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Recombinant human bone morphogenetic protein-2 for correction of unilateral cleft lip and palatal: Case report

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Abstract

The aim of this paper was to present a case report in which a unilateral cleft lip and palate was repaired with bone graft. The 11 years old Caucasian female patient was subjected to correction of unilateral cleft lip and palatal left (left side) with the rhBMP-2 (INFUSE® Bone Graft). Bone reconstruction and including canine repositioning was planned. A one and a half mm titanium mesh (was fixed by 4 titanium screws in the adjacent bone structures), to sustain collagen sponge with the protein stays in the fissure, allowing a framework and a conformation of the alveolar process. It was observed that the secondary alveolar bone graft with rhBMP-2 contributed to the rehabilitation due to the filling of bone defects caused by fissures, favoring the eruption of the adjacent canine tooth and the health of periodontal tissue. Bone morphogenetic protein is a potential substitute in bone regeneration process.

Keywords: Cleft lip and palate; Bone graft; rhBMP-2

Introduction

Cleft lip and palate are congenital deformities of high prevalence in humans [1,2] (1:650 live births) [3], presenting craniofacial malformation due to changes in embryonic development between the 4ª and 10ª week of gestation [1]. They have a multifactorial etiology, resulting from the interaction between genetic and environmental factors.

Clinically, individuals with fissure may have anatomical defects on labial, alveolar and palatal tissues, which vary according to the extent and severity of each type [3]. To complete rehabilitation move to a multidisciplinary team intervention put before compose of plastic surgeons, dentists and speech therapists [1]. In the early years of life, the patient must be subjected to the primary surgery on lip (cheiloplasty) and palate (palatoplasty) to improve the functional, aesthetic and psychological aspects [4]. This stage is critical in the initial rehabilitation, requiring other surgical interventions [1], such as bone graft [4]. The procedure provides support to adjacent teeth to fissure (erupted or

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not) and stabilizes the premaxilla in cases of bilateral clefts. In addition, provides alveolar ridge continuation, acts as a support of the alar base and nasolabial contour, besides contribute to oronasal fistula elimination [1].

Bone graft can be classified as primary, secondary and secondary late or tertiary, according to the time that it is performed. The primary is performed in the first years of life. The secondary alveolar bone graft is performed before the eruption of the permanent canine and late secondary, or tertiary, after eruption of them [4]. Ungrafted patients may develop a periodontitis at tooth adjacente to fissure due to the absence of a bone septum in this region, beyond the alveolar ridge discontinuation, precluding spontaneous eruption of teeth in the fissure area, as well as orthodontic movements [1].

Autogenous bone con be obtained from the iliac crest to reconstruct the maxilla anatomy as bone grafting [3]. However, it can bring as a result morbidity to the donor site [2,5], pain [2,6] and sensory disturbances in the long term [7]. With the advancement of tissue engineering and its applications in health [3], the grafting procedure, used for the bone defects repair, replaced the autogenous bone by bone morphogenetic proteins (BMP) [3,6,8]. These proteins are members of the Transforming Growth Factors superfamily (TGF) involve in the embryological development and skeleton formation processes [2,9]. The protein is a genetically engineered version of human natural protein, normally found in small amounts in the body, with the purpose of stimulating bone formation.

A recombinant human BMP (rhBMP) has been used in bone defects reconstruction [3]. Acts locally to concentrate the host mesenchymal cells and influence their differentiation into bone forming cells (osteoblasts). The protein has a selective mitogenic effect. In order to have a clinical effect, a super physiological doses are required, approximately 200,000 times the estimated physiological concentration of natural BMP-2, found in bone [2,3].

The aim of this paper was to present a case report in which a unilateral cleft lip and palate (left side) was repaired with rhBMP-2.

Clinical Case

Eleven years old Caucasian female patient, with lip and palate unilateral left (Figure 1A-D). The rehabilitation treatment with RhBMP2 (INFUSE® Bone Graft) (Bone Morphogenetic Protein, Medtronic, Memphis, TN, USA) was planned, avoiding the removal of donor bone of the patient. In the early years of life, the patient underwent reconstructive surgery (cheiloplasty), to correct cleft lip. This material has two components: A human recombinant, represented by Bone Morphogenetic Protein-2 (BMP-2) and a carrier/scaffold for the protein, the absorbable collagen sponge, consisting of bovine collagen type I obtained from deep flexor (Achilles tendon) [3].

The surgery was performed in a hospital under general anesthesia (tracheal intubation) in aseptic environment. After local anesthesia injection the buccal maxilla and palatal region (left side) with 2% lidocaine associated with 1:100,000 epinephrine (5ml).

Figure 1: A) Clinical aspect prior to grafting with rhBMP-2, showing the anterior and posterior crossbite (left side); B) Occlusal view, showing the upper left central incisor inclination, absence of the left maxillary lateral incisor and scar residue of primary surgery; C) cross-bite on the left side; D) Panoramic radiography, showing bone defect and absence of the left maxillary lateral incisor.

An oblique vestibular incision was made between the first molar crown center and mesial gingival papilla. Then, an intrasulcular incision extended to the lateral fissure margin bordering its gingival limit and reaching the contralateral maxilla segment, ending in the intra-sulcular region of the central incisors. From this oblique incision, the gingival flap was divided by approximately 5 mm, and the periosteum and mucosa buccal was incised, thereby obtaining a flap of the total thickness. The palatal mucosa was sutured and then the nasal floor mucosa was repositioned superiorly to promote the fistula closure and the physical space creation to carefully accommodating of the INFUSE® Bone Graft. The buccal flap was repositioned until total coating of the graft and the bone exposed (unstrained); its edges were debrided and finally incision suturing was made with simple stitches (Figure 2A-D).

It is important to note that a healthy periodontium is established especially when the flap design contributes to the keratinized mucosa covers the grafted area. A one and a half mm titanium mesh, fixed by 4 titanium screws in the adjacent bony structures to sustain collagen sponge accommodated in the fissure, allowing a framework and a conformation of the alveolar process (Figure 2D).

Patient was hospitalized for 01 day and received post-operative orientations. During the follow-up (three months), no biomaterial exposure signal was observed. The patient is already undergoing orthodontic treatment, but waiting for bone neoformation to perform tooth movement. Cone beam computed tomography (CBCT) shows the graft region (Figure 3).

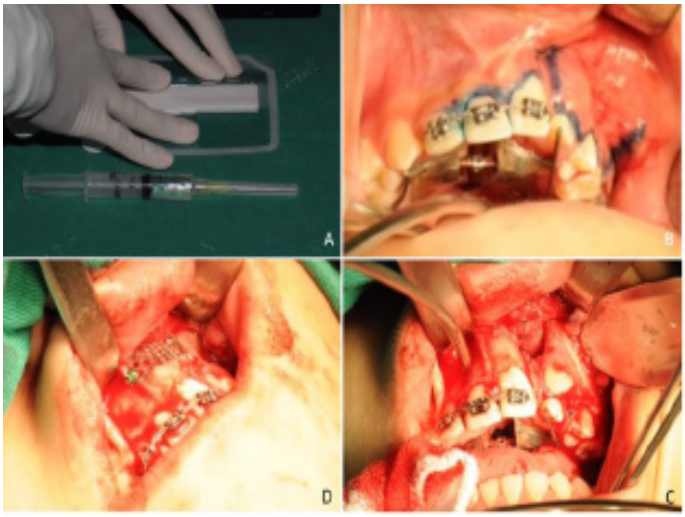

Figure 2: A) Preparation of INFUSE® Bone Graft; B) Design of surgical incisions; C) Bone defect resulting from cleft lip and palate; D) Titanium mesh fixed to the adjacent bone structure after graft in the fissure area.

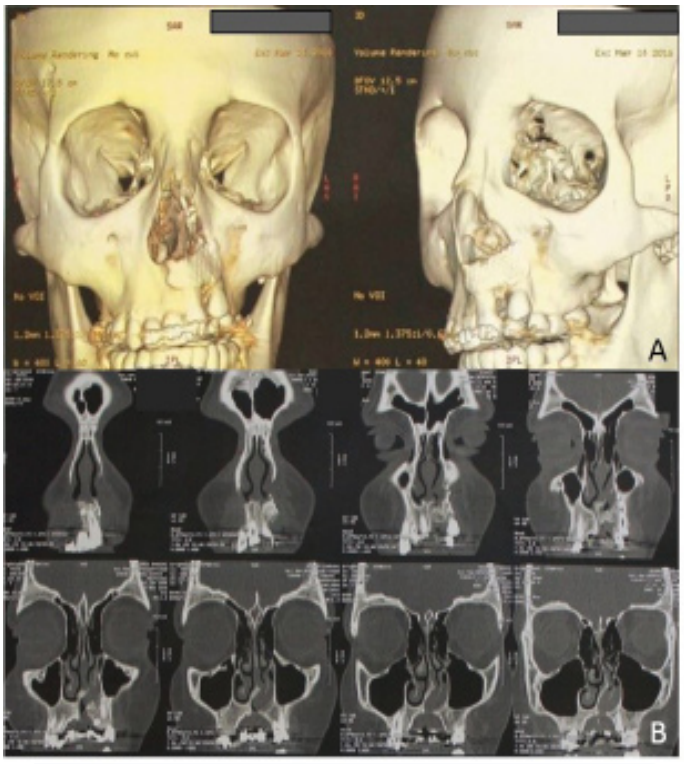

Figure 3: A) Preparation of INFUSE® Bone Graft; B) Design of surgical incisions; C) Bone defect resulting from cleft lip and palate; D) Titanium mesh fixed to the adjacent bone structure after graft in the fissure area.

Discussion

In the first years of life, the patient is subjected to primary surgery in lip and palate to improve the functional, aesthetic and psychological aspects [4], since it interfere with jaw growth. Surgical correction of the alveolar cleft is necessary bone grafts. Secondary graft is performed before the permanent canine eruption and the other (tertiary) can be performed after that eruption. Depending on the case complexity, the surgeries extend into adulthood, ever requiring a multidisciplinary team.

This graft strengthens the cleft and surrounding areas, allowing adjacent teeth movement, especially the canine and premolar, so that erupt inside this area [11]. Thus, the graft provides a normal eruption condition without skeletal disharmony in order to close the dental arch without any cleft residue, leading to a normal condition of overjet and overbite [1].

For many years, the iliac crest bone has been used as a donor site by the ease of access to get a sufficient amount of autogenous bone [3]. However, some complications are involved with this technique: The most common are: pain [2], temporary limitation of leg movements [10] and the long term sensory disturbance [7].

With the advancement of tissue engineering and its applications in health, the grafting procedure used for the bone defects repair [12,13] has replaced the autogenous bone by biomaterials, such as INFUSE® Bone Graft, showing less morbidity and excellent results [3]. As shown, this material is an absorbable collagen sponge impregnated with bone morphogenetic protein-2, which is inserted into receptor site filling the gap. The use of BMP use avoid a second surgical site, providing shorter hospitalization and less surgical time. In addition, it prevents possible complications such as: discomfort, sensory disturbances, scarring and possible infection. The most frequently reported adverse effect is the need for a second surgery due to graft failure [4,12,14,15]. Currently, there is no other bone inducer. Fortunately, in the case presented here, no complications were reported and at the time, the patient is already under orthodontic treatment.

Conclusion

The secondary alveolar bone graft with rhBMP-2 contributed to the rehabilitation due to the filling of bone defects caused by fissures, favoring the eruption of the adjacent canine tooth and the health of periodontal tissue.

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