Spontaneous Bone Regeneration of the Mandible in an Elderly Patient: A Case Report and Review of the Literature

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Spontaneous bone regeneration is an unexpected phenomenon that may take place in large mandibular defects secondary to trauma and tumor resection. One explanation for this unusual healing course is that it may be derived from the mechanism of fracture healing. A review of the literature presents several factors that may influence this process, such as the presence of periosteum and bony fragments, mandibular stabilization, soft tissue protection, the presence of infection, and a young age. Previous reports of spontaneous mandibular regeneration have all taken place in relatively young patients (5-35 years old). This paper reports a case of spontaneous bone regeneration in a 58-year-old woman who sustained an injury to her mandible from an explosive blast, and presents some explanations on how such an event could take place. *(Chang Gung Med J 2003;26:363-9)*

Key words: spontaneous bone regeneration, mandibular defect.

Spontaneous bone regeneration after avulsion or resection of a large portion of the mandible has been reported, and several explanations for this remarkable process have been proposed. These include the development of new bone from intact periosteum[1-7] or its fragments[8,9] which serve as the direct source of osteogenic cells; from a regenerated juvenile periosteum;[10] from scattered devitalized bony particles which serve as osteoinductors for mesenchymal cells in the surrounding soft tissue;[8] and from mandibular stumps which also serve as a direct source of osteogenic cells.[4,8] It has been suggested that several conditions may influence this bony regeneration including the presence of infection,[1,4,7] functional or mechanical stress on the stabilized stumps,[9] soft tissue protection of the bony gap,[10] immobilization,[7] and possible genetic factors.[7] Common among the cases reported in the past is the relatively young age of the patients (5-35 years). In this report, however, we present another case of spontaneous bone regeneration of the mandible after avulsive injury in a 58-year-old patient. This provides a new insight that age may not always be a limiting factor in the regeneration process of bone.

CASE REPORT

A 58-year-old Taiwanese woman suffered an injury from an explosive blast of an unknown nature while she was rummaging through a pile of garbage. Physical examination revealed extensive facial lacerations with soft tissue avulsion that mainly involved the left side of the mid and lower face. The maxilla was mobile and partially exposed through the lacerations. The mandible was also exposed through the lacerations and showed a continuity defect with multiple displaced bony fragments. The injuries showed marked inflammation and foul-smelling necrotic areas. The patient had no systemic problems and no
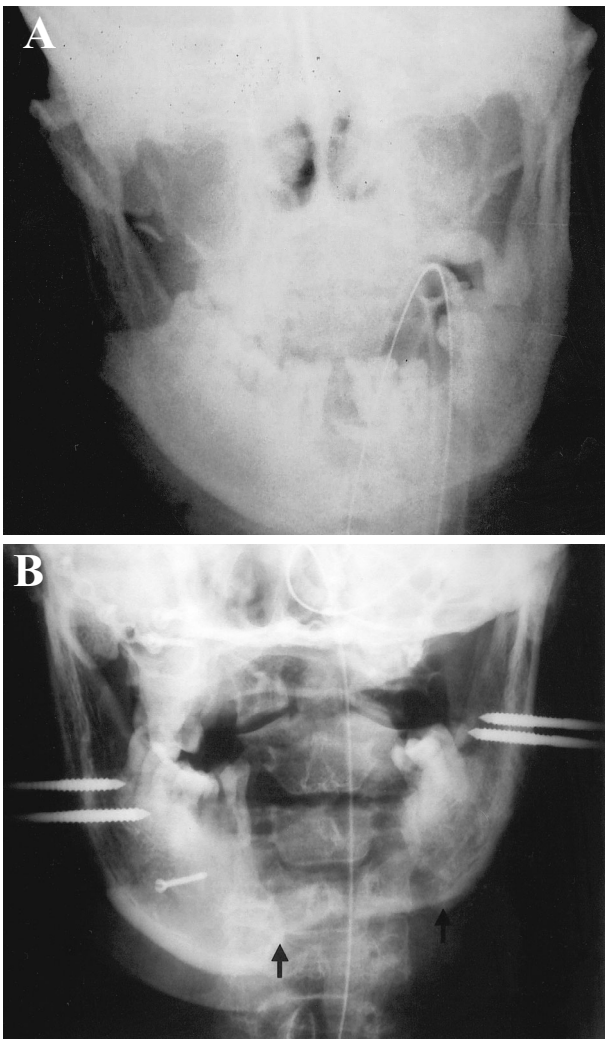
other external injuries. Initial management consisted of supportive therapy and intravenous antibiotics. Further radiographic examination revealed a minimal subarachnoid hemorrhage at the right parietal and falcotentorial junction, a Le Fort I fracture of the maxilla, and a severely comminuted fracture of the anterior and left body of the mandible (Fig. 1A).
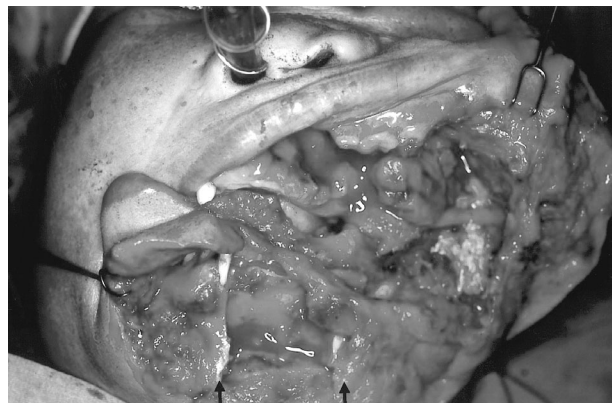
Surgical management consisted of exploration and wound debridement under general endotracheal anesthesia. The bilateral maxillary fractures were reduced and fixed with miniplates. In the mandible, a considerable amount of comminuted and infected bony fragments were resected leaving a bony defect measuring about 5 cm which extended from the right central incisor to the left second premolar area (Fig. 2). The remaining soft tissue, which had no detectable periosteum, was closed over this gap. Due to the presence of infection and extensive soft tissue loss that could favor wound dehiscence over the reconstruction plate, a modified extraoral fixation device was utilized to maintain the position of the mandibular stumps with future reconstruction in mind (Fig. 1B). The device used was an orthopedic external fixator (Colles Frame, ALTA Medical Co.) normally used for the reduction and fixation of fractures of the upper extremities. Two 3-mm-diameter steel pins, 80 mm in length were transcutaneously attached to each mandibular segment. These pins were then connected to steel rods which acted as stabilizing arms. The stabilizing arms were immobilized through additional connecting rods that extended anteriorly from the patient's face. This device held the 2 mandibular stumps rigid and prevented them from collapsing medially as the wounds healed and contracted. The postoperative course of the patient was uneventful, and she was subsequently discharged.

On follow-up, the patient had developed left submandibular cellulitis by 8 weeks after surgery. This resolved after a 2-week course of antibiotics.

Fig. 1 (A) Preoperative skull radiograph of the patient showing the mandibular fracture before resection of the comminuted and infected segments. (B) Postoperative skull radiograph of the patient showing the gap between the right and left mandibular stumps (arrows). These segments were stabilized using a modified external fixator which prevented them from collapsing into the defect.

Fig. 2 Intraoperative view of the 5-cm mandibular defect (arrows) after wound debridement. A large portion of the comminuted fractured mandible was resected leaving no clinically detectable bone or periosteum in the gap.

She also developed trismus due to contraction of the mucosal and cutaneous wounds and had a maximum mouth opening of 10 mm. Six months after surgery; the patient was scheduled for release of the mucosal scar contracture via skin grafting, removal of the extraoral appliance, and bone grafting of the mandibular defect. However, the operative findings showed new osseous tissue where the defect had originally been. The new bone was similar in appearance (color and texture) to the cortical bone of the proximal mandibular segments although it lacked height. There was continuity between the mandibular stumps and the regenerated bone, and some muscular attachments on the new bone (Fig. 3). Treatment then proceeded by grafting iliac cancellous bone in order to increase the height of this new bone. The external fixation device was also removed at this time. The patient had an uneventful healing course and was eventually discharged. On follow-up, the patient showed no signs of infection at the bone graft site and a maximum mouth opening of 25 mm. Unsatisfactory mouth opening was caused by scar contracture on the left cheek and in the submandibular area.
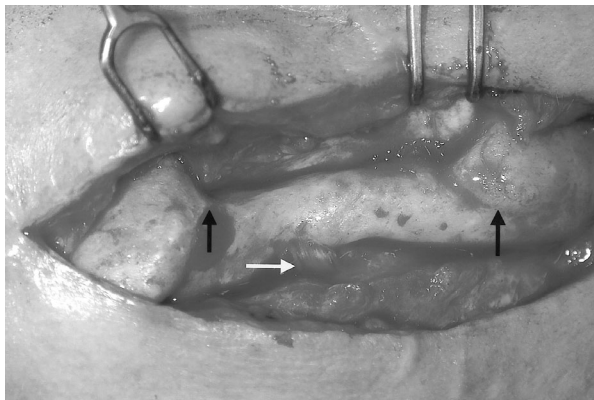
Fig. 3 Intraoperative view showing regenerated bone bridging the original defect between the right and left mandibular stumps (black arrows). Note the muscular attachments (white arrow) at the inferior border of the new bone.

DISCUSSION

Reports of spontaneous bone regeneration of the mandible in the English literature for the last 53 years are presented in Table 1. In all of these reports, authors report resecting a large portion of the mandible or repairing the remaining mandibular segments after an injury without expecting any bone regeneration to take place in such a large gap. New bone was discovered only during routine postoperative clinical and radiographic examinations. Budal[2] reported new bone formation between remaining mandibular stumps 2 weeks after resection of a large osteofibroma. The earliest radiographic evidence of bony regeneration was reported by Nagase et al.,[6] who noted eggshell radiopacity in the area of a resected condyle in an orthopantomogram taken 2 weeks postoperatively. Other authors noted similar evidence from 1 month onwards at the time when a postoperative radiograph was taken.

Boyne,[10] in a series of 6 cases of mandibular resection, noted consistent radiographic and clinical evidence of new bone formation within the empty titanium mesh tray that served as temporary reconstruction material. This new bone increased in height and thickness until approximately 9 months, at which time the regenerative growth of the bone appeared to stabilize. Whitmyer et al.[11] followed a patient 1.5 years after surgery and noted a deformation of the reconstruction plate which appeared to restrict the continued osseous regeneration. After the plate was removed, bone formation continued for 2 years postoperatively. Kisner[8] reported that the regenerated mandible in his patient had attempted to replace the missing segment not only in substance but in position as well. A 5-year follow-up of a regenerated mandible was presented by Budal[12] showing bone regeneration from the right third molar to the left second molar. Although there was no external sign of disfigurement, the new mandible was apparently deformed in the area where the ramus had been pulled upward before the formation of new bone. In our patient, definite muscular attachment in the new chin area was noted during the second surgery (6 months subsequent to the first); and there was an uninterrupted connection between the old and new bone. The above observations demonstrate that the newly regenerated bone behaved in a manner similar to that of the original bone.

An explanation for this unexpected bone regeneration may be derived from the mechanism of fracture healing. The difference is that the former process takes place in a large mandibular defect, whereas the latter occurs when the bony segments are placed in close contact with each other and fixed.

Table 1. Cases of Spontaneous Mandibular Regeneration Reported in the English Literature

Author	Case no.	Age (yr)	Gender	Diagnosis	Treatment	Periosteum status	Stabilization	Infection	New bone first detected
Kazanjian,[5] 1948	1	15	M	Ossifying fibroma	Resection from 36 to the left sigmoid notch	Preserved	Splint	No	2 months
Byars and Schatten,[3] 1960	2	8	F	Ossifying fibroma	Resection, right mandible, from ?	Preserved	Kirschner wire	No	5 weeks
	3	9	M	Fibrous dysplasia	Resection from 33 to 37	Preserved	Kirschner wire MMF, 17 days	No	5 weeks
Budal,[2] 1970	4	35	F	Osteofibroma	Resection from 48 to 37	Thin layer remained	None	No	2-3 weeks
Adekeye,[1] 1977	5	15	M	Ameloblastoma	Resection from 47 to 37	Preserved	None	Yes	7 months
Nwoku,[17] 1980	6	15	M	Recurrent ameloblastic fibroma	Resection and disarticulation of the left mandible	Preserved	MMF, 8 weeks	Yes	6 months
	7	12	F	Ossifying fibroma	Resection and disarticulation of the left mandible	Some preserved	MMF, 8 weeks	Yes	3 months
Kisner,[8] 1980	8	12	M	Shotgun blast injury, loss of mandibular segment from 46 to 34	Debridement, wound closure	Some fragments remained	Kirschner wire	No	10 months
Boyne,[10] 1980	9-14 (6 cases)	5-14	M/F	Various neoplasms	Partial resection to hemimandi-bulectomy	None	Empty titanium mesh, 10-day immobilization	No	2-3 months
Shuker,[9] 1985	15	7	M	Artillery shelling injury, 6-cm defect in mandible	Debridement, wound closure	Some strands remained	Kirschner wire	No	1 month
Nagase et al.,[6] 1985	16	12	M	Ameloblastoma	Partial mandibulectomy from 34 to the condyle, iliac bone graft for body only	Preserved	MMF, 48 days	No	2 weeks
Elbeshir,[4] 1990	17	32	F	Chronic osteomyelitis	Partial mandibulectomy from 33 to the subcondyle	Preserved	None	Yes	1 month
Whitmyer et al.,[11] 1996	18	9	F	Osteosarcoma	Partial resection from 43 to the right angle	Unknown	Reconstruction plate	No	3 months
Present case, 2002	19	58	F	Blast injury, 5 cm defect from 41 to 35	Debridement, wound closure	None detectable	Modified external fixator	Yes	3 weeks

Abbreviations: MMF: maxillomandibular fixation.

McKibbin[13] described the formation of a primary callus that appeared as an initial reaction of bone to injury. Rapid widespread cellular activity that involves the surrounding soft tissues takes place in order to form a bridging external callus whose primary purpose is to maintain the stability of the fragments. Once the bridge is formed, remodeling then proceeds to form mature bone from the temporary callus. The periosteum is believed to be the primary source of the osteogenic tissue. Einhorn[14] mentioned that the presence of committed and uncommitted undifferentiated mesenchymal cells in the periosteum contributes to the process of fracture healing by recapitulation of the embryonic intramembranous and endochondral bone formation.

According to Kisner,[8] for cases in which the periosteum is not intact, the source of the regenerated bone could be fragments of the periosteum, pieces of devitalized bone in the surrounding tissue, and the remaining mandibular stumps. Urist et al.[15] extensively discussed how mesenchymal cells in connective tissues can be induced to form new bone and bone marrow. Growth factors play a major role in this process. The soft tissue surrounding the fracture site is another important contributor to fracture healing not only as a source undifferentiated mesenchymal cells but also of the much-needed blood supply. Specifically, fracture hematoma has been found to contain the angiogenic cytokine vascular endothelial growth factor (VEGF) and has the inherent capability to induce angiogenesis and thus promote revascularization during bone repair.[16] Chalmers et al.[17] suggested that three conditions must be present for bone induction to occur: 1) an inducing agent; 2) an osteogenic precursor cell; and 3) an environment which is permissive to osteogenesis.

There is a question of whether immobilization plays a role in aiding the regeneration process. While most authors, including ourselves, stabilized the mandibular stumps through maxillomandibular fixation, Kirschner wires, reconstruction plates, and external fixation devices; others merely closed the wound and allowed the full range of motion of the remaining mandible. Shuker[9] suggested that continuous functional stresses on the regenerating area could serve as a mechanical factor in promoting osteogenesis. Therefore, we do not think that the limited mouth opening contributed to the regeneration process, but rather it was the stability provided by

the external fixator itself in this case.

When soft tissues are prevented from collapsing into the mandibular defect by a mesh tray, bone regeneration may be allowed to proceed unhindered as demonstrated by Boyne.[10] In a study on large cranial and mandibular defects by Lemperle et al.,[18] they concluded that when active osteogenic periosteum was present, defect protection alone was sufficient to allow adequate healing. However, not all of the cases reviewed, including our own, had adequate soft tissue barriers, and yet spontaneous bone regeneration still took place.

In his report of bone regeneration after resection of an infected ameloblastoma, Adekeye[1] cited the role that infection may play as a stimulus for bone regeneration. Elbeshir[4] also mentioned that periosteum provoked by slow-growing lesions or chronic infection will continue to lay down new bone. It is known that diffuse sclerosing osteomyelitis, condensing osteitis, and proliferative periostitis are inflammatory lesions that result in additional bone formation due to a certain focus of infection.[19] It is possible that infection may have influenced bone regeneration in our patient. The contaminated nature of her injury assured the presence of microorganisms in the wound, and the continued presence of a low-grade infection was shown when she developed cellulitis at the operative site after surgery. However, in the other cases presented in Table 1, infection was not a consistent finding. We are also aware of the conflicting fact that some bony non-unions occur precisely because of the presence of infection.

A common factor among the cases reviewed is the relatively young age of the patients. This has been considered essential for bone regeneration because of the active growth potential and presence of abundant osteoprogenitor cells in young individuals. Shuker[9] showed that when similar cases of mandibular injuries in older patients were repaired using the same technique employed in his young patients, spontaneous bone regeneration did not take place. This was not the case in our patient who, at 58 years old, showed a regenerative capacity equal to those of younger patients by producing bone in a short period of time. This is evidence that mature individuals may retain the potential for bone regeneration.

In summary, unexpected bone regeneration may be explained by the mechanism of fracture healing

with growth factors providing the stimulus, and the surrounding soft tissues providing nourishment for the undifferentiated mesenchymal cells to form new osteogenic tissue. However, it is still unclear as to which factors, or combinations thereof, favor this process in large mandibular defects. From the case we present, it seems that this phenomenon is not always limited by age but can remain potent throughout the lifetime of an individual and may be activated by certain conditions when the need arises.

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年長病人下頜骨自發性骨再生：病例報告及文獻回顧

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　　自發性骨再生是一種不可預期現象，它可能會發生在因外傷或腫瘤切除後導致大的下頜骨缺損處。這種不尋常的骨癒合過程可能要從骨折癒合的機轉來解釋，從文獻的回顧獲知有幾項因素，諸如：骨膜及碎骨的存在、下頜骨的穩定性、軟組織的保護、感染源的存在、及病人年齡都可能會影響此現象的發生，然而這種下頜骨自發性骨再生的現象在過去的文獻報告，皆發生在年輕人。

　　本文主要報告一位58歲女性病患因下頜骨爆炸傷致下頜骨的嚴重缺損而有下頜骨自發性骨再生的現象，並就此現象作一探討。(長庚醫誌 2003;26:363-9)

關鍵字：自發性骨再生，下頜骨缺損。