Bone Allograft: An Option for Total Mandibular Reconstruction

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Abstract

Keywords

- mandibular reconstruction
- bone allograft
- Langerhans cell tumor
- total mandibulectomy

Total mandibular reconstruction is one of the most challenging modalities in maxillofacial surgery. In this article, we try to introduce a method of total mandible reconstruction. We report a 25-year-old male patient with complete involvement of the mandible by Langerhans cell tumor. The patient underwent total mandibulectomy and reconstruction with bone allograft harvested from a donor who had died the day before. The patient has good functional and aesthetic results in a long time. It seems that bone allograft can be a good alternative to other methods in total mandibular reconstruction.

Total mandibular reconstruction is one of the most challenging modalities in oral and maxillofacial surgery. When performing mandibular reconstruction, the restoration of bony continuity should not be considered as the only measure of success. The functions of mastication, swallowing, speech, articulation, and oral competence must also be addressed. However, it is not always possible to achieve such conditions.

Various methods are available for mandibular reconstruction, including autotransplantation, allotransplantation, and biomaterials. Autogenous bone grafting is a gold standard for mandibular reconstruction,¹ and is a reliable treatment modality for the reconstruction of mandibular bone defects with predictable aesthetic and functional results.² But when total reconstruction, especially condyle, is needed, no favorable outcomes can be achieved using this method. Autogenous bone grafts may also increase the risk of morbidity by increasing the risk of infection, pain, and length of hospitalization.^{3–5} As a result, recently interest has been shown for the development of new grafting materials using allogeneic, xenogeneic, and synthetic biomaterials for reconstructive bony procedures.⁶

Some studies have compared the effectiveness of these alternatives as potential replacements for autogenous bone grafts.^{7,8} Allogeneic bone, such as demineralized bone matrix (DBM), harvested from one subject to transfer to another subject of the same species, was first used to reconstruct the skull defects in dogs more than 100 years ago.^{9,10} This method was not so popular until Dr. Marshall Urist reported the results of his research in 1965. He showed that demineralized segments of bone induced new bone formation when implanted in muscle in the rabbit. Then, scientists seriously considered demineralized allogeneic bone as a potential bioimplant for osseous repair.^{11–14} Herein we report a patient with Langerhans cell tumor, which had involved the mandible completely. The mandible was reconstructed using the allograft. The case described in this study is a new method that we cannot find in anywhere in the literature review.

Case Presentation

A 25-year-old man presented with a history of progressive, painless mandibular swelling with 6-month duration. He reported no paresthesia and the mandible was not tender

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Fig. 1 (a) Preoperative panoramic view showing multilocular lesion. (b) 3D CT scan shows massive destruction of the mandible.

on physical examination. There was neither trismus nor enlarged lymph node over the submandibular and neck region. The patient had poor oral hygiene and all of the mandibular teeth were mobile. Panoramic radiography revealed a multilocular lesion that affected the entire mandible except the right condyle (►Fig. 1a). Three-dimensional computed tomography (3D CT scan) showed massive destruction of the mandibular bone (►Fig. 1b).

Incisional biopsy of the oral cavity was done under local anesthesia and eosinophilic granuloma was reported. The patient was then scheduled for total mandibulectomy via submandibular incision accompanied by reconstruction with a transplant bone. We have taken a surgical consent from the patient that was approved by the Urmia University Ethical Committee.

During the operation, the skin flap was raised and retracted superiorly exposing the whole mandible (►Fig. 2). Then total mandibulectomy was performed and the transplanted mandible was located in the site of the mandible. Inferior alveolar dental nerve was not preserved, but the discs of temporomandibular joints were preserved bilaterally. As the inter-condylar distance of the new mandible was greater than the previous one, osteotomy was done in the right mandibular body region and the mandibular condyles were adjusted in glenoid fossa bilaterally (►Fig. 3). Coronoidec-tomy was done on both sides, and at the end of the surgery, all

masticatory muscles were intact and replaced to their positions. All muscles were fixed to the bone by 4–0 PDS sutures. The skin flap was sutured with 5–0 nylon (►Fig. 4).

The transplanted bone was freeze-dried bone prepared according to the latest version of the guidelines of the American Association of Tissue Banks (AATB).¹⁵

The donor was a 38-year-old man who had died in a car accident and his mandible was harvested on the next day. Before harvesting his mandible, physical examination and

Fig. 2 Intraoperative image shows involvement and destruction of the mandible.

Fig. 3 Osteotomy was done in the right site and fixed with miniplate.

required laboratory examinations were performed. The donor did not have any high-risk behavior and his laboratory tests for anti-HIV1, anti-HIV2, anti-hepatitis C virus (anti-HCV), hepatitis B surface antigen (HBsAg), cytomegalovirus, and fungal culture were negative.

The preparation, including physical and chemical treatment, was done by the Iranian Tissue Bank and Research Center. It was sterilized by 25 kGy gamma irradiation. The postoperative period was uneventful and feeding was started via nasogastric tube for 3 days and then the tube was removed and a soft diet was started. He was discharged from the hospital on day 5 after operation.

Histopathologic evaluation showed clusters and sheets of uniform, ovoid histocytes with abundant acidophilic cytoplasm and lobulated nuclei admixed with chronic inflammatory cells especially eosinophils. Osteoclast-like giant cells, necrosis, and fibrosis were present as well (►Fig. 5a, b). These cells were positive for CD1a (►Fig. 6a) and S100 (►Fig. 6b). Based on the immunohistochemical finding, the diagnosis of Langerhans cell histiocytosis was made.

At the first follow-up (2 weeks later), the patient had no significant complaint, except a mild, clear discharge from the incision site on the right side. The diagnosis was parotid fistula which was treated by compression bandage for 10 days. Three months after the surgery, radiographic exami-

Fig. 4 Photography of the lateral view after surgery.

Fig. 5 (a) Histopathologic evaluation showed a Langerhans cell histiocytosis, large histiocytes surrounded by an inflammatory infiltrate of lymphocytes, eosinophils, and osteoclast-like giant cells. (b) A mixture of Langerhans cells, eosinophil, mandibular bone, and fibrosis.

nation showed no bone resorption (►Fig. 7) and in the follow-up 6-month postsurgery, an adequate and stable restoration of facial contour was evident. The maximum inter-incisional opening was 40 mm. Tc-99m MPD bone scintigraphy was

Fig. 6 (a, b) Langerhans cells are positive for CD1a and S100 by immunohistochemical staining.

Fig. 7 Three months postoperative panoramic view.

performed 9 months postoperatively (►**Fig. 8**). There was a mild bone resorption in the panoramic radiography and 3D CT scan 2 years after operation (►**Figs. 9 and 10**). The mouth movements including opening and closing were normal 2 years after surgery. Our future plan is construction of the occlusion by dental implant.

Discussion

Mandibular reconstruction after total resection can be achieved by various methods. There are various types of material for bone reconstruction, including autograft, allograft, xenograft, and synthetic materials. The successful use of these modalities is dependent on various biological, physiological, and biomechanical factors, each of which affects the result of the transplant.^{16,17} The most common method for reconstruction of the mandible is use of reconstruction plate with or without bone graft.¹⁸ It has some disadvantages, including plate exposure, fistula, and interface with radiation therapy.^{19,20} Vascularized free fibula flap has become the preferred method of mandible reconstruction after oncologic surgical ablation. The fibula flap was first described by Taylor et al²¹ and was used for the first time in mandibular reconstruction by Hidalgo.²² It has some disadvantages, such as increased operating time and complications of the harvested site. Despite the high success rate of total mandibular reconstruction with vascularized fibula flap,^{23,24} it is not suitable for condylar reconstruction.

There are three mechanisms in which a bone graft may possess: osteoconduction, osteoinduction, and osteogenesis.²⁵ Osteoconduction is the process by which the graft provides a 3D structure that facilitates the ingrowth of capillaries and mesenchymal stem cells to support new bone formation on the graft. Osteoblasts from the margin of the defect that is being grafted utilized the bone graft material as a scaffold upon which to spread and generate new bone. Osteoinduction is the process by which mesenchymal

stem cells from the graft or the host tissue are induced to differentiate into chondroblasts or osteoblasts that then begin new bone formation. Growth factors such as bone morphogenic proteins (BMPs), interleukins, and platelet-derived growth factor can influence the recruitment and differentiation of mesenchymal stem cells.²⁶ A bone graft material that is osteoconductive and osteoinductive will not only serve as a scaffold for currently existing osteoblasts but will also trigger the formation of new osteoblasts, theoretically promoting faster integration of the graft. Osteogenesis is the process of new bone formation by cells from the host or the graft. Both autologous cancellous and cortical grafts can provide cells capable of producing bone, but cancellous autografts with their trabecular structure lined with osteoblasts and large surface area provide for much more potent osteogenesis.

There are three forms of bone allograft available: fresh or fresh-frozen bone, freeze-dried bone allograft (FDBA), and demineralized freeze-dried bone allograft (DFDBA).

FDBA provides an osteoconductive scaffold and elicits resorption when implanted in mesenchymal tissues.²⁷ DFDBA also provides an osteoconductive surface. In addition, it provides a source of osteoinductive factors. Therefore, it elicits mesenchymal cell migration, attachment, and osteogenesis when implanted in well-vascularized bone. It also induces endochondral bone formation when implanted in tissues that would otherwise not form bone.¹¹ The decision about which form of allograft to use should be based on the clinical condition of the site to be grafted. Because it is still mineralized, FDBA may have better physical characteristics. The effect of drying on the mechanical properties of cortical bone is very limited and consider as insignificant method on the mechanical properties of trabecular bone.²⁸ Although no significant differences have been found clinically between FDBA and DFDBA in primarily intraosseous defects, in sites where regeneration may be more problematic, DFDBA may be a more appropriate choice.^{29,30}

Fig. 8 Scintigraphy 9 months postoperative: (a) whole body scan; (b) flow phase; (c) pool phase.

Fig. 9 There was a mild bone resorption in the panoramic radiography 2 years after operation.

One of the most important problems in bone allotransplant is the potential for transmission of infections as HIV; therefore, various techniques are used for this purpose, including irradiation, ethylene oxide, and chemical sterilization. The effect of radiation is more controversial. Although a

15- to 25-kGy dose is commonly used, many authors stated that 15 kGy would not reliably inactivate HIV in bone.³¹⁻³³ Bacterial sterilization is achieved at the usual dose of 25 kGy.³³ Irradiation of dried bone will substantially reduce its mechanical capacity.³⁴ Gamma radiation adversely affects the

Fig. 10 There was a mild bone resorption in the 3D CT scan 2 years after operation.

mechanical and biological properties of bone allografts by degrading the collagen in bone matrix. Specifically, gamma rays split polypeptide chains.³⁵ In the frozen state, damage to collagen is reduced because of the smaller amounts of free radicals generated by ionization of frozen water, in comparison to the room temperature.³⁶ The American Association of Tissue Bank (AATB) sets guidelines for tissue procurement, processing, and sterilization of bone grafts (available online at: www.aatb.org/American-Association-of-Tissue-Banks). AATB's guidelines apply to quality control and compliance, ensuring safety. The U.S. Food and Drug Administration does have guidelines for implants manufactured from biomaterials, indicating upper limits on residuals and contaminants introduced during processing, including ethylene oxide (ETO)

sterilization. At least with respect to ETO, these guidelines must be applied to banked bone.¹⁵ The AATB29 advocates excluding collection of bone from donors with the following circumstances:

1. Donors from high-risk groups, as determined by medical testing and/or behavioral risk assessments
2. Donors with positive test for HIV antibody confirmed by ELISA
3. Donors whose autopsy reveals occult disease
4. Donors with positive bone tests for bacterial contamination
5. Donors with positive bone test for HBsAg or HCV
6. Donor with positive tests for syphilis

Table 1 Summary of the reported cases of total mandibular reconstruction

No	Age (y)	Cause of mandibular loss	Reconstruction technique	Source	Date of report	Follow-up period
1	56	Trauma	Free fibula flap	Takahiro et al ³⁹	2011	5
2	24	Mandibular neuroma	Free fibula flap	Jambehkar Et al ⁴⁰	2015	–
3	55	Gorham–Stout syndrome	Free fibula flap	Paley et al ⁴¹	2005	4
4	58	Ameloblastic carcinoma	Free fibula flap	Jeremic et al ⁴²	2010	<1
5	52	Ameloblastoma	Iliac crest bone	Orringer et al ⁴³	1999	2
6	19	Osteosarcoma	Radial forearm free flaps	Grinsell et al ⁴⁴	2014	4
7	56	Infection	Free fibula flap	Winters et al ⁴⁵	2012	<1
8	Not available	Adenocystic carcinoma	Pectoralis major composite flap	Bhathena et al ⁴⁶	1986	<1

There have been no reports of virus contamination or acquired pathology from FDBA, although this material is in wide use clinically.^{32,37,38} Although nowadays partial reconstruction of the mandible is a common treatment, there are a few literature about total mandibular reconstruction (►Table 1). The case described in this study is a new method of total mandibular reconstruction that we cannot find in anywhere in the literature review. It seems that it can be the first choice when total mandibular with condylar reconstruction is needed.

Funding

None.

Conflict of Interest

None.

Ethical Approval

Not required. I have received patient consent to re-use the image.

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