Bone Substitute: Alveolar Bone Grafting (ABG) with rhBMP-2 (Recombinant Bone Morphogenic Protein-2)

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Alveolar bone grafting was first introduced to Brazil by the Bauru Cleft Team in 1993, brought from Oslo, Norway (Abyholm et al. 1981a). Since that time, the use of autologous bone grafting harvested from the iliac crest using Boyne's technique has become the gold standard for the rehabilitation of the vast majority of cleft patients worldwide (Boyne and Sands 1972). Secondary alveolar bone grafting is ideally performed at 8–10 years of age, when dental development is finishing and the canine is partially formed, with a root of at least 2/3 of final size, ready to erupt into the maxilla. Preoperatively, the use of transverse maxillary expansion and orthodontics for dental alignment facilitates greatly the alveolar bone grafting procedure (Abyholm et al. 1981a, b).

As this procedure is often performed in children under 10 years of age, alternatives to the use of an iliac crest donor site must be considered. Complications at the donor site are quite common with incidence rates reported to be between 2.5 and 40%, ranging from surgical site infection to pain (Ochs 1996; Hall and Posnick 1983; Daw and Patel 2004; Clarke et al. 2015). Beyond the risk of surgical complications, there is also a risk of encountering a lack of sufficient bone for grafting, and a need for secondary and tertiary intervention in the future (David et al. 2005). Patient's parents are always very concerned when the necessity of a donor site is mentioned for children in this age group. Scars and pain are the main concern for then.

Many studies have evaluated possible alternatives to bone substitution and have suggested the use of stem cells, tricalcium phosphate, and bovine bone among others, especially useful when there isn't a sufficient donor site to be harvested. These

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alternatives show promise for the future but raise many concerns regarding the quality of newly formed bone, mainly in children (Raposo-Amaral et al. 2014; de Mendonca et al. 2008; Bueno et al. 2009).

Since 1965 when M. Urist first described a new protein from the family of growth factors that could induce bone formation many improvements in bone healing have happened. Just because this protein had the ability to direct the formation of bone from neighboring cells many researchers felt that would be the solution for bone substitution in the future (Urist 1965). The very first use in clinical cases was done in tibial nonunion and spinal fusions in 2001and 2002 (Baskin et al. 2003; Boden et al. 2000). In maxillofacial defects the approval of FDA occurred in 2007 with many restrictions (Carstens et al. 2005a, b; Chin et al. 2005).

Studies evaluating the use of recombinant bone morphogenic protein 2 (rhBMP-2) for cleft patients in Brazil began in 2008, based off of previous work done by Chin et al. (2005), Carstens et al. (2005a, b).

Initially described by Chin et al., rhBMP-2 was used (Carstens et al. 2005a, b; Chin et al. 2005) at very early age replacing alveolar bone graft at mixed dentition. Our protocol started as was described by Boyne and Sands (1972) ensuring that any failure of BMP-2 implantation could be followed by an ABG. At the Hospital das Clinicas, University of São Paulo Medical School, a prospective randomized study was performed with eight patients, comparing rhBMP-2 and ABG. The methodology to compare both groups was radiologic and clinical evaluation of the patients (Fig. 17.1).

CT scan was taken pre- and 1 year postoperative, and bone volume and alveolar height were measured. On clinical evaluation, complication in donor site, pain and infection, and hospital stay were used for final comparison. The canine eruption and correction of oronasal fistula were compared. The final results after 1 year showed no significant differences with respect to the three primary outcomes of interest: quality and quantity of newly formed bone, tooth eruption, and complications related to rhBMP-2 (Alonso et al. 2010). Canan et al. presented a comparative study among rhBMP-2, ABG, and gingivoperiosteoplasty and found better performance of rhBMP-2 when the bone volume was evaluated (Canan et al. 2012) (Fig. 17.2).

Beginning in 2010, the cost-effectiveness of rhBMP-2 was studied in 23 consecutive patients operated on with the same technique. These patients included unilateral cleft, bilateral cleft, secondary, and tertiary alveolar bone grafting patients. Differences were found with regard to late postoperative edema, which was dose dependent (Leal et al. 2015) (Fig. 17.3).

Leal et al. found late facial edema higher in rhBMP-2 than ABG in 150 patients (Leal et al. 2015).

At 8-year follow-up, no major complications have been recorded. Recent long-term evaluation is being done to evaluate the cost-effectiveness and the rate of success of BMP-2 maxillary alveolar implants in cleft patients. Interim results show

high-quality neo-bone formation, elimination of the need for a donor site, a shorter hospitalization, less operative time, and fewer long-term problems in rhBMP-2 patients compared to ABG patients (Lima Junior 2014).

Repair of maxillary cleft is important for final cosmetic outcomes in cleft lip and palate patients, and patients with defects in their maxillary alveolar bone will often

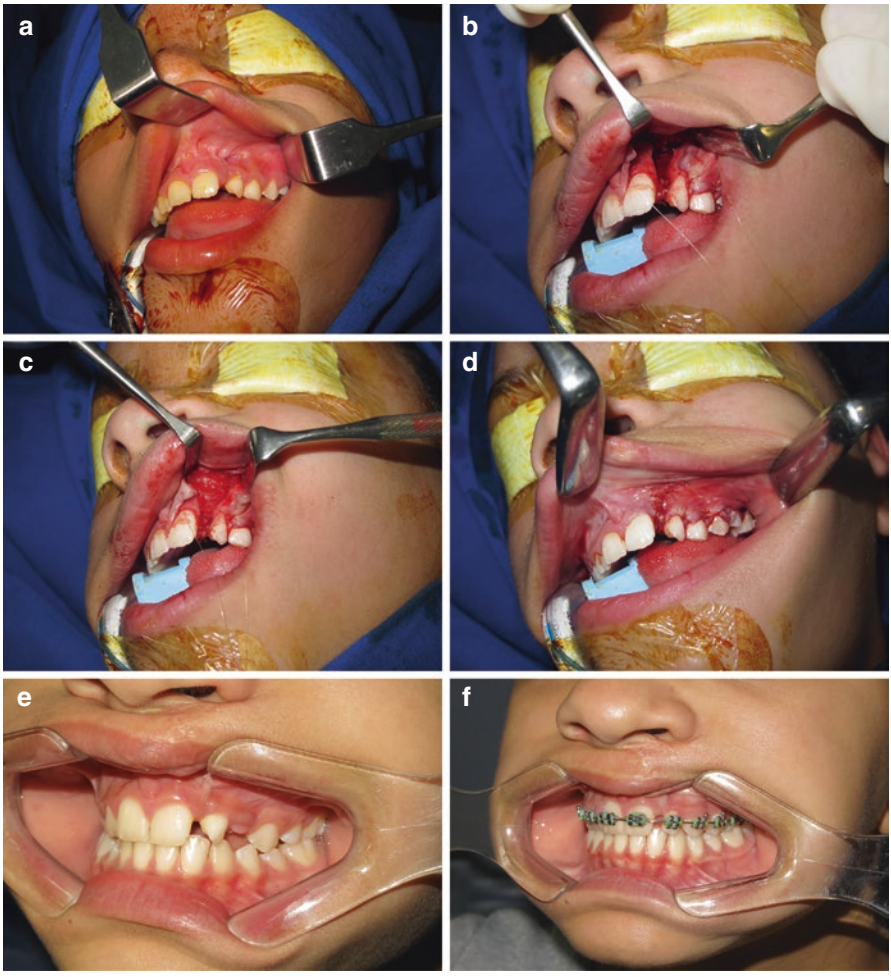
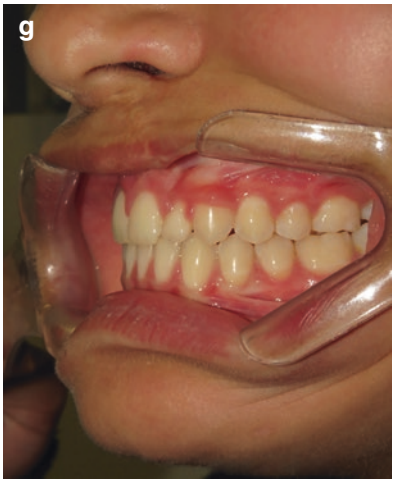


Fig. 17.1 Left unilateral cleft patient age of mixed dentition 10 years old. (**a**) Intraoperative view of the cleft, (**b**) gingivoperiosteal flap raised and nasal mucosa sutured, (**c**) rbBMP-2 with collagen sponge in place without any fixation, (**d**) oral flap in place final suture, (**e**) 6 months after surgery, (**f**) permanent canine irrupted and orthodontic treatment started, (**g**) final dental occlusion 4 years after ABG

Fig. 17.1 (continued)



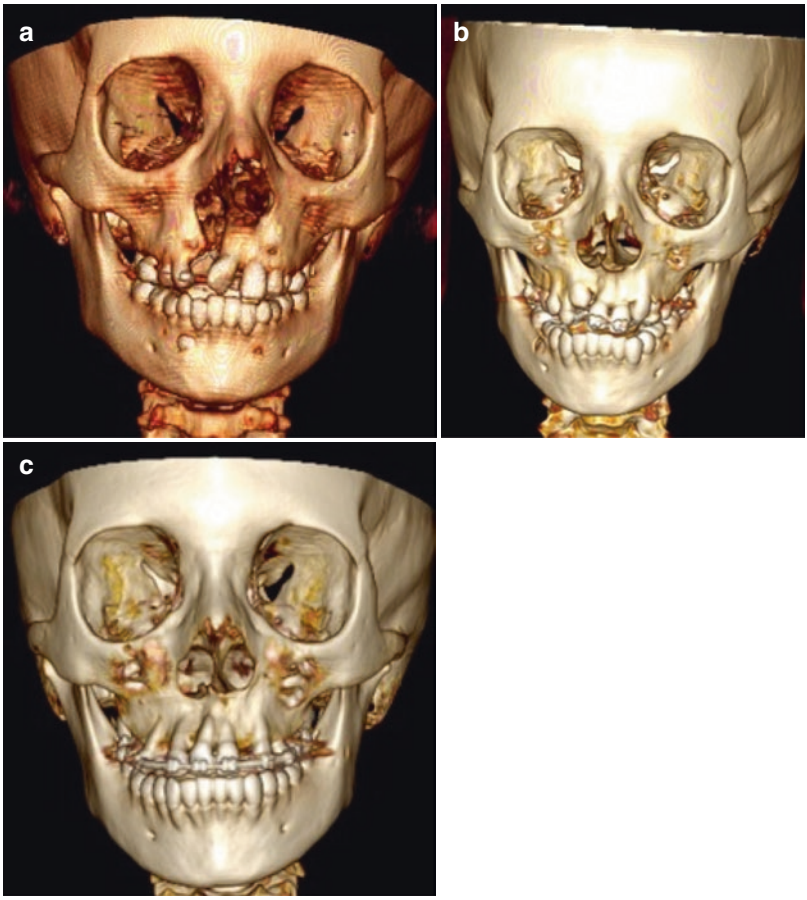


Fig. 17.2 Right unilateral cleft patient before canine eruption. (**a**) CT scan preoperative, (**b**) CT scan during canine eruption, (**c**) CT scan at the end of eruption

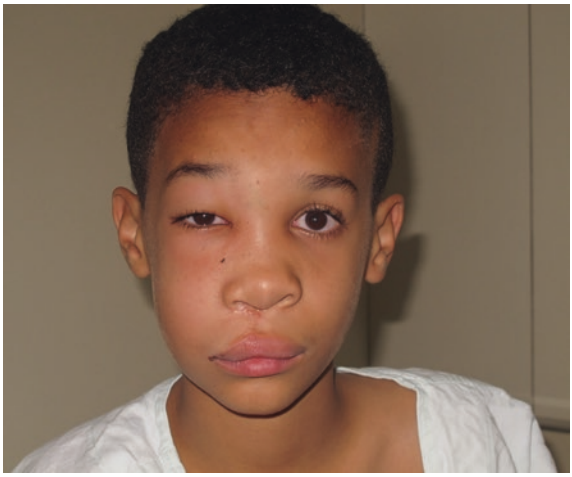


Fig. 17.3 At 5 days PO large facial edema

come in requesting rhinoplasty. If rhinoplasty is performed without first correcting the bony defect, the patient will continue to return at intervals ranging from months to years requesting follow-up rhinoplasty. A preferred sequence is to first correct the alveolar maxillary defect using either an ABG or an rhBMP-2, and then perform a staged rhinoplasty. Several studies at our institution have shown no difference in nasal symmetry and overall cosmetic outcomes between ABG and rhBMP-2 for maxillary cleft repair (Alonso et al. 2014; Raposo-Amaral et al. 2015, 2016).

Bone donor site in children will be always a great challenge not just for lack of available bone but also for the complications related to its local harvesting. New bone substitutes have very good perspectives with new tissue engineering technique associated with genetic stem cell studies (Bueno et al. 2009; Tissiani and Alonso 2016; Tanikawa et al. 2013).

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