for the chemotaxis of undifferentiated mesenchymal cells and for the induction of their differentiation into osteoprogenitor cells (Faverani et al., 2014).

The xenogeneic graft promotes an increase in the alveolar ridge, creating an adequate volume and providing sufficient structure for the implant to be installed in its correct position. In order to eliminate immune and inflammatory responses in the patient, the molecular structure of xenogeneic grafts in blocks is made up of deproteinized inorganic bone matrix. It acts as a scaffold for the proliferation of host bone cells, allowing native bone to grow slowly and be procedurally replaced by newly formed bone. This process is slow, depending on the type of biomaterial. Thus, especially in aesthetic areas, low resorption rates are associated with bone volume preservation (Loyola, Ancoski, Ramires, Mello & Mello, 2018).

The US Food and Drug Administration (FDA, 2007) granted approval for recombinant human bone morphogenetic protein (rhBMP-2) to be used in maxillary sinus and alveolar ridge augmentation. This approval was based on data from 312 patients enrolled in a total of 5 clinical studies (Cicciù, Herford, Stoffella, Cervino & Cicciù, 2012). Currently, BMP is mostly used in off-label treatments as adjuvants for allografts or bone autografts (Oliveira, Martins, Lima & Gomes, 2017).

Bone morphogenetic proteins (BMPs) are members of the transforming growth factor-β superfamily that have the ability to induce bone formation and eliminate autograft-associated morbidity (Kelly, Vaughn & Anderson, 2016). The emergence of recombinant human bone morphogenetic protein (rhBMP-2) becomes a viable alternative to common bone grafts, eliminates the need to remove bone from the iliac crest or other sites, minimizes morbidity associated with these procedures, and increases the degree of new bone formation (Cicciù et al., 2012).

Thus, this paper aims to present and discuss a case of atrophic maxillary reconstruction in which rhBMP-2 was used in association with a particulate xenogeneic graft stabilized with titanium mesh, emphasizing the indications, contraindications and possible limitations of this technique that has been increasingly employed in clinical practice.

CASE REPORT

Female patient, with 75 years old, with chewing and phonation issues, and pain in the left TMJ; in addition to medical history of arterial hypertension and anxiety. An extraoral clinical examination revealed reduced vertical dimension, poor lip support, and a condition compatible with angular cheilitis. Intraorally, it was possible to detect upper total edentulism associated with severe maxillary bone resorption, and lower partial edentulism. Cone Beam Volumetric Tomography showed a generalized and significant reduction in bone thickness, as well as bilateral pneumatization of the maxillary sinuses, as it can be seen in Figure 1.

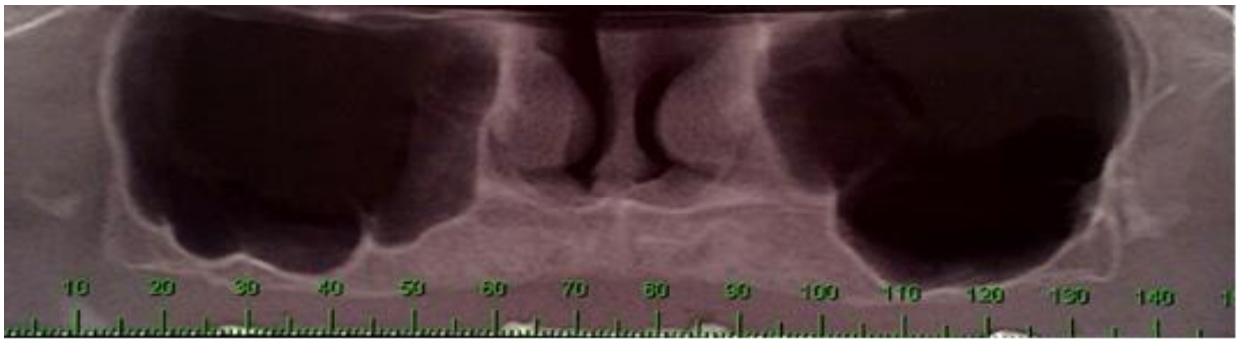

Figure 1. Cone beam tomography showing severe maxillary resorption associated with bilaterally pneumatization of the maxillary sinuses
Source: The authors.

Maxillary reconstruction was planned with rhBMP-2 (Medtronic Sofamor Danek, Memphis, TN, USA), using collagen sponge (Cerasorb, Kleinosheim, Germany), in association with xenogeneic bone graft (particulate Bio-Oss®). The procedure was started by extraoral asepsis with 2% chlorhexidine, and intraorally with 0.12% chlorhexidine digluconate, through a mouthwash for 1 minute and apposition of sterile operative fields. The patient was anesthetized with mepivacaine (2% and epinephrine 1:100,000). Two relaxing incisions were made in the posterior maxilla, bilaterally, joined through an incision in the crest of the bone ridge, using a scalpel handle number 3 and blade 15. With the aid of a Molt-type periosteum, the full-thickness flap was lifted, exposing the entire area and providing an adequate view of the surgical bed to be reconstructed. Subsequently, osteotomies were performed with a number 6 spherical drill under abundant irrigation with saline solution for the sinus lifts, and the Schneiderian membranes were carefully detached with curettes for maxillary sinus and sinus lifts (Figure 2).

Figure 2. Maxillary osteotomy and lifting of the Schneiderian membrane of the right maxillary sinus.
Source: The authors.

After the membranes were lifted, both maxillary sinuses and the anterior maxillary remnant were filled with the reconstructive materials. Following the manufacturer's recommendations, a dose of 4.2 mg of rhBMP-2, at a concentration of 1.5 mg/ml, and two collagen-carrying sponges were used for grafting. Incorporated into this material, a xenogeneic bone graft (particulate Bio-Oss®) was used. Both were incorporated in the floor of the maxillary sinuses and in the entire extension of the maxilla. The grafted material was placed under a titanium mesh previously shaped in accordance with the desired region for bone augmentation and stabilized with graft screws (Figure 3).

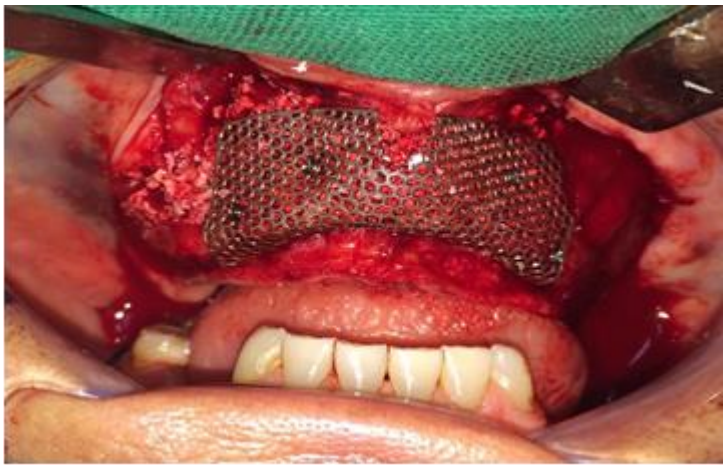

Figure 3. Maxillary reconstruction with Rh-BMP, Bio-Oss®, and titanium mesh and screws.
Source: The authors.

The flap was placed in position and sutured with 5-0 nylon monofilament thread; the relaxing incisions were sutured with simple stitches, and the alveolar crest, with continuous Ford-interlocking stitches. The patient was instructed on the postoperative recommendations and prescribed Amoxicillin 500 mg every eight hours, for seven days, Nimesulide 100 mg every 12 hours, for four days, and Dipyrone 1g every six hours, for three days.

The patient evolved without major postoperative complications, presenting a moderate and well-located edema in the upper lip region, associated with ecchymosis, but without pain complaints.

DISCUSSION

Disuse atrophy, hormonal-metabolic action, use of dental prosthesis, traumatic occlusion, parafunctional habits and iatrogenic causes lead to bone resorption and generate maxillary atrophy with poor quality and quantity of residual bone. This rehabilitation becomes challenging due to the resorption patterns that this area presents after tooth loss. Furthermore, according to Cruz, Peixoto, Aguiar, Camargo e Homs (2017), pneumatization of the maxillary sinus can make the rehabilitation of the posterior region of the maxilla even more difficult, which makes sinus lift and precise placement of grafting materials essential procedures (El-Ghareeb, Pi-Anfruns, Khosousi, Aghaloo & Moy, 2012).

The assessment of possible alterations in the maxillary sinuses is observed in the preoperative planning of implant in the posterior region of the maxilla. Panoramic radiography, computed tomography (CT) and cone beam computed tomography (CBCT) have been used as an aid in the planning of rehabilitation in this area (Toraman, Peker, Degerli, Cebeci & Sadik, 2016). For Liang et al. (2010), CBCT is recommended as an excellent and low-cost technique to evaluate the maxillary sinus with only a slightly higher dose of ionizing radiation compared to panoramic radiography, and much lower compared to CT.

The fear of surgery is related to expectations, doubts and worries about what will happen. It is important that the patient is prepared for the surgery and trusts the professional who will operate on them.

The techniques of maxillary reconstruction with bone grafts inevitably present some risk component, since they require: good surgical technique, good quality of the soft tissues that cover the graft, great cooperation on the part of the patient, and general health condition that favors the repair. Factors such as discomfort, abstinence from the use of removable prosthesis, and costs make the procedure difficult. Success will depend on a set of factors, which together respond directly to the results of the oral treatment. Research conducted by Faé, Ferreto and Hoshi (2009) shows that 91% of respondents agree that the success of the implant depends on its location in the mouth, on the patient's cooperation as to having good oral hygiene, and regular visits to the dentist.

The type of maxillary sinus lift technique should be discussed together with the patient; it is mainly based on the height of the residual vertical bone, on marginal bone width, on internal sinus anatomy and on the number of teeth to be replaced, although other factors such as surgical training and experience may interfere with the success of the procedure.

According to Cariello (2018), the effectiveness of this technique can be determined by the quantity of vital bone formation after graft maturation and by the long-term preservation of the implants placed in this region. Two main approaches are commonly used: the lateral window technique and the osteotome intrusion technique. The lateral window technique, used in the reported case, is commonly indicated when large bone gains are required in a severely resorbed maxilla.

The gold standard in approaches involving grafting is the use of autogenous bone, due to its osteogenic, osteoinductive and osteoconductive characteristics. However, Herford and Boyne (2008) reveal that, with the advancement of tissue engineering and the substantial increase in the number of studies related to regenerative medicine, there is an increasing tendency to seek less invasive reconstructive treatments that result in less morbidity, that are quicker and that achieve an ideal aesthetic-functional rehabilitation of patients.

Thus, it is possible to observe in the literature that rhBMP-2 can stimulate osteoblastic differentiation of stem cells, resulting in newly formed bone that has the same composition as natural bone, becoming one of the most promising growth factors for the regeneration of bone defects. Furthermore, it overcomes most problems associated with autogenous and allogeneic bone grafts (Alraei, Sharqawi, Harcher & Ghita, 2020). Among the functions of BMPs, highlight can be given to: induction of cell replication, chemotaxis, induction of differentiation, anchorage-dependent cell fixation, osteocalcin synthesis or mineralization, and alkaline phosphatase activity (Zakrzewski, Dobrzynski, Rybak, Szymonowicz & Wiglusz, 2020).

Govender et al. (2002), in a study with four hundred and fifty patients, observed that the use of rhBMP-2 was safe and, when at a concentration of 1.5 mg/ml, presented a superior result in reducing the frequency of secondary interventions and in the general invasiveness of the procedures, accelerating fracture resolution and improving wound healing. Other clinical studies related to maxillary sinus lift and edentulous alveolar ridge reveal that the use of rhBMP-2 (added to absorbable collagen), at a concentration of 1.5 mg/ml, induced significant bone formation, both quantitatively and qualitatively, similar to native bone, thus enabling rehabilitation with implants (Woo, 2012). In the described case, 2.8 ml of the solution at a concentration of 1.5 mg/ml were used, in association with a collagen sponge and xenogeneic bone graft.

Pasquali et al. (2014) emphasize that the materials tested in association with BMP include hydroxyapatite, resorbable collagen sponges, expanded polytetrafluoroethylene, xenogeneic bone and autogenous bone. The most used carriers are hydroxyapatite and collagen, as they are compounds present in the bone structure, naturally absorbing BMP.

In the reported case, the biomaterials were used in a meticulous way, in accordance with the morpho-physiological patterns of the receptor sites, as well as with the manufacturer's specifications. The functions of the collagen sponge (carrier) are basically to keep the BMP in the specific surgical bed, preventing a possible systemic toxicity from the protein, optimizing osteoinduction by a gradual release of this growth factor (Herford, 2009). However, because it is easily deformable, its use alone is inadequate to maintain the bone regeneration space, oftentimes requiring additional methods for local stabilization, such as the use of titanium mesh and screws.

Side effects of BMP-2 use are related to postoperative inflammation (edema), ectopic bone formation, osteoclast-mediated bone resorption, and inadequate adipogenesis. A better understanding of these side effects by scientists will help determine the most appropriate and safe use of BMP-2 in the clinical setting (James, 2016).

For Lowery and Rosen (2018), BMPs can be beneficial in treating human diseases and in improving the patient's quality of life, and few tools are currently available to set this pathway in the clinical environment. The only FDA-approved application at this time is for recombinant ligands administered in relatively few clinical scenarios, such as open or ununited fractures, vertebral fusion, and maxillofacial bone augmentation.

CONCLUSION

The use of new materials, adjuvants to the technique of reconstruction of the atrophic maxilla involving maxillary sinus lift, such as morphogenetic proteins, are being well reported in the literature, with safety and efficacy being noted. In the case report, the patient evolved without major complications, the result was considered satisfactory, and she awaits the necessary time for rehabilitation with an implant-supported prosthesis.

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