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CLINICAL PAPER

Spontaneous Regeneration of Bone in Segmental Mandibular Defect

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Abstract
Aim To highlight the spontaneous regeneration of mandibular segmental defects in young and pediatric cases and to review the literature of this unusual and rare phenomenon.
Methodology Two case reports of a 17-year old male and a 8-month-old infant has been presented who underwent resection of mandible for benign tumors. These two cases have been compared with the existing literature of 61 cases published till date.
Inference Spontaneous regeneration of mandible as a viable reconstructive option is not practically feasible. The consistency and predictability of the phenomenon is questionable. Bone grafting should probably be done immediately in all cases, even in young patients if a delay would interfere with quality of life. In infants and small children though, we propose that immediate reconstruction may be avoided to allow some regeneration at the defect site. If it does not occur, secondary reconstruction may then be considered.

Keywords Spontaneous regeneration · Periosteal regeneration · Resection of mandible · Reconstruction of mandible · Pediatric jaw tumors

Introduction

Spontaneous bone regeneration (SBR) or spontaneous regeneration of mandible (SRM) is defined as the rapid, usually unexpected, formation of new cortical bone in a previous mandibular defect and has been sparsely described in the literature [1]. It has been reported to occur in mandibular resection surgeries undertaken to manage both benign and malignant lesions as well as gunshot and blast injuries (Table 1). The size of regenerated bone ranges from a few centimeters to the formation of the whole mandible. The bone is also reported to be of sufficient quality to allow rehabilitative prosthetic procedures, implant therapy and even distraction. Some factors like preservation of periosteum, young age of the patient, use of fixation or stabilization devices, maintenance of soft tissue architecture and genetic predisposition have been variably proposed for this phenomenon [2]. This article reports two such cases with a comprehensive literature review and explores the factors contributing to a successful spontaneous regeneration.

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Table 1 Review of the literature of spontaneous regeneration of bone in mandible

Author	Years	No. of patients	Age/sex	Pathology	First radiographic evidence of bone formation	State of periosteum	Immobilization/fixation device	Grafting
Kazanjian [1]	1946	1	10/M	Ossifying fibroma	3 months	Preserved	Intraoral retaining device	None
Budal [2]	1970	2	35/F,18/F	Osteofibromas	3 weeks	Preserved	Elastic banding	None
Adekeye [3]	1977	1	15/M	Ameloblastoma	7 months	Preserved	None	None
Kisner [4]	1980	1	12/M	Gunshot wound	10 months	Fragments remained	K wire	None
Boyne [5]	1983	6	8 (mean)	Variable	2–3 months	Fragments remained	Titanium mesh	None
Nagase [6]	1985	1	12/M	Ameloblastoma	2 weeks	Preserved	MMF for 48 days	None
Shuker [7]	1985	1	7/M	Gunshot Injury	2.5 years	Hardly detectable	K wire	None
Elbeshir [8]	1990	1	32/F	Osteomyelitis	5 months	Preserved	None	None
Kamegai [9]	1990	1	12/F	Ewing's sarcoma	1 year	Fragments remained	Reconstruction plate	Secondary iliac crest grafting
Ruggiero [10]	1991	2	27/M, 27/F	Variable	1 year	Fragments remained	–	–
Whitmeyer [11]	1996	1	9/F	Osteosarcoma	3 months	Preserved	Reconstruction plate	Secondary rib allograft
De villa [12]	2003	1	58/F	Blast injuries	6 months	Hardly detectable	External orthopedic fixator	Secondary iliac crest grafting
Pramono [13]	2004	1	6/M	Ameloblastoma	6 months	Preserved	Reconstruction plate	None
Martin [14]	2004	1	14/M	Ossifying fibroma	2 years	Partially preserved	None	None
Ogunlewe [15]	2006	1	10/M	Ameloblastoma	2.5 months	Preserved	Archbars	None
Espinosa [16]	2006	1	7/M	Juvenile ossifying fibroma	6 months	Preserved	Reconstruction plate	None
Khodayari [17]	2011	1	19/M	Odontogenic keratocyst	1 year	Preserved	Recon plate	None
Abdulai [18]	2012	1	12/F	Ameloblastoma	6 weeks	Preserved	No	None
Ahmad [19]	2012	1	16/M	Ameloblastoma	4 months	Preserved	Recon plate	None
Adebayo [20]	2012	1	16/M	Odontogenic myxoma	3 months	Preserved	MMF	None
Sharma [21]	2013	4	6–11, 3 M: 1F	Variable	2 months	Preserved	In one case	In one case
Bataineh [22]	2016	1	10/F	Oseteosarcoma	2 months	Preserved	K wire	Secondary iliac crest graft and recon plate
Cardinal [23]	2016	1	7/F	Post-traumatic osteonecrosis	60 days	Preserved	Recon plate	Secondary distraction
Okoturo	2016	8	10.75 (Mean), 6 M: 2F	Variable, Predominantly Ameloblastoma	8 weeks	Preserved	Variable	None
Anyanechi [24]	2016	13	26.6 (mean), 7 M: 6F	Variable, Predominantly Ameloblastoma	9–17 weeks	Partially preserved (5), Excised (8)	MMF	None
Guven [25]	2017	2	10/F, 23/F	TMJ ankylosis	2–7 years	Preserved	Stock TMJ prosthesis in one case	None

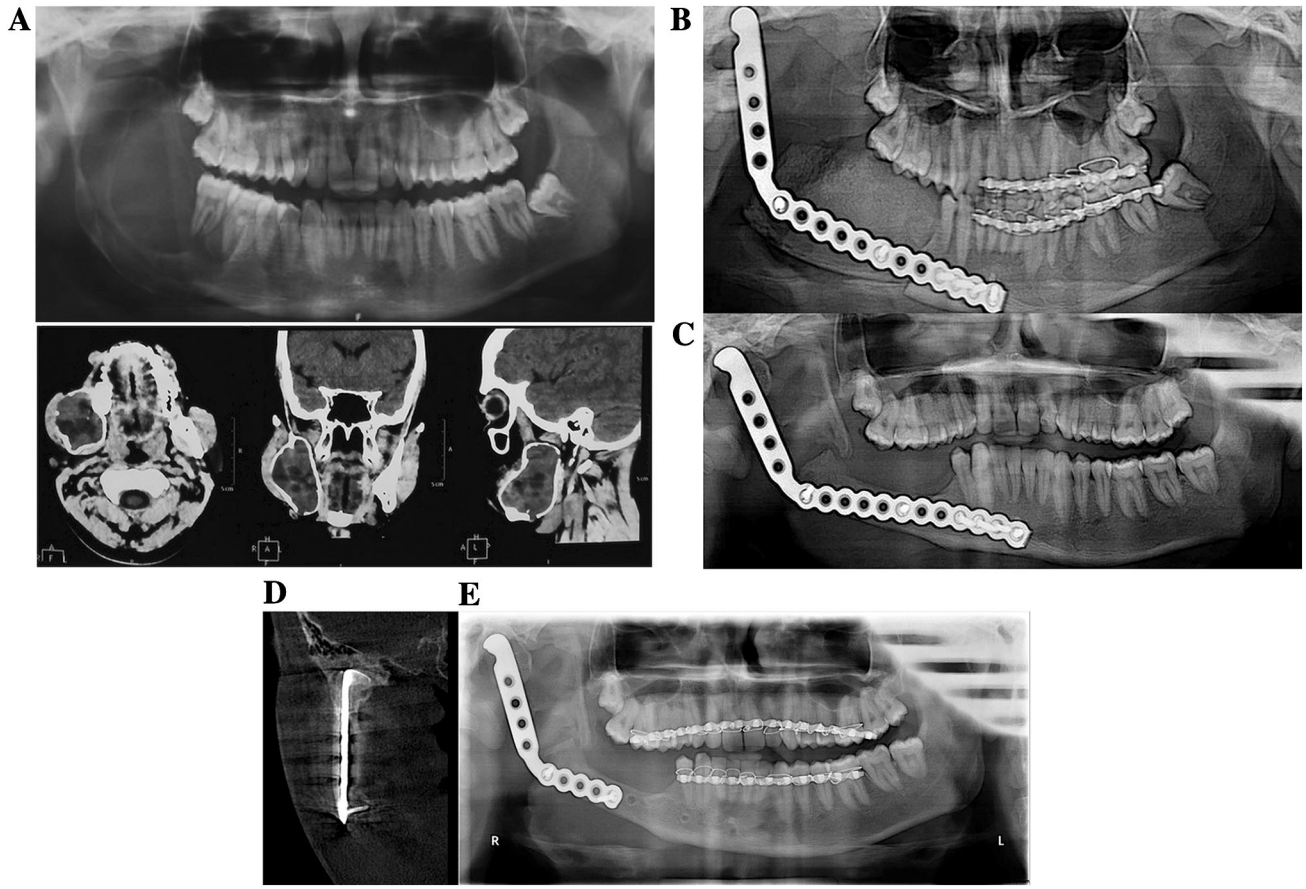

Fig. 1 **a** Osteolytic lesion in the right body of the mandible extending up to the condyle and coronoid process. **b, c** Immediate postoperative radiograph depicting reconstruction of the dentate segment with iliac crest and titanium reconstruction plate (**b**). Postoperative radiograph after 6 months depicting spontaneous regeneration of the ramus–condyle–coronoid unit (**c**). **d, e** Coronal CBCT section of the condyle showing engulfing of the titanium condylar head with the regenerated bone (**d**). Postoperative radiograph at 3 years showing consolidated bone. A part of the reconstruction plate was removed intraorally to facilitate prosthetic rehabilitation. The ramal–condylar segment was left due to new bone growth around it (**e**)

Case 1

A 17-year-old male patient of ameloblastic fibroma of mandible was planned for resection and reconstruction with non-vascularized iliac crest graft (Fig. 1a). The dentate segment and the angle of the mandible were restored with the graft, whereas the reconstruction plate alone formed the ramus–condyle unit (Fig. 1b). Postoperative course was uneventful, and his regular follow-ups showed consolidation of the graft and spontaneous regeneration of the angle–ramus–condyle unit (Fig. 1c). Further, in the course, his CBCT scan showed new bone engulfing the condylar head of the titanium reconstruction plate (Fig. 1d). Revision surgery was performed to remove the dentate part of the reconstruction plate intraorally, but the vertical component engulfed in the new bone was left as such (Fig. 1e). The dentate segment was rehabilitated with prosthesis in further follow-ups.

Case 2

A 7-month-old male infant presented with melanotic neuroectodermal tumor of infancy (MNTI) in the anterior mandible (Fig. 2a, b). Wide resection was planned, and a continuity defect was created with primary closer and no reconstruction. Within 3 months of regular follow-up, the child showed the clinical sign of bone regeneration and his regular annual follow-up shows naturally regenerated bone (Fig. 2c, d).

Discussion

The paper highlights the natural phenomenon of spontaneous regeneration of the mandible in a young male and an infant. A comprehensive literature search presented 60 such cases including the ones presented in this article (Table 1). The age range was 5–58 years with the majority

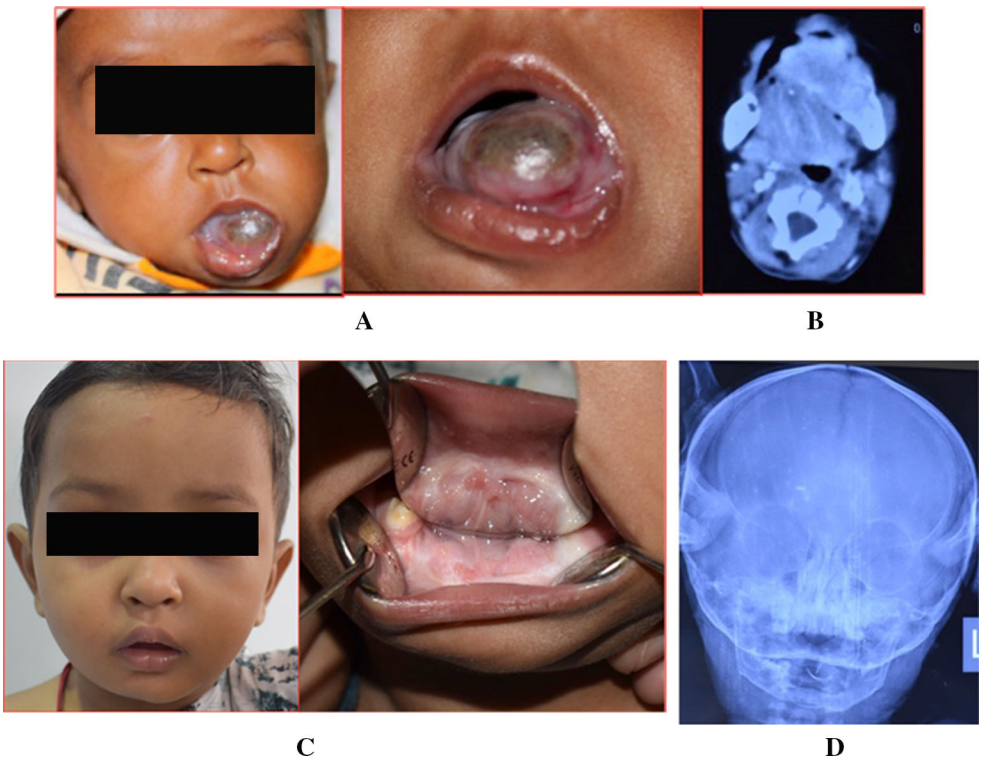

Fig. 2 **a**, **b** Clinical and radiographic picture (*axial section*) of the infant with MNTI. **c** Clinical picture of the child at the end of 2 years. **d** Extra-oral radiograph showing consolidated bone at the end of 1 year

of younger individuals and slight male preponderance. Ours is the first report of SRM occurring in an infant.

The phenomenon of SRM is postulated to be a form of bone healing. The formation of a primary callus after the bone injury that eventually undergoes maturation and remodeling forms the regenerated bone. The presence of an intact periosteum or at least a part of it is an often-documented prerequisite for this phenomenon [5, 7, 16, 17]. The periosteum acts as a reservoir of osteoprogenitor cells and provides vascular supply for the newly formed bone, while its intact state is thought to provide a barrier to infiltration of granulation tissue, thus creating a permissive environment for osteogenesis. A case report describing a full mandibular regeneration after resection for ameloblastoma where periosteum was the sole osteogenic tissue remaining, further consolidates this assertion [16].

The earliest reported bone formation is around 2 weeks [7], but in most cases, the first radiographic appearance of new bone is observed between 2 and 3 months after resection, which collates with our cases where the bone formation was first evident at 3 months. The bone formation usually reaches a threshold and then stabilizes. Various studies have shown the bone regeneration occurring up to a period of 9 months to 2 years [6, 12, 25]. A 5-year follow-up of a regenerated mandible was presented by Budal showing bone regeneration from the right third molar to the left second molar [2]. In our first patient, the new bone gradually gained size for almost 2 years after which it appeared to undergo stabilization and consolidation. The second patient, however, had almost fully consolidated bone 1 year after the surgery.

This phenomenon is mostly reported in younger individuals. The mean age of the patients in various case series ranges from 9 to 28 years. Better bone regeneration in young subjects is thought to be due to higher cellular content and abundant mesenchymal tissue to form osteogenic tissue [16]. Other factors like the absence of infection, general health of the patient and stability of the segment may have equal influence on the regenerating potential [25]. Thus, the age of the patient, though not a limiting factor, is nonetheless an important contributory parameter and has a strong influence over osteogenesis.

Immobilization with the stability of the defect and adequate soft tissue coverage are also important factors in SRM. In our first case, the bone graft and the reconstruction plate maintained the dimensions of the lost part of the mandible. The periosteum was meticulously sutured with the graft and the plate. This resulted in a favorable environment for the new bone to grow in volume. On the contrary, our second case showed spontaneous regeneration when neither grafts nor segment stabilization was done, and the wound was simply closed in layers and

routine functional movements allowed. The young age of the patient favored new bone formation.

Spontaneous regeneration of mandible as a viable reconstructive option is not practically feasible. The consistency and predictability of the phenomenon are questionable. In their retrospective study, Sharma et al. followed a protocol with benign conditions of the mandible that advocated preservation of periosteum, space maintenance with a reconstruction plate and delaying reconstruction to see whether bone forms spontaneously in young children. In 636 cases operated over a period of 23 years by segmental mandibular resection, only 2.0% of the patients had spontaneous bone regeneration [22]. Even in cases where regeneration was observed, secondary bone grafting was still required either to bridge the gap between new and the old bone or to achieve sufficient height and width for rehabilitative procedures. Considering this, bone grafting should probably be done immediately in all cases, even in young patients if a delay would interfere with quality of life. In infants and small children though, we propose that immediate reconstruction may be avoided to allow for SRM at the defect site. If SRM does not occur, secondary reconstruction may then be considered.

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Compliance with Ethical Standards

Conflict of interest No conflict exists. Both the authors, Sachin Rai and Vidya Rattan, declare that they have no conflict of interest.

Ethical Approval This is an observational study conducted after routine surgery and did not need ethical approval. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study to publish their postoperative results and pictures.

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