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Research Article

Vertical Guided Bone Regeneration with Recombinant Human Bone Morphogenetic Protein-2: A Retrospective Evaluation of Two Clinical Cases

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Abstract

Objectives: The present study evaluated the effectiveness of recombinant human bone morphogenetic protein-2 (rhBMP-2) application in vertical augmentation of the severely resorbed mandibular alveolar ridges for dental implant placement.

Material and Methods: Two alveolar ridge defects in two patients were reconstructed with composite grafts contained in a titanium mesh. Composite grafts consisted of rhBMP-2/absorbable collagen sponge (ACS) mixed with deproteinized bovine bone mineral (DBBM) in a 1:1 ratio. A total of five dental implants were placed in two patients. The results of bone augmentation were analyzed clinically and radiologically.

Results: The healing period was uneventful. Both patients showed radiographic signs of bone formation by as early as 7 months after surgery. At the time of re-entry for implant placement, an adequate volume of viable bone was observed, allowing for the implants to be placed successfully without any issues. The overall dental implant success and survival rates were 100% and remained unchanged at a follow-up period of 1 to 4 years.

Conclusions: The results of this study demonstrated that a composite graft of rhBMP-2/ACS and DBBM can result in predictable reconstruction of a large bone volume of the alveolar ridges for dental implant placement and functional loading.

Keywords: *Recombinant Human Bone Morphogenetic Protein-2, Guided Bone Regeneration, Dental Implant Survival Rate, Dental Implant Success Rate*

Introduction

Vertical bone augmentation presents a considerable challenge in the field of implant dentistry. It involves restoring a substantial volume of useful bone necessary for the proper placement and osteointegration of dental implants, particularly in patients with compromised healing due to prior inflammation, failed surgeries, or age-related factors [1,2].

While a variety of grafting materials are available, autogenous bone remains the “gold standard” due to its excellent osteogenic and osteoinductive qualities. However, autogenous bone grafts come with several limitations and drawbacks such as lengthy surgical procedures, increased costs, potential complications, and a longer recovery period, particularly when using donor sites outside the mouth and restricted availability of bone from intraoral donor sites due to anatomical differences or prior surgical interventions [3,4,5].

Moreover, the osteogenic capacity of autogenous bone tends to decrease with age due to a decline in osteoprogenitor cells in the bone marrow, which are often replaced by fibro-fatty tissue [6,7,8]. Also, over time, autogenous bone grafts may experience significant resorption, with volume loss ranging from 8.3% to 42%. This resorption can be influenced by various factors, including the patient's age, the nature of the bone defect, and the embryological characteristics of the graft (intramembranous vs. endochondral) [9,10].

Growth factors and bone morphogenetic proteins (BMPs) are promising next-generation agents that can be effectively utilized for alveolar ridge reconstruction. BMPs, part of the transforming growth factor beta superfamily, have the ability to initiate and enhance normal bone formation processes and can promote the differentiation of mesenchymal cells into osteogenic cells upon implantation. Research has shown that the osteogenic effects of rhBMP-2 can lead to bone formation comparable to that of autogenous bone [1,11].The FDA approved rhBMP-2, delivered in an absorbable collagen sponge, for orthopedic use in 2002 and for oral and maxillofacial applications in 2007 [12].

This case series aims to evaluate the effectiveness of rhBMP-2 in reconstructing of the severely resorbed alveolar ridges for dental implant placement, as well as to assess the long-term survival and success rates of implants placed in rhBMP-2-induced bone.

Materials and Methods

A retrospective evaluation was performed on two patients with edentulous posterior mandibles (Class V–VI according to Howell–Cawood classification) who were treated from June 2017 to February 2022. Patients did not have any known medical conditions. The defects were grafted with a composite graft consisting of a combination of rhBMP-2/ACS manufactured by Infuse Bone Graft (Medtronic, Memphis, TN, USA) and deproteinized bovine bone mineral (DBBM) Bio-Oss spongiosa granules of 1–2 mm (Geistlich AG, Wolhusen, Switzerland).

The operations were performed under a combination of local anesthesia and intravenous sedation. In each case a mid-crestal incision was made to expose the edentulous alveolar crest. The mandibular left alveolar ridge defects were reconstructed with composite grafts contained in a titanium mesh. Titanium mesh was fixed with monocortical screws. The graft consisted of a mixture of an acellular collagen sponge soaked with solubilizing rhBMP-2 and cut into 0.5-cm square pieces and DBBM particles in a 1:1 ratio, a 0.7 cc of BMP-2 for each two-tooth segment. The mucoperiosteal flaps were repositioned and sutured with resorbable sutures [Figure. 1-4b, Fig. 9-10].

In both cases alveolar defects on the right side were reconstructed with autogenous bone grafts harvested from mandibular ramus [Figure. 4c-d, Fig.11].

Postoperative CBCT scans were obtained immediately after bone augmentation and at the time of implant placement [Figure. 5a,b, Fig.12].

All dental implants were inserted using a two-stage approach with good primary stability (minimum insertion torque of 35 N/cm). Changes in bone quality and peri-implant crestal bone level were evaluated using CBCT images during follow-up visits for a period of 1 to 4 years [Figure. 8a,b, Figure.16a-c].

Results

Two female patients were included in the study. Healing was uneventful, both patients showed radiographic signs of bone formation by as early as 7 months after surgery. At the time of re-entry for dental implant placement, an adequate volume of viable bone was observed, allowing for the implants to be placed successfully without any issues.

A total of five implants were placed, successfully osseointegrated, and functionally loaded after 4 months [Figure.7a-c, Fig.15a-c]. At the time of follow-up (ranging from 1 to 4 years), no implants were lost. Therefore, the implant success and survival rates, according to Albrektsson's criteria, were 100%. Analysis of CBCT images during follow-up visits for a period of 1 to 4 years revealed stable peri-implant crestal bone level and increased density of the augmented bone.

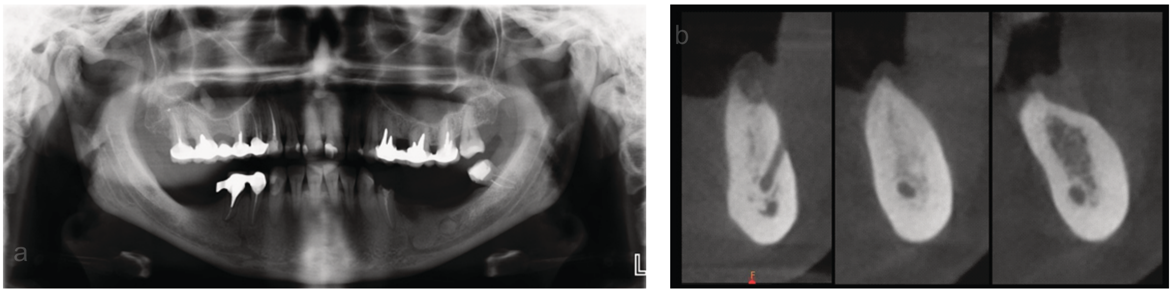


Figure 1a, b. Case #1. Preoperative panoramic radiograph and CBCT scans of the left side showing deficient bone in posterior mandible.

Figure 2a, b. Preoperative intraoral images. Note bone deficiency and lack of keratinize gingiva in the edentulous areas.

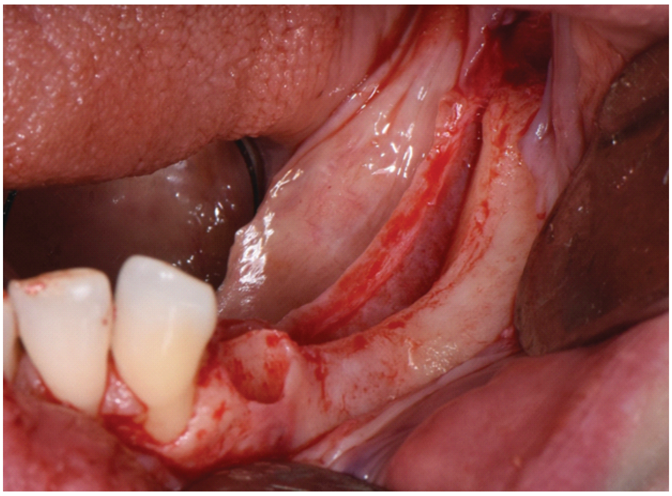


Figure 3. The edentulous alveolar ridge is exposed. Note a bone defect after previous surgeries.

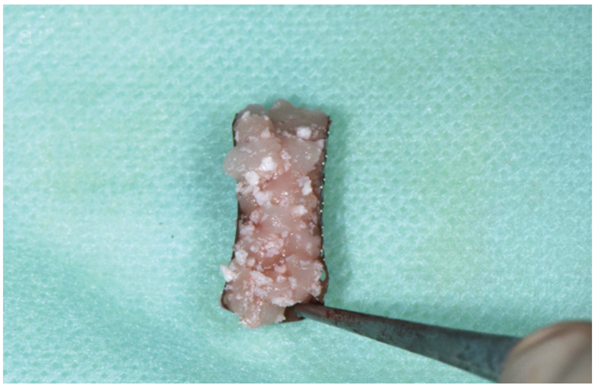


Figure 4a. Titanium mesh with a composite graft before placement. The graft consisted of a mixture of an acellular collagen sponge soaked with solubilizing rhBMP-2 and cut into 0.5-cm square pieces and DBBM particles in a 1:1 ratio.

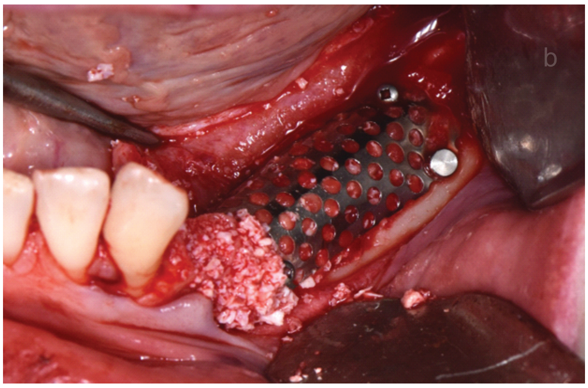
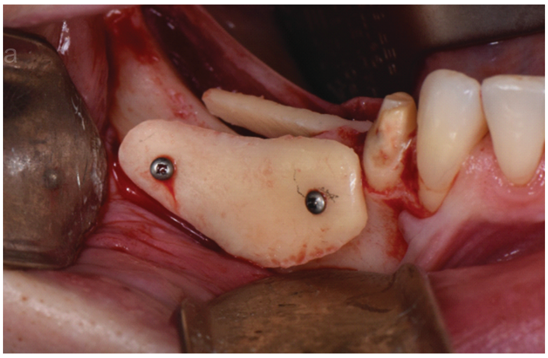


Figure 4b. Titanium mesh is fixed with monocortical screws and pins.



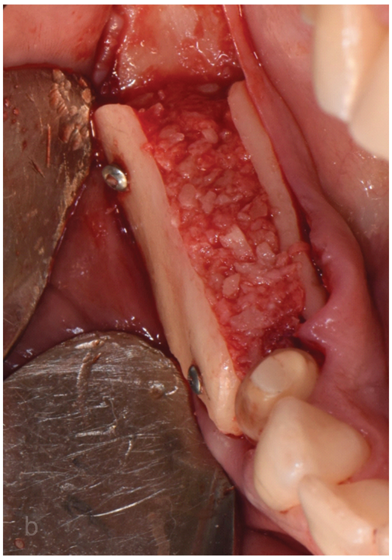
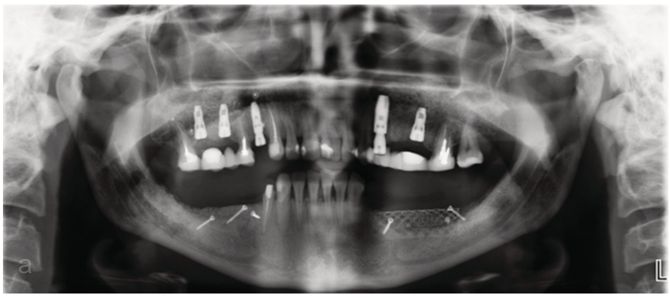


Figure 4c, d. Reconstruction of alveolar defect on the right side with autogenous bone grafts.



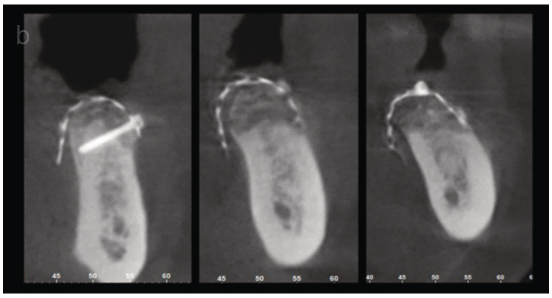
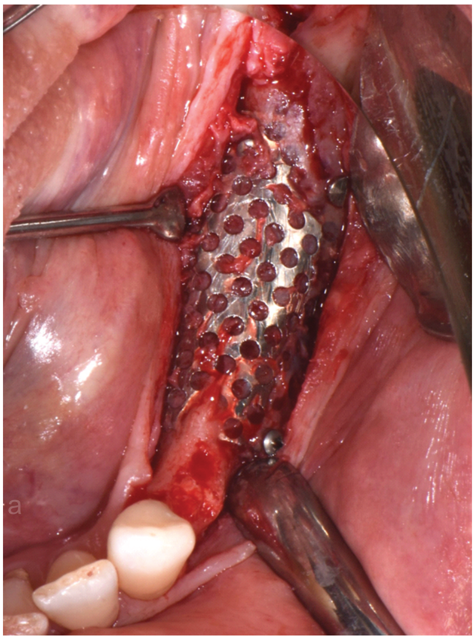


Figure 5a, b. Six months postoperative radiograph.



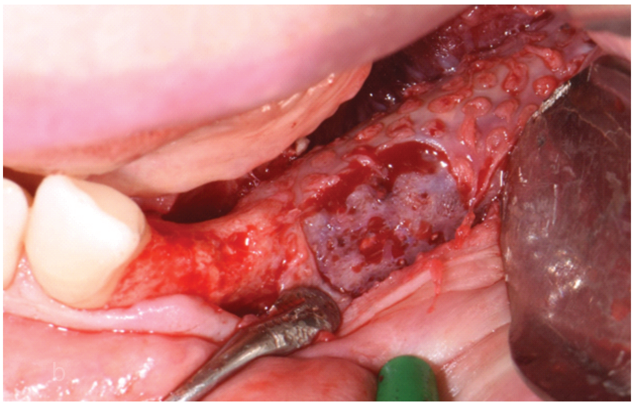


Figure 6a, b. Augmented alveolar ridge is exposed and titanium mesh is removed. Note complete bone regeneration in augmented area.

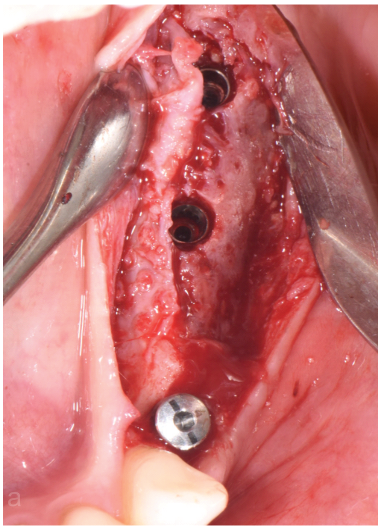


Figure 6c. Placement of dental implants.

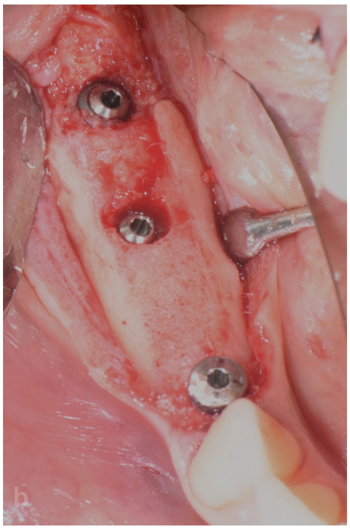


Figure 6d. Placement of dental implants on the right side (after bone blocks augmentation).

Figure 7a-c. Final restoration.

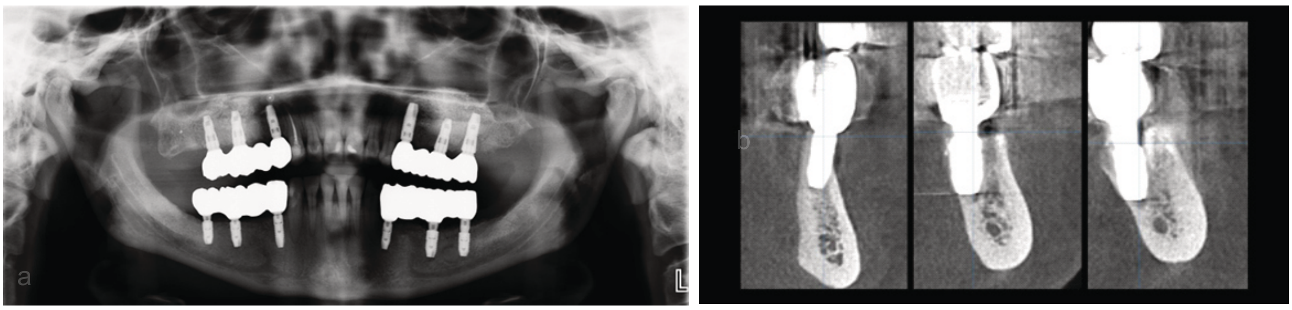


Figure 8a, b. Panoramic radiograph and CBCT scans three years after the delivery of the final prothesis.

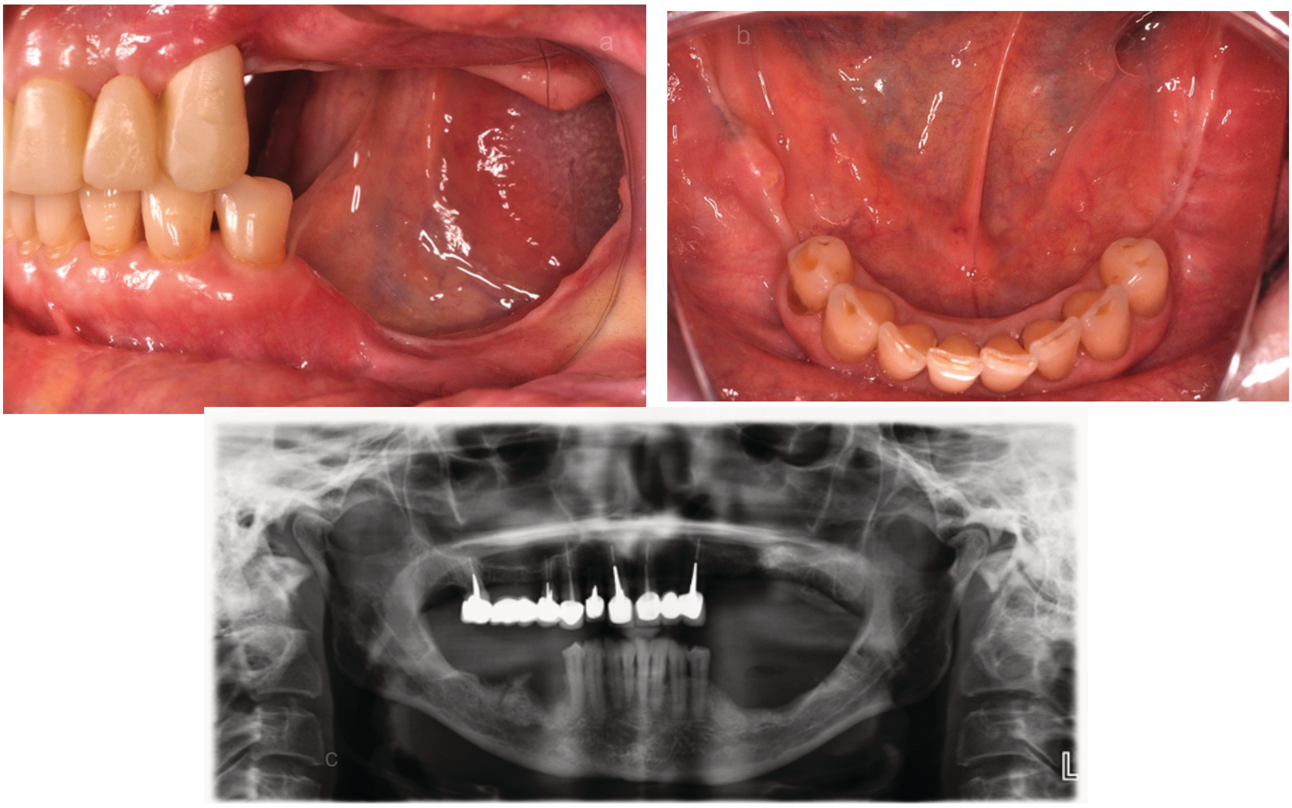


Figure 9a-c. Case #2. Preoperative intraoral images and panoramic radiograph showing deficient bone in posterior mandible.

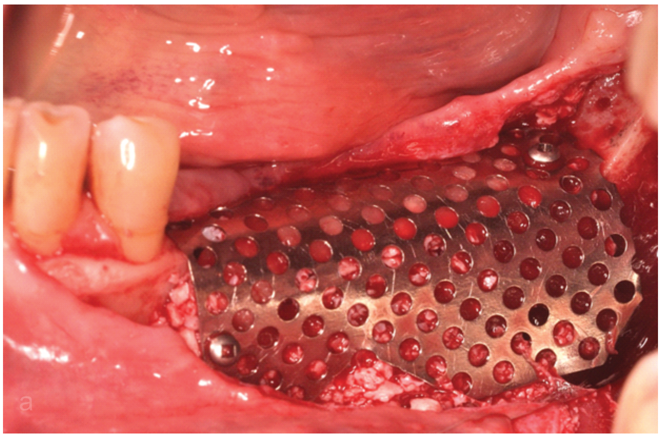


Figure 10. Reconstruction of alveolar ridge on the left side with rhBMP-2.

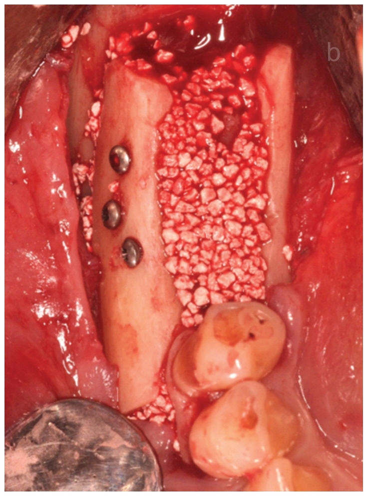


Figure 11. Autogenous bone block augmentation on the right side.

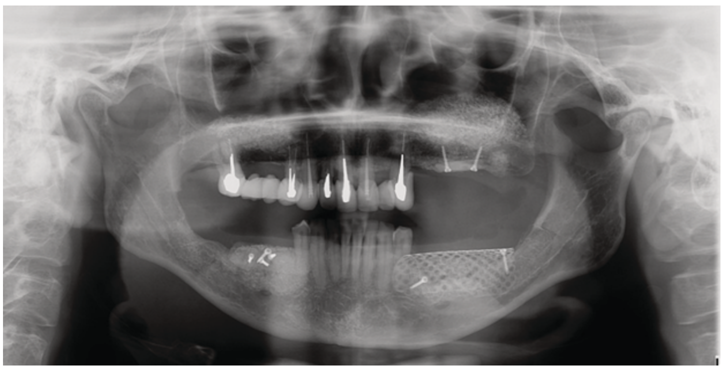


Figure 12. Six months postoperative radiograph.

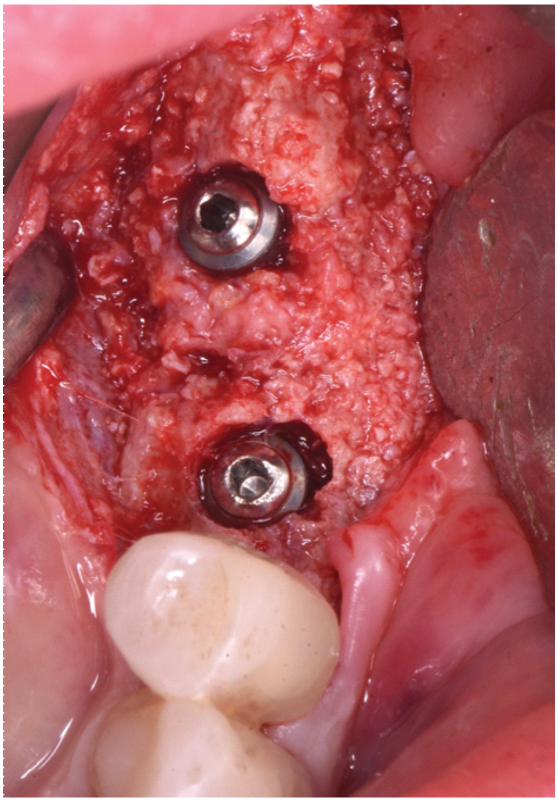


Figure13. Placement of dental implants on the left side. Alveolar ridge grafted with rhBMP-2 /ACS and DBBM.

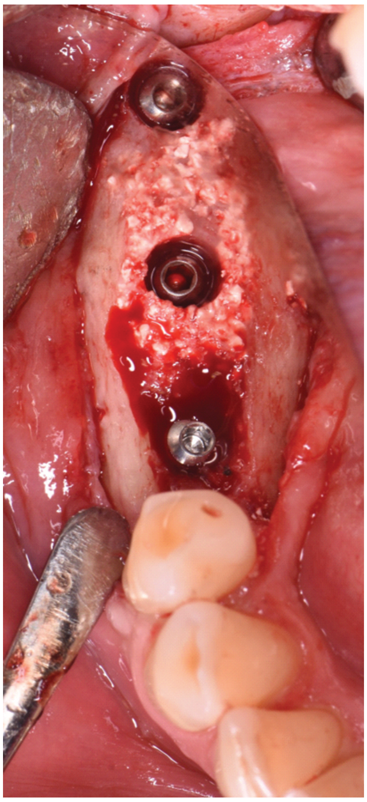


Figure 14. Placement of dental implants on the right side (augmented with bone blocks).

Figure 15a-c. Final restoration.

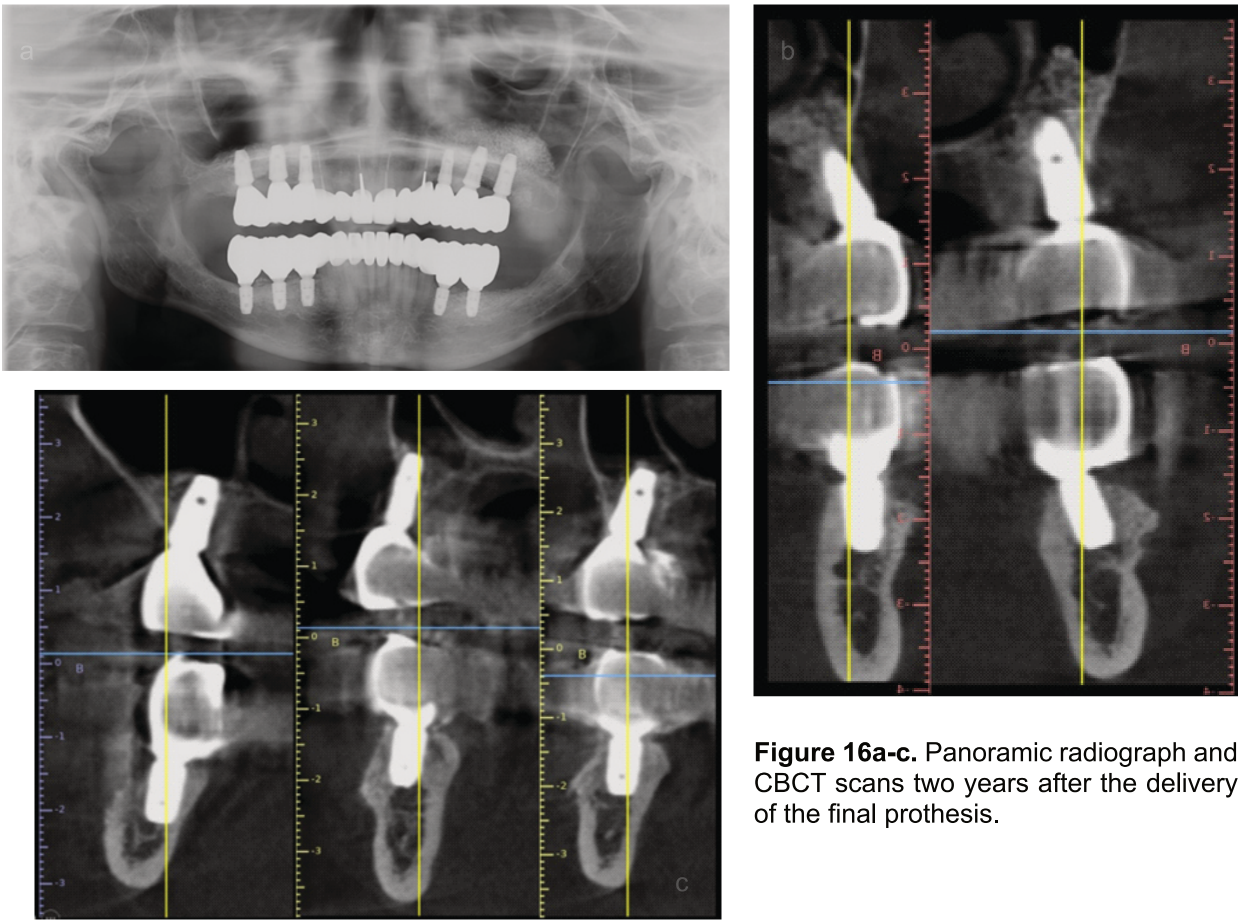


Figure 16a-c. Panoramic radiograph and CBCT scans two years after the delivery of the final prothesis.

Discussion

According to the results of our retrospective case series, a composite graft consisting of rhBMP-2/ACS mixed with DBBM withing a titanium mesh can be used for the successful reconstruction of critical size ridge defects. The results of grafting with composite material were equivalent to that seen for sites augmented with autogenous grafts in terms of total bone regeneration, implant osseointegration and functional restoration [1,13].

A combination of rhBMP-2 /ACS and DBBM completes the tissue-engineering triangle, where the rhBMP-2 signal attracts mesenchymal stem cells and hematopoietic stem cells, providing cellular proliferation, capillary ingrowth, and osteoid formation. An acellular collagen sponge (carrier) and DBBM (xenograft) represent an upregulated matrix that attaches cell adhesion molecules (fibrin, fibronectin, and vitronectin), thereby creating a framework for cell migration and subsequent tissue formation [1,11,13].

Additionally, rhBMP-2 promotes soft tissue healing by stimulating vascular endothelial growth factors [1,13,14]. Thus, its application could be beneficial for the treatment of bone defects with impaired blood supply. All patients in our case series fell into this category due to prior inflammation, failed surgeries, or age-related factors.

Titanium mesh perfectly serves to stabilize the graft and maintain the space preventing compression of ACS soaked with rhBMP-2, however it tends to erode thin mucosa. Mesh exposure is one of the potential complications after the surgery and can occur in 27%-50% of cases. However, if it occurs more than 3 weeks after the surgery, it doesn't lead to graft loss because by that time the augmented bone should be well vascularized to resist infection [1,13,14].

Herford AS and Boyne PJ utilized rhBMP-2 in the reconstruction of large critical-sized mandibular defects secondary to osteomyelitis or neoplastic diseases. In all 14 cases of successful osseous restoration of the edentulous area, followed by prosthetic treatment, rhBMP-2 was used alone with the collagen carrier, without concomitant bone materials. A superior border plate or titanium mesh were utilized to maintain the space by "tenting" the periosteum of the soft-tissue walls of the defects. [13].

Robert E. Marx et al. found out that a composite graft of recombinant human bone morphogenetic protein-2/acellular collagen sponge (rhBMP-2/ACS), crushed cancellous freeze-dried allogeneic bone (CCFDAB), and platelet-rich plasma (PRP) within a titanium mesh crib regenerates bone as predictably as 100% autogenous graft with less morbidity, equal cost, and more viable new bone formation without residual nonviable bone particles, but with more edema. This composite graft embodies an in-situ tissue engineering conception that can deliver results comparable to autogenous grafts for significant vertical ridge augmentations without the need for donor bone harvesting [1].

Jung et al. investigated the influence of rhBMP-2 on GBR when combined with Bio-Oss. The results of their study showed that the combination of xenorgaft (Bio-Oss) with rhBMP-2 could enhance bone maturation and accelerate GBR therapy [15].

The most notable disadvantage of using rhBMP-2 is edema, which is generally larger and persists longer than that with autogenous bone grafting. In addition, this type of edema is less responsive to steroids. This was attributed to two factors: rhBMP-2 hypertonicity and increased cellular content at the surgical site. Steroids are less effective in edemas caused by noninflammatory cells [1].

Also, there are some concerns among clinicians that growth and differentiation factors and rhBMP-2 could cause uncontrolled differentiation of mesenchymal cells, similar to cancer [16,17]. Several arguments have been made regarding this notion. First, growth and differentiation factors do not enter the cell or cell nucleus, releasing their effects through cell membrane receptors. They were only active for 3 weeks. Additionally, they are not mutagenic. Finally, no control studies have shown a higher incidence of cancer among rhBMP-2 users [13,18].

Conclusion

The current study showed that severely resorbed mandibular alveolar ridges could be successfully augmented with a combination of rhBMP-2 /ACS and DBBM. RhBMP-2/ACS has great osteogenic potential and can be used as an alternative to autogenous bone. Advanced surgical skills and protocols for rh-BMP-2 preparation and utilization are required to perform this technique. Further studies are needed to support the safety and effectiveness of rhBMP-2 in preprosthetic and reconstructive surgeries.

Abbreviations

rhBMP-2: recombinant human bone morphogenetic protein-2; DBBM: deproteinized bovine bone mineral; ACS: absorbable collagen sponge; BMGCs biomaterial-associated multinucleated giant cells; FDA: The United States Food and Drug Administration; CBCT: cone-beam computed tomography; HbA1c glycated hemoglobin; GBR: guided bone regeneration; IGF-1,2: insulin-like growth factors 1 and 2.

Acknowledgements

Not applicable

Author's Contribution

GD: conceived the presented study, performed literature search, analyzed the data, wrote the manuscript. ES: conceived the presented study, analyzed the data, wrote the manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

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