Self-Regeneration of the Mandible Following Hemimandibulectomy for Ameloblastoma: A Case Report and Review of Literature

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Abstract Resection of the mandible with immediate or delayed graft reconstruction is widely used in the treatment of ameloblastoma involving a large portion of the mandible. The purpose of reconstruction is mainly to restore the esthetic appearance and mandibular function of the patient. Spontaneous regeneration of the mandible after resection is rarely encountered. This article reports a rare case of spontaneous regeneration of the mandible after hemimandibulectomy for ameloblastoma in a 16-year-old male patient. We discuss the theories pertaining to the mechanism and source of the new bone formation in this case and review the English literature.

Keywords Regeneration · Mandible · Periosteum · Ameloblastoma · Resection

Background

Ameloblastoma is a relatively common benign odontogenic tumor constituting about 10 % of odontogenic tumors and 1 % of the all maxillofacial cysts and tumors. However; malignant and metastasizing ameloblastomas

have been reported. Ameloblastoma is mainly localized in the third molar–ramus area of the mandible [1].

Although conservative surgical procedures such as enucleation, curettage, and marsupialization had been advised for the treatment of ameloblastoma in the literature; however, segmental resection of the lesion with healthy bone margins and immediate reconstruction with free vascularized graft and subsequent dental rehabilitation is the current accepted treatment modality. This is aimed at radical resection and adequate reconstruction of the surgical defect for restoring masticatory function and facial esthetics [2].

Spontaneous bone regeneration of the mandible is rarely reported in the literature. The exact factors controlling spontaneous bone regeneration are not fully identified; however, the age of the patient, presence of infection, preservation of periosteum, immobilization, and genetic factors have been suspected [3–8].

In this report, we present a rare case of spontaneous regeneration of the mandible after hemimandibulectomy for ameloblastoma in a 16-year-old male patient, and discuss the theories pertaining to the mechanism and source of the new bone formation in the light of previous literature.

Case Report

A 16-year-old Hispanic male patient was referred from private dental practice to Department of Oral and Maxillofacial Surgery at University of Connecticut School of Dental Medicine for a 1-month history of slowly enlarging painless swelling of the left side of face. Visual inspection showed mild swelling in the posterior portion of the left mandible. Manual examination showed diffuse, non-tender, hard-texture swelling of the posterior left mandible.

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Fig. 1 Panoramic radiograph showing ameloblastoma of the left posterior mandibular body and ramus

Intraoral examination showed bucco-lingual expansion of the mandibular alveolus in the molar region with normal overlying mucosa. All Molar teeth were present and showed grade II and I mobility. Left submandibular lymph nodes were palpable, mobile and non-tender. There was no history of lip paresthesia or significant weight loss. Patient's medical history was otherwise unremarkable.

On initial panoramic examination, there was a well-defined, expansile, multilocular radiolucent lesion of the left mandibular ramus and posterior body. The lesion had caused thinning of the inferior mandibular and anterior ramal borders, and gross expansion of what was likely to be the buccal cortex of posterior body and ramus. The lesion has also caused moderate to severe root resorption of the molar teeth. There was no internal content of the lesion except for sparse, long, and thin septa. The inferior alveolar canal could not be traced within the lesion (Fig. 1).

Multi-slice CT (MSCT) examination showed the lesion extending anteriorly from the mesial root of the mandibular first molar to the coronoid process and notch posteriorly, sparing the condylar process. There was severe thinning, with intermittent cortical perforations, and ballooning of coronoid (sigmoid) notch, anterior ramal border, and buccal and lingual cortices; however, lingual expansion was more pronounced (Fig. 2).

The lesion was explored by intraoral incisional biopsy under local anesthesia as a chair side procedure. Aspiration was performed immediate prior to the biopsy procedure and revealed clear yellow fluid. The biopsy confirmed the provisional diagnosis of ameloblastoma (Fig. 3).

Surgery was planned as disarticulation resection of the left mandible from the region of the canine via a sub-mandibular approach. So the canine was extracted and osteotomy was made through the extraction socket, and the left mandible was then disarticulated from the glenoid fossa (Fig. 3). Intra-operatively the periosteum was intact, so it was bluntly dissected from the cortical surfaces and preserved (subperiosteal resection). A reconstruction plate was fixed across the surgical defect with four titanium screws to restore the mandibular contour (Fig. 4). The plate was intended for temporary reconstruction and pre-adapted through a stereolithographic prototype. The surgical wound was closed in four layers. The post-operative course was uneventful. Further histologic examination of the gross specimen again confirmed the diagnosis of ameloblastoma (Fig. 3).

A 4-month follow-up panoramic radiograph showed spontaneous bone regeneration forming what was likely to be a new mandible (Fig. 4); 8 months later, a cone beam CT scan demonstrated a complete self-regenerated mandible (Figs. 5, 6). Therefore, no further reconstructive procedure was planned and the patient was referred to the Department of Prosthetic Dentistry for dental rehabilitation with osseointegrated dental implants.

Discussion

A comprehensive literature search was made online through the PubMed interface of MEDLINE (National Library of Medicine). Including the present case, our final search showed that 32 reports of spontaneous regeneration of the mandible had been published in the English literature

Fig. 2 Coronal (a) and sagittal (b) CT images showing thinning and expansion of the buccal and lingual mandibular cortices and root resorption of the mandibular molars

Fig. 3 Macroscopic specimen, lateral radiographic view (a). High-power microscopic image shows multiple islands of odontogenic epithelium with peripheral ameloblast-like cells and central stellate reticulum-like cells in connective tissue stroma (b)

Fig. 4 Panoramic radiographs, immediate post-operative (a), and 4-month follow-up (b) showing regeneration of the left mandible

since 1946 [3]. Among the 32 reports, there were 22 males and 10 females; 26 patients were younger than 17 years of age at the time of presentation (mean age; 12 years). There were 28 cases of spontaneous mandibular regeneration reported after resection for various benign conditions, three cases after blast injury, and one case after resection for malignant lesion (Table 1). Periosteum was totally or partially preserved in 22 cases, whereas it was removed, undetected, or unstated in ten cases. The earliest radiographic evidence of new bone formation was reported by Nagase et al. [4] at 2 weeks post-operatively; however, the average time of first observation of osteogenesis was 4 months.

Fig. 5 CBCT-reconstructed panoramic image, generated by curvilinear multi-planar reformatting (MPR) made along the curve of the newly formed bone, showing regeneration of the left mandible with well-shaped condylar and coronoid processes (long arrows) and inferior alveolar canal (short arrows), 12-month follow-up

The mechanism of spontaneous regeneration of the mandible is not clearly understood; however, several influential factors have been suggested. These include preservation and intactness of the periosteum, the age of patient, presence of local infection, post-operative immobilization, and functional or mechanical stress on the mandibular stumps [5–8].

Periosteum is a specialized connective tissue forming a thin but tough fibrous membrane firmly attached to bone surface. The structure of periosteum varies with age. In young individuals it is thicker, more vascular, active, and loosely attached. With age, it gets thinner, less vascular, inactive, and tightly adherent. Periosteum has a crucial role in osteogenesis [9]. This potential of new bone formation is stimulated by infection, trauma, and growing lesions. The osteogenic potential of periosteum is proportional to its vascularity [10, 11]. Many studies have shown that periosteum regenerates bone as well as cartilage from its progenitor cells [11, 12]. The periosteum consists of two discrete layers: an outer fibrous layer containing fibroblasts,

Fig. 6 Coronal CBCT image showing well-defined corticalized bone regeneration with spongy pattern (*arrow*)

blood vessels, and Sharpey's fibers; and an inner cambium layer containing nerve fibers, capillaries, osteoblasts, and undifferentiated mesenchymal stem cells. The latter are able to differentiate into osteoblasts and chondroblasts as a

source of growth factors play an important role in the healing and remodeling process at the outer surface of the cortical bone [11, 12].

The essential role of periosteum in fracture healing, bone grafting, and probably spontaneous bone regeneration is recognized. Ruggiero et al. [13] reported spontaneous mandibular regeneration within irradiated field over the first post-operative year. This observation indicates that irradiated periosteum will still maintain some degree of osteogenic activity. Bridges and Pritchard [14] using rabbits, found that the periosteum of the mandible and the capsular tissues of the temporomandibular joint regenerated the body of the mandible and the condyle following subperiosteal resection with disarticulation. Ogunlewe et al. reported spontaneous regeneration of the whole mandible after total that mandibulectomy with bilateral disarticulation occurred in a 13-year old sickle-cell patient without the need for bone graft. Interestingly, the spontaneous bone regeneration in their case was noticed 10 weeks post-operatively; and by

Table 1 Reported cases of spontaneous mandibular regeneration in the English literature

Author	Case no.	Age (years)	Sex	Diagnosis	Periosteum status	Bone formation first seen
Kazanjian [3]	1	15	M	Ossifying fibroma	Preserved	2 months
Byars and Schatten [24]	2	8	F	Ossifying fibroma	Preserved	5 weeks
	3	9	M	Fibrous dysplasia	Preserved	5 weeks
Budal [25]	4	35	F	Osteofibroma	Preserved	2–3 weeks
Adekeye [7]	5	15	M	Ameloblastoma	Preserved	7 months
Nwoku [20]	6	15	M	Ameloblastic fibroma	Preserved	6 months
	7	12	F	Ossifying fibroma	Preserved	3 months
Kisner [19]	8	12	M	Gunshot injury	Fragments remained	10 months
Boyne [26] ^a	9–14 (6 cases)	5–14	M/F	Various benign lesions	None	2–3 months
Shuker [6]	15	7	M	Artillery shelling injury	Fragments remained	1 month
Nagase et al. [4]	16	12	M	Ameloblastoma	Preserved	2 weeks
Elbeshir [8]	17	32	F	Chronic osteomyelitis	Preserved	1 month
Ruggiero [13]	18	27	M	Odontogenic keratocyst	Preserved	IIG
	19	27	M	Ewing's sarcoma	Removed	1 year
Whitmyer et al. [16]	20	9	F	Osteosarcoma	ING	3 month
De Villa et al. [22]	21	58	F	Blast injury	Not detectable	3 weeks
Pramono [27]	22	6	M	Ameloblastoma	Preserved	6 months
Martins and Avila [28]	23	14	M	Fibroma	Preserved	2 years
Espinosa et al. [29]	24	7	M	Ossifying fibroma	Preserved	6 months
Ogunlewe et al. [15]	25	10	M	Ameloblastoma	Preserved	10 weeks
Khodayari et al. [5]	26	19	M	Odontogenic keratocyst	Preserved	1 year
Adebayo et al. [30]	27	16	M	Odontogenic myxoma	ING	3 months
Sharma et al. [23]	28	11	M	Ossifying fibroma	Preserved	2 months
	29	7	F	Aneurysmal bone cyst	Preserved	2 months
	30	12	M	Hemangioendothelioma	Preserved	6 months
	31	6	M	Ossifying fibroma	Preserved	2 months
Present case (2012)	32	16	M	Ameloblastoma	Preserved	4 months

IIG inadequate information given, ING information not given

^a Individual patient's age, gender, and diagnosis were not specified

1 year of the operation, there was regeneration of the entire mandible with well-shaped condyles [15]. Moreover; dental implants have been placed successfully in spontaneously regenerated bone after mandibular resection [16]. Khodayari et al. [5] in their case report, examined the osseous histology of newly regenerated bone; the microscopic evaluation demonstrated dense trabecular formation with osteocytes and fibrous connective tissue in bone marrow spaces. We did not have the chance to examine the structural quality of the regenerated bone; however, our investigation was mainly through clinical and radiographic evaluations.

Spontaneous regeneration of a lost portion of bone is not limited to the jaws. It has also been reported in the long bones of the lower extremity after injuries [17, 18]. According to Kisner [19], for cases in which the periosteum is not intact, the source of osteogenesis could be residual fragments of the periosteum, small particles of bone—bone dust—remained in the surgical bed, and the mandibular stumps. In our case, we believe that the preserved intact periosteum, coupled with the young patient's age, was the stimulant factor in the spontaneous bone regeneration.

Low-grade infection is believed to activate periosteal bone regeneration [7, 20]. Elbeshir [8] stated that periosteum provoked by chronic infection would continue to lay down new bone. It is known that chronic osteomyelitis results in additional periosteal bone formation [21]. In our case, infection was not encountered during the course of treatment.

Immobilization of the mandibular stumps has been suggested to promote osteogenesis [13, 17, 22]. In our case, the remainder mandible was stabilized by a reconstruction plate. Mechanical stress is another factor that has been implicated in spontaneous bone regeneration. However, this seems to be contradictory to the hypothesis of immobilization. Because the exact factors that enable the periosteum to regenerate bone are not fully understood, it has been suggested that the periosteum should always be preserved when carrying out mandibular resection for benign lesions that have not perforated the cortical plates and invaded the surrounding soft tissues [15].

Sharma et al. presented a series of four case reports of spontaneous mandibular regeneration in children after subperiosteal resection for benign lesions; consequently, they advocated a pediatric protocol of deferral of graft reconstruction of the mandible in order to give a chance for spontaneous bone regeneration to occur [23].

Spontaneous bone formation can usually be noticed radiographically by 3 months post-operatively. If it is detected at this stage then further monitoring is recommended until no further bone formation can be seen radiographically, or until the defect is filled. The planned

delayed reconstruction meant that these patients would not need any bony reconstruction, or would need less than had originally been anticipated. If no spontaneous formation can be seen at 3 months, then conventional delayed reconstruction is performed [23].

As a conclusion, with consideration to preservation of periosteum, patient's age, and mandibular stabilization, spontaneous bone regeneration following mandibular resection should be expected.

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Conflict of interest None declared.

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