

# Three-Dimensional Alveolar Bone Reconstruction with a Combination of Recombinant Human Platelet-Derived Growth Factor BB and Guided Bone Regeneration: A Case Report



Massimo Simion, MD, DDS\*  
 Isabella Rocchietta, DDS\*\*  
 Maurizio Monforte, MD, DDS\*\*\*  
 Emilio Maschera, MD, DDS\*\*\*

A report of a patient who presented with severe disfigurement of the maxillary left lateral incisor and canine area following oncologic surgery is presented. The bone defect extended 20 mm from the cervical line of adjacent teeth up to and including the nasal cavity. Treatment was performed with a 1:1 ratio of autogenous bone graft (harvested from the retromolar region) and deproteinized bovine bone particles. The composite graft was hydrolyzed with recombinant human platelet-derived growth factor BB and covered with a titanium-reinforced nonresorbable membrane. Second-stage surgery was performed at 6 months, at which point the membrane was removed and two titanium dental implants were successfully placed. The elapsed time from initial surgery to definitive prosthesis placement was 14 months. (Int J Periodontics Restorative Dent 2008;28:239–243.)

Guided bone regeneration has been an effective means of enhancing bone volume for the purpose of implant placement. Several materials, including particulated autogenous bone with and without a xenograft or a barrier membrane, have demonstrated success with this technique.<sup>1</sup> A 1:1 ratio of intraoral autogenous bone chips supplemented with deproteinized bovine mineral was shown to successfully accomplish vertical ridge augmentation.<sup>2</sup> Biopsies obtained from patients treated with this technique show that this composite graft presented the normal cascade of events of bone remodeling, from woven to lamellar bone. The application of tissue engineering to these projects has the potential to enhance outcomes, as it reduces or eliminates the morbidity associated with harvesting autogenous bone.

The safety and efficacy of recombinant human platelet-derived growth factor (rhPDGF-BB) have been demonstrated repeatedly by periodontal regeneration.<sup>3</sup> rhPDGF-BB is contained in the alpha granules of blood platelets and participates in regenerative activities, including chemotaxis and proliferation of progenitor cells,

\*Professor and Chairman, Department of Periodontology, School of Dentistry, University of Milan, Italy.

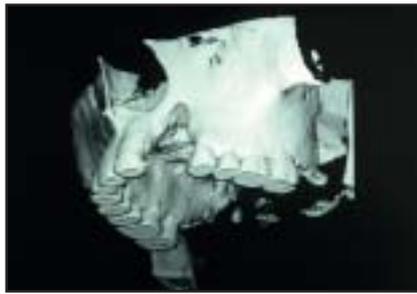
\*\*Research Fellow, Department of Periodontology, School of Dentistry, University of Milan, Italy.

\*\*\*Institute for Dental Research and Education, Milan, Italy.

Correspondence to: Dr Isabella Rocchietta, Department of Periodontology, University of Milan, Via della Commenda 10, Milan 20100, Italy; e-mail:isabella.rocchietta@gmail.com.



**Fig 1** Clinical appearance of the defect. The previous oncolytic resection resulted in the loss of the maxillary left lateral incisor and canine.



**Fig 2** Three-dimensional CT scan reconstructions reveal severe bone loss that is in direct continuity with the nasal cavity.



matrix formation, and the initiation of capillary budding.<sup>4</sup> A significant volume of regenerated bone in a canine model was obtained by infusing a xenograft block with rhPDGF-BB and fixing the block to native bone with two osseointegrated implants.<sup>5</sup> This treatment was then applied to two clinical cases, resulting in a considerable volume of new bone formation surrounding the xenograft.<sup>6</sup>

The application of this growth factor treatment regimen to repair a significant loss of bone to an oncologic lesion is the basis of this case report.

## Case presentation

A 36-year-old female Caucasian patient presented with severe disfigurement of the maxillary left lateral incisor and canine area following oncologic surgery that had resulted in the loss of both teeth (Fig 1). The patient

had been previously diagnosed with epidermoid carcinoma, for which she underwent a surgical resection of the lesion corresponding to the maxillary left lateral incisor and canine. The patient was never treated with chemotherapy or radiotherapy. A computerized tomography (CT) scan confirmed a bone defect with direct nasal cavity continuity (Figs 2a and 2b).

The patient's chief concerns were both esthetic correction, including tooth replacement with dental implants, and functional. She was very encouraged by the possibility of successful treatment and decided to follow the recommendation of bone reconstruction, implant placement, and a fixed restoration. There were no systemic complications, and surgery was performed under local anesthesia.

A midcrestal full-thickness incision was made in the edentulous area and continued intrasulcularly to the adjacent proximal teeth. A partial-

thickness flap was elevated where bone was absent. The bone defect extended 20 mm from the cervical line of adjacent teeth up to and including the nasal cavity (Fig 3). The bone surface was curetted to remove all residual soft tissue and decorticated to expose the medullary spaces that contained the elements necessary for bone regeneration.<sup>7</sup>

Two tenting screws (ACE Surgical Supply) were inserted to help guide the height and thickness of the regenerated bone and to tent the overlying barrier membrane (Fig 4). Autogenous bone was then harvested from the mandibular retromolar area and was supplemented with deproteinized bovine bone particles (Bio-Oss, Geistlich Pharma) in a 1:1 ratio. The composite material was then hydrolyzed with 1.2 mg/mL of rhPDGF-BB (BioMimetic Therapeutics) (Fig 5). A titanium-reinforced Gore-Tex augmentation membrane (expanded



**Fig 3 (left)** Clinical appearance of the defect after full-thickness flap elevation. The vertical bone loss approaches 20 mm.



**Fig 4 (right)** Two tenting screws are positioned to support the composite graft and prevent collapse of the overlying membrane and soft tissues.



**Fig 5 (left)** The composite graft (autogenous bone and deproteinized bovine bone in a 1:1 ratio) is placed and compacted in the deficient site. Prior to this, the graft was hydrolyzed with rhPDGF-BB.



**Fig 6 (right)** The overlying e-PTFE membrane is carefully trimmed and secured by buccal and palatal tacks to the defect area.



**Fig 7 (left)** Tension-free soft tissue closure is achieved with horizontal and interrupted sutures.



**Fig 8 (right)** Re-entry of the site after 6 months reveals complete bone fill of the defect with the tenting screw heads visible. The e-PTFE membrane is removed and two titanium dental implants are placed.

polytetrafluoroethylene [e-PTFE], TR-GTAM, W. L. Gore) was shaped appropriately and fixed palatally and buccally with four tacks. The membrane was trimmed to limit its extent to 1 mm from the adjacent tooth surfaces to decrease the likelihood of membrane exposure, infection, and compromised healing (Fig 6).

Soft tissue closure was ensured by vertical releasing incisions so as to

advance the buccal flap and completely coapt the soft tissues over the wound. A periosteal flap, prepared as described by Triaca et al,<sup>8</sup> provided additional elasticity and tension-free adaptation of the flap surfaces. The wound was closed with horizontal mattress and interrupted Gore-Tex (W. L. Gore) and polypropylene sutures (Fig 7).

A provisional acrylic resin-bonded prosthesis was provided for the area 12 days after surgery. The tissue appearance was excellent at that time, and the site demonstrated complete closure.

The augmentation membrane was removed after 6 months (Fig 8), and two titanium implants (MKIII Natural Platform 3.3 × 15 mm and Speedy Groovy 4 × 15 mm, Nobel Biocare) were placed in the lateral incisor and



**Fig 9a** Periapical radiograph of the initial defect.



**Fig 9b** The tenting screws in place with the overlying e-PTFE membrane.



**Fig 9c** The two titanium dental implants are completely surrounded by regenerated bone.



**Fig 10a** (left) Clinical appearance of the definitive prosthesis in situ.

**Fig 10b** (right) Periapical radiograph of the implants and the definitive prosthesis.



canine sites, respectively (Figs 9a to 9c). Second-stage surgery was performed after 4 months with a soft tissue punch that exposed the cover screws, which were replaced with healing abutments. The time elapsed from initial surgery to definitive prosthesis placement was 14 months (Figs 10a and 10b).

## Discussion

The present patient presented with a severe bone defect resulting from oncologic surgery, which created esthetic and functional problems. The treatment goal was to augment the bone defect to allow dental implant placement and an acceptable implant

prosthesis. The clinical results show complete regeneration of the bone lost during the previous surgery, allowing optimal implant placement and an esthetically acceptable prosthesis.

A composite graft of a growth factor (rhPDGF-BB), deproteinized bovine bone, and autogenous bone in combination with a nonresorbable barrier

membrane was used. The buccal tissue was advanced to provide complete membrane closure, and in fact the site did heal with no exposure. A soft tissue dehiscence over a non-resorbable membrane may result in severe infection of the site, jeopardizing the final outcome.<sup>9</sup> Previous studies have described the positive role played by PDGF in enhancing the healing of soft and hard tissues.<sup>4,5</sup>

The osteopromotive properties of PDGF are seen in its mitogenic, chemotactic, and angiogenic characteristics, which lead to extensive bone reconstruction. One area in which PDGF exerts its properties most markedly is the periosteum.<sup>10</sup> Osteoblasts and precursor cells appear to readily migrate from the periosteum and medullary space to populate the graft matrix. However, a barrier membrane appears to block the chemotaxis of bone progenitor cells from the periosteum and thus compromise the outcome.<sup>5</sup> Although we were able to achieve ideal osseous reconstruction for implant placement, nevertheless we may have decreased PDGF's chemotactic potential by using a non-resorbable membrane. To the best of our knowledge, no data are available regarding the use of PDGF with a non-resorbable membrane.

The result achieved in this patient highlights the potential of adding PDGF to a known technique and its potential beneficial effects on both soft and hard tissue healing. This implies that the use of PDGF may increase the predictability of results and prevent healing complications in cases of three-dimensional bone augmentation.

## References

1. Camelo M, Nevins ML, Lynch SE, Schenk RK, Simion M, Nevins M. Periodontal regeneration with an autogenous bone-Bio-Oss composite graft and a Bio-Gide membrane. *Int J Periodontics Restorative Dent* 2001;21:109–119.
2. Simion M, Fontana F, Rasperini G, Maiorana C. Vertical ridge augmentation by e-PTFE membrane and a combination of intraoral autogenous bone graft and deproteinized anorganic bovine bone (Bio Oss). *Clin Oral Implants Res* 2007;18:620–629.
3. Nevins M, Giannobile WV, McGuire MK, et al. Platelet-derived growth factor stimulates bone fill and rate of attachment level gain: Results of a large multicenter randomized controlled trial. *J Periodontol* 2005;76:2205–2215.
4. Lynch SE. Introduction. In: Lynch SE, Genco RJ, Marx RE (eds). *Tissue Engineering: Applications in Maxillofacial Surgery and Periodontics*. Chicago: Quintessence, 1999:xi–xviii.
5. Simion M, Rocchietta I, Kim D, Nevins M, Fiorellini J. Vertical ridge augmentation by means of deproteinized bovine bone block and recombinant human platelet-derived growth factor-BB: A histologic study in a dog model. *Int J Periodontics Restorative Dent* 2006;26:415–423.
6. Simion M, Rocchietta I, Dellavia C. Three-dimensional ridge augmentation with xenograft and recombinant human platelet-derived growth factor-BB in humans: Report of two cases. *Int J Periodontics Restorative Dent* 2007;27:109–115.
7. Cushing M. Autogenous red marrow grafts: Their potential for induction of osteogenesis. *J Periodontol* 1969;40:492–497.
8. Triaca A, Minoretti R, Merli M, Merz B. Periosteoplasty for soft tissue closure and augmentation in preprosthetic surgery: A surgical report. *Int J Oral Maxillofac Implants* 2001;16:851–856.
9. Simion M, Maglione M, Iamoni F, Scarano A, Piattelli A, Salvato A. Bacterial penetration through Resolut resorbable membrane in vitro. An histological and scanning electron microscopic study. *Clin Oral Implants Res* 1997;8:23–31.
10. Allen MR, Hock JM, Burr DB. Periosteum: Biology, regulation, and response to osteoporosis therapies. *Bone* 2004;35:1003–1012.