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Case report

Continuity resection of the mandible after ameloblastoma – feasibility of oral rehabilitation with rhBMP-2 associated to bovine xenograft followed by implant installation

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ABSTRACT

Recombinant human morphogenetic protein (rhBMP) is a graft alternative for extensive mandibular reconstruction after tumor resections. However, the feasibility of rhBMP-2 to receive osseointegrated implants and prosthetic rehabilitation has been rarely reported. This study reports on a case of an extensive solid ameloblastoma along the mandibular body. The treatment consisted of resection followed by off-label use of rhBMP type 2 associated with bovine bone xenograft. Eleven months postoperatively, the patient was prosthetically rehabilitated with dental implants, without evidence of resorption or complications. The literature on mandibular reconstructions using rhBMP and their feasibility for future osseointegrated implant placement was also reviewed. Based on the presented case, the association between rhBMP-2 and a bovine bone xenograft could be considered a feasible option for the reconstruction and rehabilitation of large mandibular defects after tumor resection. According to the literature, the use of rhBMP as a graft material is encouraging, with good clinical outcome. However, there are no long-term studies demonstrating success and survival rates of implants placed in these grafts. Future investigations will be required to ascertain the long-term survival of implants in areas grafted with rhBMP. Also, there is a lack of information regarding the prosthetic rehabilitation of these patients.

1. Introduction

Mandibular continuity defects due to tumor resection can lead to significant morbidity that requires reconstruction techniques (Cicciù et al., 2014) in order to reestablish patient function and aesthetics. Given that iliac crest autograft and microvascularized graft can cause further morbidity and pain, and that the resulting graft often lacks in quality and height (Herford and Cicciù, 2010), the off-label use of recombinant human bone morphogenetic protein (rhBMP) has been considered as an alternative in such cases (Lustosa et al., 2014). The two most studied bone morphogenetic proteins (BMP) for oral and maxillofacial application are the rhBMP-2 and rhBMP-7, which have been demonstrated to possess osteoinductive properties.

Although the US Food and Drug Administration (FDA) has approved the use of recombinant human morphogenetic proteins only for sinus augmentations and for localized alveolar ridge augmentations in defects associated with extraction sockets (Physician labeling, 2007), some studies have used these proteins for reconstructions of mandibular defects in animals (Toriumi et al., 1991, 1999; Boyne, 1996; Wang et al., 2004) and humans (Chao et al., 2006; Carter et al., 2008; Herford and Boyne, 2008; Balaji, 2009; Glied and Kraut, 2010; Herford and Cicciú, 2010; Zétola et al., 2011; Cicciú et al., 2012, 2014; Desai et al., 2013; Lustosa et al., 2014).

In 1991, Toriumi et al. performed a functional, histologic, and biomechanical evaluation of the rhBMP-2 for mandibular reconstruction in dogs. The biomechanical strength of the defects reconstructed with BMP-2 increased significantly from 3 to 6 months and was related to degree of mineralization and thickness

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of bone bridging the defect (Toriumi et al., 1991). A pilot study in monkeys was undertaken by Boyne (1996) to observe the effect of the rhBMP-2 on bone regeneration following hemimandibulectomies, using a collagen I sponge as the carrier. The reconstructed areas were implanted and brought into occlusion. In all animals, the alveolar ridges were regenerated completely with restoration of contour and cortical bone, indicating that rhBMP-2 can bring about osseous regeneration of critical-sized hemimandibulectomy defects (Boyne, 1996). Toriumi et al. (1999) determined the degree of bone resorption and stability of canine mandibular defects reconstructed with rhBMP-2 and a bioerodible particle carrier. The rhBMP-2–induced bone stabilized by 11 months after reconstruction, and no further resorption was noted. The newly formed bone successfully integrated with existing host bone, creating a stable union capable of withstanding the forces of masticatory function in dogs (Toriumi et al., 1999). The preliminary study of Wang et al. (2004) investigated the potential of the rhBMP-7 (OP-1) collagen formulation stabilized with carboxymethylcellulose (CMC) in mandibular defects in miniature pigs. The results suggested that the rhBMP-7 delivered with a CMC-stabilized type I collagen matrix may have an effective osteoinductive potency and excellent space-keeping properties (Wang et al., 2004).

Some studies have successfully and predictably used rhBMP-2 (Chao et al., 2006; Carter et al., 2008; Herford and Boyne, 2008; Balaji, 2009; Heford and Cicciú, 2010; Zétola et al., 2011; Cicciú et al., 2012, 2014; Desai et al., 2013; Lustosa et al., 2014) and rhBMP-7 (Clokie and Sándor, 2008) (off-label) for reconstructions of mandibular defects in humans after tumor resections, alone or in association with another grafts. However, most of these studies did not mention the rehabilitation of these defects with dental implants and prostheses.

The insertion of bovine bone xenograft in association with rhBMP-2 is presented in the literature as a scaffold to maintain space, allowing rhBMP-2 to develop its function as an osteoinductive graft (Lustosa et al., 2014). Tarnow et al. (2010) showed that this association reduced the shrinkage of the graft and produced higher density in the newly formed bone, when compared with allografts in sinus lift procedures (Tarnow et al., 2010).

Implant placement in grafted sites after mandibular reconstruction with autogenous grafts have shown high survival and success rates (Chiapasco et al., 2006, 2008; Zou et al., 2013). Despite that, bone grafts harvested from extraoral sites cause morbidity to patients (Zou et al., 2013). Hence the recent interest in the use of rhBMP-2 and rhBMP-7 as an alternative graft. However, studies reporting on the placement of dental implants in rhBMP-2–grafted areas after mandibular reconstruction are rare, and do not mention the prosthetic rehabilitation or the outcome of dental implants in the long term (Herford and Boyne, 2008; Cicciù et al., 2012).

Therefore, the present study aimed to report a case of an extensive mandibular solid ameloblastoma treated with segmental resection and the immediate reconstruction with off-label use of rhBMP-2 associated with bovine bone xenograft, followed by prosthetic rehabilitation with osseointegrated implants. Additionally, a review of the literature on mandibular reconstruction after the removal of extensive tumors or cystic lesions followed by dental implant rehabilitation was conducted using the following two inclusion criteria: studies conducted in humans, and articles published in English. The database sources were Medline and Lilacs and the search terms used were “rhBMP-2” OR “rhBMP-7” OR “OP-1” AND “mandible” AND “reconstruction”. Twelve relevant articles were found, and their methods and results were summarized in Table 1, including the present study.

2. Case report

A 44-year old Caucasian/white male patient presented with persistent swelling in the right mandibular body for 24 months, without other symptoms. Panoramic radiography and computed tomography (CT) revealed a multilocular hypodense lesion in the mandible extending from the distal portion of the right canine to the second molar, involving the lower edge of the mandible (Fig. 1). Incisional biopsy followed by microscopic examination revealed proliferation of cell nests, similar to ameloblasts, in palisade with inverted polarization, with central areas resembling the stellate reticulum, compatible with solid ameloblastoma (Fig. 2).

The treatment consisted of segmental subperiosteal mandibular resection under general anesthesia with alveolar inferior nerve resection. Combined extra- and intraoral access was performed. A 2.4-mm locking reconstruction plate (Neoortho, Curitiba, Brazil) was preadjusted and placed in position to maintain the mandibular perimeter. The defect was filled with 12 mg of rhBMP-2 (Infuse, Medtronic Safamor Denek) in absorbable collagen sponge (1.5 mg/mL), and 2 g of bovine bone xenograft (Bio-Oss, Geistlich Biomaterials) covered by a titanium mesh (Fig. 3). The histopathologic characteristics of the specimen confirmed the solid ameloblastoma diagnostic.

The purified rhBMP-2 is freeze-dried in vials. These vials are assembled into marketed kits. One vial contains sterile water for injection and another contains the rhBMP-2. The kit also contains a sterile absorbable collagen sponge. The bone graft was prepared according to the manufacturer's instructions. The rhBMP-2 protein was mixed with sterile water. The solution was then soaked onto the absorbable collagen sponge. After 15 min, the rhBMP-2 binds to the collagen sponges and becomes stable, allowing cutting the membrane into small pieces. These fragments are then mixed with the bovine bone xenograft in a 1:1 ratio. This mixing allows cavity filling with greater dimensional stability and provides slower reabsorption, ensuring the maintenance of the fill.

Follow-up consisted of weekly appointments within the first month postoperatively, then again at the end of the third and sixth months, and finally the surgery for implant placement was scheduled on the eleventh month after the resection surgery, when bone formation was considered satisfactory and no recurrence was observed (Fig. 4). The second surgery was conducted under local anesthesia for the placement of four dental implants (Straumann SLActive, Tapered Effect, 3.3, Regular Neck; Institute Straumann AG, Basel, Switzerland) in the grafted area (Fig. 5). Two months after implant placement, prosthetic rehabilitation with an implant-supported partial denture was initiated. Eighteen months after the first surgery and 5 months of prosthetic load on the dental implants, the patient had fully recovered from the treatment and regained normal function (Fig. 6). All of the implants have survived.

3. Discussion

Ameloblastomas can be locally aggressive and may involve a large portion of the mandible when detected late. The recommended treatment consists of tumor resection with a 1-cm margin, followed by immediate reconstruction (Sham et al., 2009). The resection can produce a large defect and, depending on its size, mandibular continuity may be lost. The gold standard in these cases is the reconstruction with autogenous bone graft (Herford and Cicciù, 2010).

Of the total 28 cases of mandibular reconstruction after the removal of extensive tumors or cystic lesions with rhBMP-2 or rhBMP-7, the most frequently used surgical procedure was resection (26 cases), whereas enucleation and curettage was performed

Table 1
Review of the literature of studies using rhBMP-2 and rhBMP-7 to reconstruct human mandible.

Authors, year	Lesion	Type of surgery	Defect size (cm)	rhBMP	Associated graft	Results	Follow-up (months)	Rehabilitation
Present study	Solid ameloblastoma	Resection	4	2	Bovine bone xenograft	Bone neoformation	11	4 implants
Cicciú et al., 2014	Solid ameloblastoma	Resection	7.5	2	Allograft	Bone neoformation	18	None
Lustosa et al., 2014	Central giant cell lesion	Enucleation and curettage	5	2	Bovine bone xenograft	Bone neoformation	24	None
Desai et al., 2013	Giant cell reparative granuloma	Resection	3.5	2	Matrix of beta tricalcium phosphate and platysma flap	Good Healing	28	NR
	Recurrent ameloblastoma		12		Allograft and Matrix of beta tricalcium phosphate	Poor Healing	36	NR
	Ameloblastoma		11		Allograft	Good Healing	39	NR
	Odontogenic keratocyst		10		Matrix of beta tricalcium phosphate	Good Healing	50	NR
	Odontogenic keratocyst		6		Matrix of beta tricalcium phosphate	Good Healing	51	NR
Cicciú et al., 2012	Dentinogenic ghost cell tumor	Resection	NR	2	Allograft	Bone neoformation	9	4 implants
Zétola et al., 2011	Ameloblastoma	Resection	NR	2	Autograft and hidroxiapatyte beta tricalcium phosphate	Bone neoformation	7	None
Herford and Cicciú, 2010	Central giant cell lesion	Resection	NR	2	Autograft	Bone neoformation	6	None
Glied and Kraut, 2010	Ameloblastoma	Resection	8	2	Allograft	Little Bone Formation	12	None
	Ameloblastoma		4.5			Little Bone Formation	12	None
Balaji, 2009	Aneurysmal bone cyst	Resection	6	2	Autograft	Bone neoformation	6	None
Herford and Boyne, 2008	Aggressive juvenile ossifying fibroma	Resection	±6.1	2	No associations	Bone neoformation	6	Conventional prosthesis
	Ameloblastoma						8	None
	Ameloblastoma						8	5 implants
Clokie and Sándor, 2008	Ameloblastoma	Resection	9	7	Demineralized bone matrix (DBM) suspended in a reverse-phase medium	Bone neoformation	Minimum of 9 months	4 out of 9 patients had dental implants placed
	Ameloblastoma		5					
	Ameloblastoma		3					
	Ameloblastoma		3					
	Ameloblastoma		7					
	Ameloblastoma		6					
	Ameloblastoma		5					
	Ameloblastoma		5					
	Ameloblastoma		7					
Carter et al., 2008	Dentigerous cyst	Tooth extraction, enucleation, and curettage	NR	2	Microfibrillar collagen	Bone neoformation	6	None
Chao et al., 2006	Juvenile ossifying fibroma	Resection	12	2	Matrix of beta tricalcium phosphate and Hydroxyapatite	Bone neoformation	9	None

NR, not reported.

in two cases (Carter et al., 2008; Lustosa et al., 2014). Bone size defects ranged from 3.5 cm (Desai et al., 2013) to 12 cm (Chao et al., 2006; Desai et al., 2013). Follow-up time varied from 6 months (Chao et al., 2006; Balaji, 2009; Herford and Cicciù, 2010) to 51 months (Desai et al., 2013); bone neoformation was observed in 89.3% of the cases, whereas in the remaining 10.7% of cases little bone formation or poor healing was found. Concerning the types of graft used, in three cases the authors associated rhBMP-2 with β-tricalcium phosphate matrix (Desai et al., 2013); in five cases it was associated with allografts (Glied and Kraut et al., 2010; Cicciù et al., 2012, 2014; Desai et al., 2013); three cases presented no associations (Herford and Boyne, 2008); in two cases it was associated with bovine bone xenograft (Lustosa et al., 2014); in two cases with autografts (Balaji, 2009; Herford and Cicciù, 2010); in one case with microfibrillar collagen (Carter et al., 2008); in one case with autograft, hydroxyapatite and β-tricalcium phosphate matrix (Desai et al., 2013); in one case with allograft and β-tricalcium phosphate matrix (Desai et al., 2013), in nine cases with 10 mL of demineralized bone matrix (DBM) suspended in a reverse-phase medium (DynaGraft Putty) (Clokie and Sándor, 2008), and in one case with hydroxyapatite and β-tricalcium phosphate matrix (Chao et al., 2006). Dental implant rehabilitations were presented only in four studies, including the present report (Herford and Boyne, 2008; Clokie and Sándor, 2008; Cicciù et al., 2012) (1).

In 2007, the US FDA approved the use of rhBMP-2 (on-label) as an alternative to autogenous bone graft for sinus augmentations and alveolar ridge augmentations after teeth extractions (Physician labeling, 2007). However, before that, Moghadam et al., in 2001, had already reported on the use of native BMP-2 in the reconstruction of a 6-cm mandibular defect. Nine months after the procedure, the graft showed osteogenesis, demonstrating the capacity of BMP-2 to induce bone formation in a segmentally resected mandible (Moghadam et al., 2001). Despite FDA limitations on the use of rhBMP-2, since the findings of Moghadam et al. (2001), other studies have also reported success with the off-label use of rhBMP-2 in the reconstruction of mandibular defects (Herford and Boyne, 2008; Desai et al., 2013; Lustosa et al., 2014). Thus, rhBMP-2 is increasingly becoming a feasible alternative for mandibular reconstructions, avoiding the need for a second surgical intervention and the consequent morbidity and pain resulting from bone harvest, as well as the loss in graft quality and height (Herford and Cicciù, 2010).

However, in some cases, rhBMP-2 is unable to produce enough bone volume to reestablish patients' function and aesthetics. The

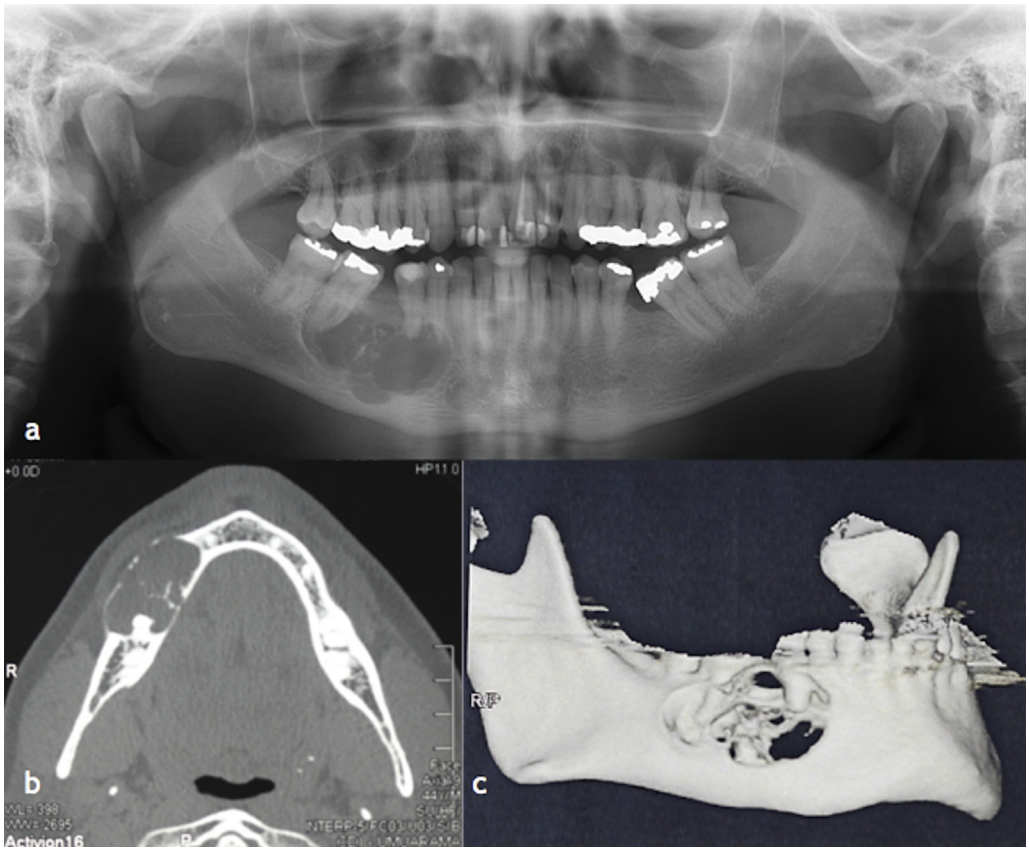

Fig. 1. (a) Panoramic radiograph showing a multilocular radiolucent area extending from the distal portion of the right canine to the second molar, involving the lower edge of the mandible. (b) Computed tomographic axial plane demonstrating the cortical expansion due to the presence of an extensive lesion. (c) Three-dimensional reconstruction showing bone loss on the buccal cortical plate.

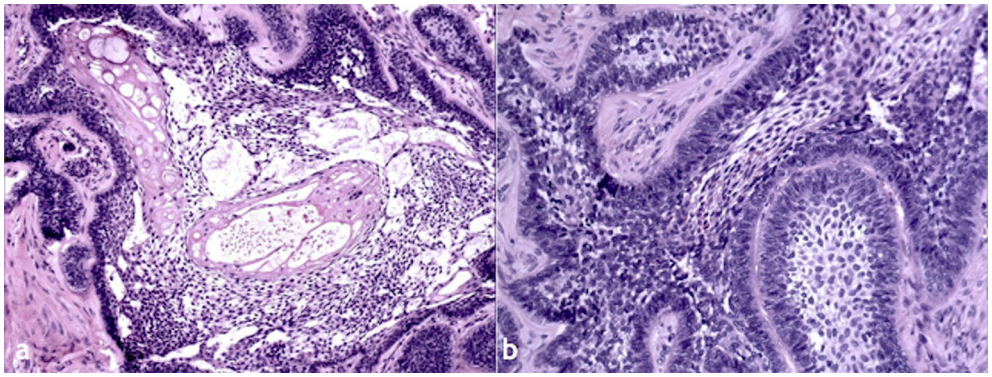

Fig. 2. Proliferation of cell nests, similar to ameloblasts, in palisade with inverted polarization, and central areas resembling the stellate reticulum, confirming the diagnosis of solid ameloblastoma; ×100 (a) and ×200 (b) magnification. Hematoxylin and eosin staining.

main factors to be taken into account in graft failures or insufficient bone formations are graft placement in infected areas, or in areas without sufficient scaffolding to prevent the compression by soft tissue swelling of the collagen sponge that contains rhBMP-2 (Carter et al., 2008; Glied and Kraut, 2010). To prevent the compression of the collagen sponge, the use of titanium meshes becomes an interesting alternative (Herford, 2009). Titanium meshes provide stability to the soft tissue, preventing it from collapsing into the rhBMP-2 graft, and permitting adequate bone formation.

In the present case, as a marginal resection was performed (a fragment involving the mandibular inferior margin was removed), the use of a titanium mesh retained the graft material in position, with more stability. If only a reconstruction plate was used, the bone xenograft could drain to the adjacent soft tissues. However, the mesh must be removed before surgical installation of the implants, since it may block the placement of the implants, as well as cause bone resorption and/or stress shielding.

In a critical-sized defect model in rat calvaria, the association of bovine bone xenograft with rhBMP-2 showed superior results in terms of bone formation when compared to freeze-dried bone allograft associated with rhBMP-2, and autograft (Mokbel et al., 2013). Boyne and Shabahang (2001) also demonstrated bone formation and implant osseointegration clinically and histologically

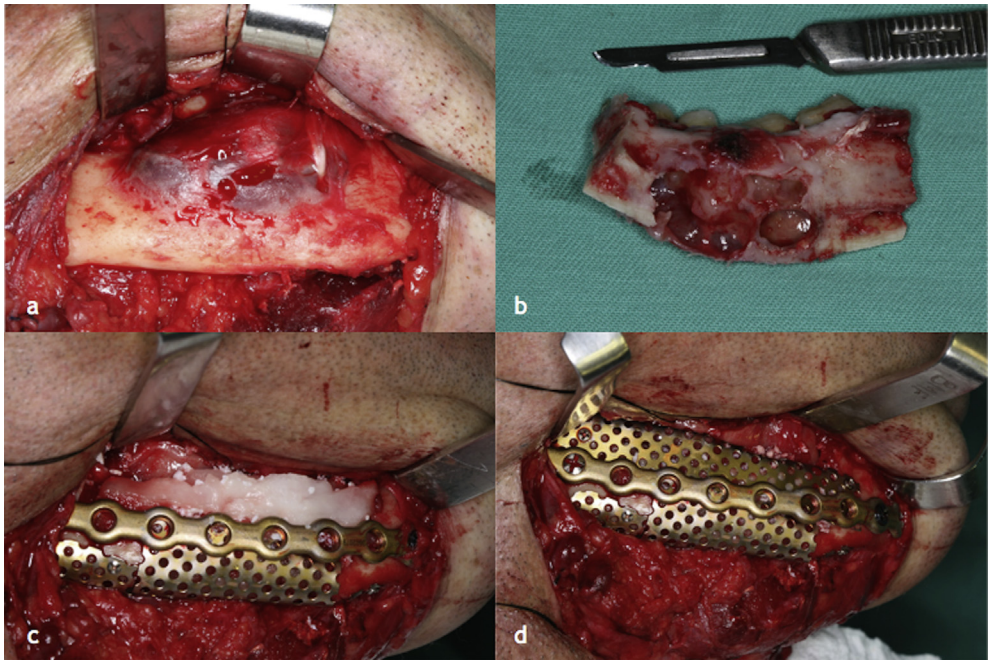

Fig. 3. Surgical procedure. (a) Access to lesion, showing loss of buccal cortical plate. (b) Specimen obtained from surgical resection (c) and (d) Mandibular reconstruction with rhBMP-2, bovine bone xenograft, a 2.4-mm locking reconstruction plate, and a titanium mesh.

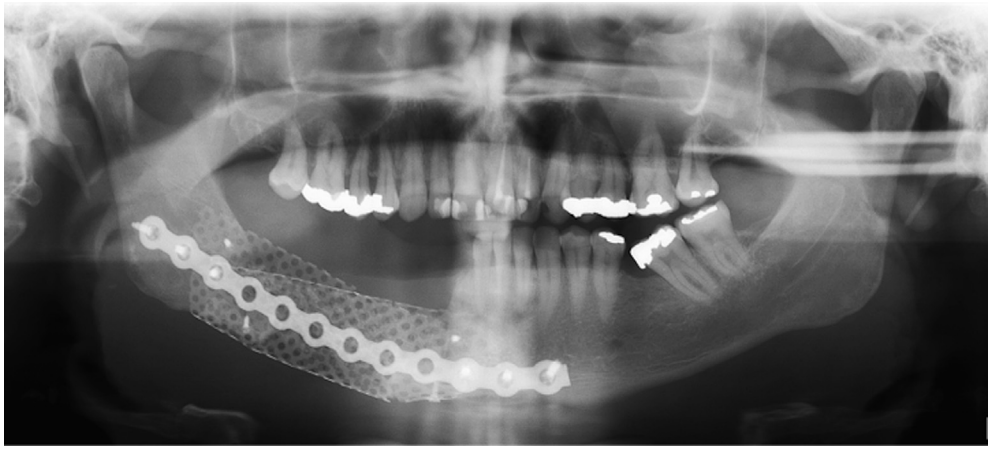

Fig. 4. Eleven-month follow-up panoramic radiograph showing bone neoformation.

with the association of rhBMP-2 and bovine bone xenograft for the reconstruction of 2.0 × 1.4-cm mandibular defects in monkeys (Boyne and Shabahang, 2001). Other studies in animals with rhBMP-7 using the bovine bone xenograft as a noncompressible carrier also presented bone neoformation and good results for critical-sized defects (Terheyden et al., 1999, 2001). The association of rhBMP-2 with bovine bone xenograft in humans has been reported only three times in the literature: in one case of enucleation and curettage of an extensive central giant cell lesion in the mandibular body and symphysis (Lustosa et al., 2014), in a sandwich technique in an anterior maxillary defect (Herford et al., 2013), and in a bilateral sinus lift (Tarnow et al., 2010). The present case is the first to report on the association of rhBMP-2 and bovine bone xenograft to reconstruct a segmental defect of the mandible, followed by prosthetic rehabilitation with dental implants.

It has been suggested that bovine bone xenograft can help with the stability of rhBMP-2, working as a space maintainer (Lustosa et al., 2014). In the present case, the use of rhBMP-2 together with bovine bone xenograft associated the qualities of both grafts—osteoinduction and osteoconductivity, respectively—producing sufficient mandibular bone neoformation to be rehabilitated with implants 11 months after the surgery. Furthermore, the preservation of the periosteal tube of the mandible facilitated the reconstruction and provided blood supply to consolidate the graft. The distribution of the rhBMP-2 graft along the bovine bone xenograft induced satisfactory bone formation both in thickness and in height. The reason for that lies in the fact that the bovine bone xenograft functioned as a non-compressible carrier for the rhBMP-2 and as a structural scaffold for the rhBMP-2 in a three-dimensional framework. Hence, the combination of off-label use of rhBMP-2, bovine xenograft, and a titanium mesh should be considered a feasible alternative to reconstruct the mandibular continuity.

Despite rhBMP-2 capacity to reconstruct extensive mandibular resections after the removal of tumors or cystic lesions, implant

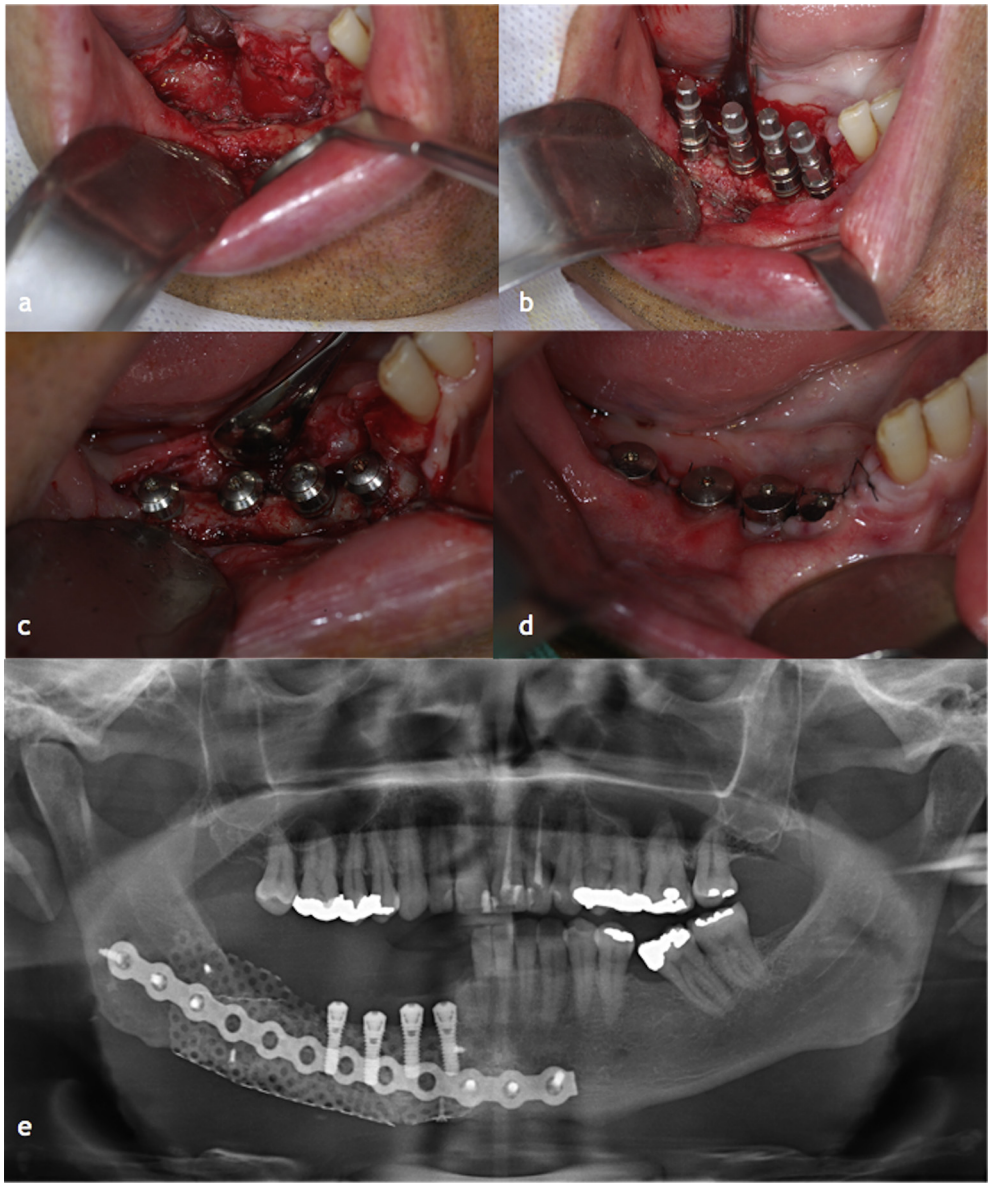

Fig. 5. Surgical procedure for dental implant placement. (a) Surgical exposure of the grafted area. (b and c) Dental implants placement. (e) Healing caps placement. (f) Panoramic radiograph of dental implants in position.

rehabilitation in those cases have rarely been reported. Most studies have addressed the successful reconstructions of the jaw, but did not mention the esthetic and functional rehabilitation of these patients. This is an important phase of the treatment, since only after the prosthetic rehabilitation will patients restore their occlusion and their confidence.

According to Zou et al. (2013), dental implant rehabilitation in mandibular reconstructions with autologous vascularized bone graft presented a high survival and success rate (96.4% and 91.8%, respectively) in an 8- to 12-year follow-up (Zou et al., 2013). Survival and success rates in nonvascularized iliac crest, calvaria, and fibula have also been high, ranging from 93.1% to 98.6% (Chiapasco et al., 2006, 2008). However, despite the high survival and success rates in dental implant rehabilitation in the autogenous bone grafts, these techniques submit patients to long stays in the hospital, postoperative pain, sensory disturbances, and walking problems (Fasolis et al., 2012) when compared to reconstructions with rhBMP-2.

Considering that the use of rhBMPs as graft materials is relatively new, there are no long-term studies demonstrating success and survival rates of implants placed in these grafts. The present report illustrates a successful case in which the patient was prosthetically rehabilitated. The four dental implants have been receiving prosthetic load for 5 months without any complications, demonstrating that the reconstruction and rehabilitation in grafted areas with rhBMP-2 and bovine bone xenograft is feasible and should be considered. Nonetheless, future studies will be required to ascertain the long-term survival of implants in areas grafted with rhBMP-2.

4. Conclusion

In conclusion, the use of the recombinant human morphogenetic protein as a graft material is encouraging, with good clinical outcome. The presented case reports a successful association between rhBMP type 2 and bovine bone xenograft, demonstrating that the implants placed in the grafted area were maintained without evidence of resorption or complications. Thus, this

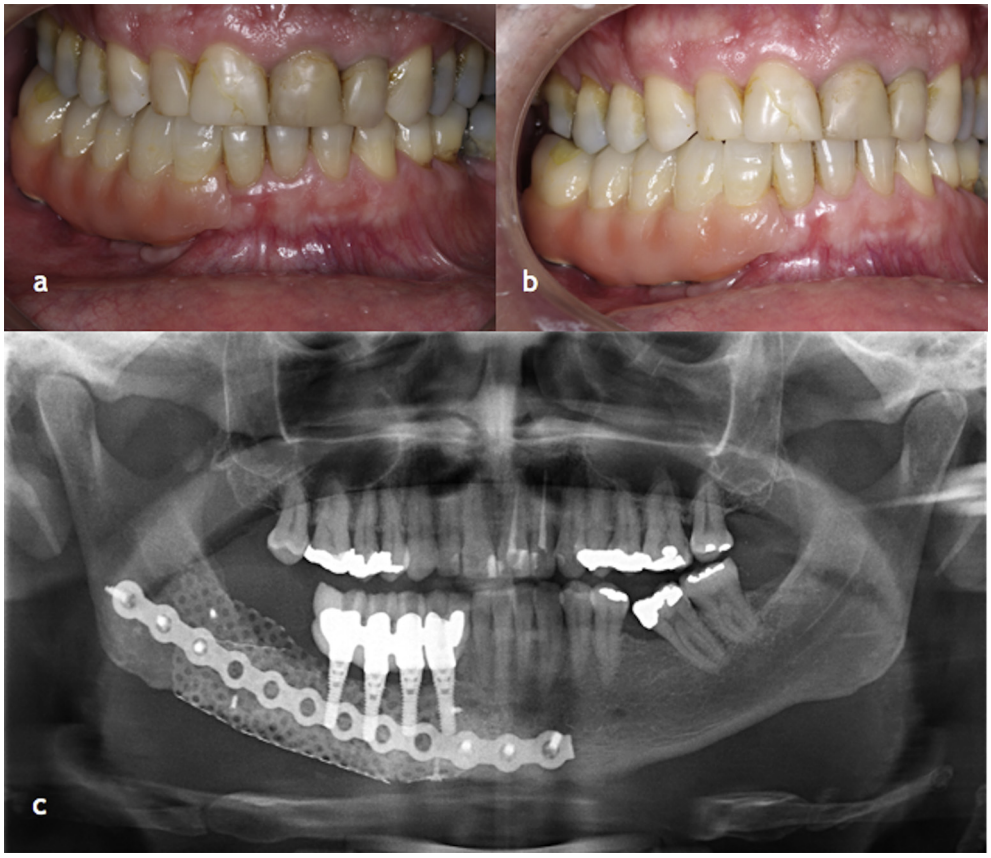

Fig. 6. Prosthetic rehabilitation. (a) Frontal view and (b) lateral view of the implant-supported partial denture in occlusion. (c) Eighteen-month follow-up panoramic radiograph showing prosthetic rehabilitation with dental implants and implant-supported partial denture.

association could be considered a feasible option for the reconstruction and rehabilitation of large mandibular defects.

References

Balaji SM: Mandibular cystic defect: a composite approach with rhBMP-2 and rib graft. J Maxillofac Oral Surg 8: 27–30, 2009

Boyne PJ: Animal studies of application of rhBMP-2 in maxillofacial reconstruction. Bone 19(1 Suppl): 83S–92S, 1996

Boyne PJ, Shabahang S: An evaluation of bone induction delivery materials in conjunction with root-form implant placement. Int J Periodont Restor Dent 21: 1–11, 2001

Carter TG, Brar PS, Tolas A, Beirne OR: Off-label use of recombinant human bone morphogenetic protein-2 (rhBMP-2) for reconstruction of mandibular bone defects in humans. J Oral Maxillofac Surg 66: 1417–1425, 2008

Chao M, Donovan T, Sotelo C, Carstens MH: In situ osteogenesis of hemi-mandible with rhBMP-2 in a 9-year-old boy: osteoinduction via stem cell. J Craniofac Surg 17: 405–412, 2006

Chiapasco M, Biglioli F, Autelitano L, Romeo E, Brusati R: Clinical outcome of dental implants placed in fibula-free flaps used for the reconstruction of maxilo-mandibular defects following ablation for tumors or osteoradionecrosis. Clin Oral Impl Res 17: 220–228, 2006

Chiapasco M, Colletti G, Romeo E, Zaniboni M, Brusati R: Long-term results of mandibular reconstruction with autogenous bone grafts and oral implants after tumor resection. Clin Oral Impl Res 19: 1074–1080, 2008

Cicciù M, Herford AS, Stofella E, Cervino G, Ciccù D: Protein-signaled guided bone regeneration using titanium mesh and rh-BMP2 in oral surgery: a case report involving left mandibular reconstruction after tumor resection. Open Dent J 6: 51–55, 2012

Cicciù M, Scott A, Cicciù D, Tandon R, Maiorana C: Recombinant human bone morphogenetic protein-2 promote and stabilize hard and soft tissue healing for large mandibular new bone reconstruction defects. J Craniofac Surg 25(3): 860–862, 2014

Clokie CM, Sándor GK: Reconstruction of 10 major mandibular defects using bio-implants containing BMP-7. J Can Dent Assoc 74(1): 67–72, 2008

Desai SC, Sclaroff A, Nussenbaum B: Use of recombinant human bone morphogenetic protein 2 for mandible reconstruction. JAMA Fac Plast Surg 15: 204–209, 2013

Fasolis M, Boffano P, Ramieri G: Morbidity associated with anterior iliac crest bone graft. Oral Surg Oral Med Oral Pathol Oral Radiol 114: 586–591, 2012

Glied AN, Kraut RA: Off-label use of rhBMP-2 for reconstruction of critical-sized mandibular defects. N Y State Dent J 76: 32–35, 2010

Herford AS: rhBMP-2 as an option for reconstructing mandibular continuity defects. J Oral Maxillofac Surg 67: 2679–2684, 2009

Herford AS, Boyne PJ: Reconstruction of mandibular continuity defects with bone morphogenetic protein-2 (rhBMP-2). J Oral Maxillofac Surg 66: 616–624, 2008

Herford AS, Cicciù M: Recombinant human bone morphogenetic protein type 2 jaw reconstruction in patients affected by giant cell tumor. J Craniofac Surg 21: 1970–1975, 2010

Herford AS, Tandon R, Stevens TW, Stofella E, Cicciù M: Immediate distraction osteogenesis: the sandwich technique in combination with rhBMP-2 for anterior maxillary and mandibular defects. J Craniofac Surg 24: 1383–1387, 2013

Lustosa RM, Iwaki LCV, Tolentino ES, Chicarelli MS, Lazarin RO, Iwaki LF: Mandible reconstruction using rhBMP-2: case report and literature review. Quintessence Int 45: 869–874, 2014

Moghadam HG, Urist MR, Sandor GK, Clokie CM: Successful mandibular reconstruction using a BMP bioimplant. J Craniofac Surg 12: 119–127, 2001

Mokbel N, Naaman N, Nohra J, Badawi N: Healing patterns of critical size bony defects in rats after grafting with bone substitutes soaked in recombinant human bone morphogenetic protein-2: histological and histometric evaluation. Br J Oral Maxillofac Surg 51: 545–549, 2013

Physician labeling: Infuse bone graft for certain oral maxillofacial and dental regenerative uses. Important med inf, Rx only http://www.fda.gov/cdrh/pdf5/p050053c.pdf, 3/8/2007; . Available at:

Sham E, Leong J, Maher R, Schenberg M, Leung M, Mansour AK: Mandibular ameloblastoma: clinical experience and literature review. ANZ J Surg 79: 739–744, 2009

Tarnow DP, Wallace SS, Testori T, Froum SJ, Motroni A, Prasad HS: Maxillary sinus augmentation using recombinant bone morphogenetic protein-2/acellular collagen sponge in combination with a mineralized bone replacement graft: a report of three cases. Int J Periodont Restor Dent 30: 139–149, 2010

Terheyden H, Jepsen S, Möller B, Tucker MM, Rueger DC: Sinus floor augmentation with simultaneous placement of dental implants using a combination of deproteinized bone xenografts and recombinant human osteogenic protein-1. A histometric study in miniature pigs. Clin Oral Implant Res 10(6): 510–521, 1999

Terheyden H, Warnke P, Dunsche A, Jepsen S, Brenner W, Palmie S, et al: Mandibular reconstruction with prefabricated vascularized bone grafts using recombinant human osteogenic protein-1: an experimental study in miniature pigs. Part II: transplantation. Int J Oral Maxillofac Surg 30(6): 469–478, 2001

Toriumi DM, Kotler HS, Luxenberg DP, Holtrop ME, Wang EA: Mandibular reconstruction with a recombinant bone-inducing factor. Functional, histologic, and biomechanical evaluation. Arch Otolaryngol Head Neck Surg 117(10): 1101–1112, 1991

Toriumi DM, O'Grady K, Horlbeck DM, Desai D, Turek TJ, Wozney J: Mandibular reconstruction using bone morphogenetic protein 2: long-term follow-up in a canine model. Laryngoscope 109(9): 1481–1489, 1999

Wang H, Springer IN, Schildberg H, Acil Y, Ludwig K, Rueger DR, et al: Carboxymethylcellulose-stabilized collagenous rhOP-1 device-a novel carrier biomaterial for the repair of mandibular continuity defects. J Biomed Mater Res A 1 68(2): 219–226, 2004

Zétola A, Ferreira FM, Larson R, Shibli JA: Recombinant human bone morphogenetic protein-2 (rhBMP-2) in the treatment of mandibular sequelae after tumor resection. Oral Maxillofac Surg 15: 169–174, 2011

Zou D, Huang W, Wang F, Wang S, Zhang Z, Zhang C, et al: Autologous ilium grafts: long-term results on immediate or staged functional rehabilitation of mandibular segmental defects using dental implants after tumor resection. Clin Implant Dent Relat Res: 1–11, 2013