Management of Central Giant Cell Granulomas of the Jaws: An Unusual Case Report with Critical Appraisal of Existing Literature

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Abstract

Central giant cell granuloma (CGCG) is an uncommon, benign but aggressive osteolytic neoplasm of the craniomaxillofacial region, histologically characterized by an abundance of evenly distributed multinucleated giant cells within a sea of spindle-shaped mesenchymal stromal cells, scattered throughout the fibrovascular connective tissue stroma containing areas of hemorrhage. A rapid diagnostic assessment, together with an adequate histopathologic verification, is essential to improve the management and the prognosis of this locally destructive lesion. A rare case of a large destructive CGCG involving the entire right angle of mandible, causing extensive bony resorption, and buccal, medial as well as inferior border cortical expansion with multiple perforations, in a young child is presented. It was treated successfully by enucleation and aggressive curettage followed by peripheral ostectomy preserving the continuity of the mandible. Two adjunctive measures were employed; first, chemical cauterization of the residual bony walls to prevent possible recurrence, for which this tumor is notorious, and second, placement of fresh autologous platelet-rich fibrin within the bony defect to hasten bone fill and reossification, thus obviating the need for a bone graft.

Keywords: Aneurysmal bone cyst, central giant cell granuloma, giant cell lesions, giant cell tumor, platelet-rich fibrin

INTRODUCTION

Central giant cell granuloma (CGCG) is an uncommon, histologically benign but locally aggressive and destructive osteolytic lesion of osteoclastic origin that occurs in the craniofacial region, especially in jaw bones.[1] It is a solitary lesion, presenting radiographically as a multilocular radiolucency with scalloped margins and a honeycomb or soap bubble-like appearance. It accounts for <7% of all benign tumors of the jaws, the mandible being more frequently affected than the maxilla, with a relative proportion ranging from 2:1 to 11:9. In the mandible, it usually occurs in the body region, anterior to the first molars. It usually affects younger patients under the age of 30 years (80% of the patients being under the age of 20), with a clear female predilection (62%).[2]

Another very similar entity is the giant cell tumor (GCT) which affects long bones and is histologically as well as immunohistochemically indistinguishable from the CGCG.[3,4] These are principally located in long metaphysis like the femur and tibia (accounting for more than 50% of GCTs) and

spine (12%–30%).[5] It has been proposed that CGCG of the jaws and GCT of long bones could represent the development of a single pathologic process, modified by age of the patient, location and presentation of the lesion, and possibly other unknown factors.[6,7] Some literature reports even suggest the aneurysmal bone cyst synonymous with the GCT and a rapidly proliferative variant of the latter.[2]

WHO has defined CGCG as "A localized benign but sometimes aggressive, osteolytic proliferation consisting of fibrous tissue with hemorrhage and hemosiderin deposits and presence of osteoclast-like giant cells with reactive bone formation."[8]

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Clinically, CGCG may behave variably, exhibiting characteristics ranging from asymptomatic, indolent, and slow growth to aggressive and rapid hollowing out of bone, with cortical expansion, thinning and perforation, root resorption, displacement of adjacent structures including teeth and nerves, accompanied by pain. Perineural invasion and infiltration into adjacent soft tissues are generally not seen, and although the lesion is unencapsulated, it expands, pushing away and displacing adjacent structures, rather than invading or infiltrating into them. It is associated with a relatively high recurrence rate of 15%–20%; the more aggressive the lesion, the higher the chances of its recurrence.[8]

Etiology of CGCG is debatable. Jaffe considered this tumor to be a locally reparative reaction of bone to inflammation, local trauma, or hemorrhage. Although originally termed as giant cell *reparative* granuloma, the clinical behavior of these lesions has been inconsistent with a reparative process, as it is neither self-limiting nor self-healing, but requires to be removed or treated, so the term "reparative" has been omitted today.[9] It is not considered an odontogenic lesion.[10] It has been suggested that it might be an inflammatory lesion, a reactive lesion, a true tumor, or an endocrine lesion. One hypothesis suggests that CGCG belongs to the spectrum of mesenchymal proliferative vascular primary jaw lesions.[10]

Although the origin of the cells present in giant cell lesions has been investigated through histochemistry, ultrastructural, and immunohistochemical methods, the pathogenesis and nature of these lesions is still unclear.[11]

Alteration in the hemostatic–vascular equilibrium of bone has been suggested as a possible etiological factor. The best and the most accepted theory of relationship between GCT, CGCG, and traumatic bone cyst is presented by Hillerup and Hjørting-Hansen,[12] who proposed that these lesions are different manifestations of the same general process, the cause of which is a "vascular mishap" resulting from trauma, primary bone disease, or malformation.

Treatment options advocated vary from case to case depending on the clinical characteristics and behavior and range from surgical excision or resection with continuity defect, cryotherapy, to enucleation and aggressive local curettage with or without chemical cauterization.[13] Prognosis is good when complete removal is achieved, and excision by curettage with removal of peripheral bone margins is the gold standard. Early intervention and treatment produce a better outcome.

Case Report

An 8-year-old female child was brought by her parents with the complaints of a slowly enlarging, painless swelling on the right side of her face in the region of the lower jaw. It had been first noticed 8 months ago which had slowly increased in size and prominence lately over the past month. On examination, a roughly spherical, smooth, bulbous, bony hard, and nontender swelling was noted in the right angle region of the mandible with expansion of both the inferior border as well as the medial aspect/surface [Figure 1a-h]. The skin overlying the swelling appeared normal, with no visible pulsations or secondary changes. On palpation, the swelling was bony hard in consistency, nontender, noncompressible, and nonpulsatile. No paresthesia was noted. The expansion of the inferior border in the angle region was significant, extending onto the medial aspect. Mouth opening was unrestricted, and temporomandibular joint and condylar movements were bilaterally synchronous, full, and free. There was no regional lymphadenopathy noted. Intraorally, there was appreciable expansion of the buccal cortical plate in the molar and retromolar regions as well as the lowermost aspect of the ascending ramus. "Egg shell crackling" could not be elicited. There was no disturbance of the dental arches or of the occlusion, and no displacement of teeth was noted in the region. The patient was in the mixed dentition stage [Figure 1g]. The oral mucosa showed no breach, secondary changes, or sinus opening and was of the normal coral pink color and appearance.

Orthopantomogram [Figure 1i] showed the jaws in the mixed dentition stage typical for the age of the patient. It revealed a large multilocular radiolucency, with scalloped margins and a soap bubble and honeycomb appearance in the region of the right angle of the mandible, extending anteriorly up to the root tips of the adjacent first molar, which showed evidence of resorption. Posteriorly, the multilocular lesion extended posterior to the developing second molar tooth bud and its follicle, past the angle region of the mandible. There was noted diverging and expanding margins of the lesion, with cortical thinning as well as sclerotic margins at places. There was seen a pronounced expansion along the inferior border of the mandible in the angle region, causing its eccentric ballooning with periosteal new bone formation [Figure 1i]. Thin radiopaque septae separated the locules. Fine bony trabeculations in the lesion give a typical "soap bubble appearance."

Noncontrast computed tomographic (NCCT) scan was carried out, and 5-mm contiguous, axial sections were obtained for the maxillofacial region without administration of iodinated contrast [Figure 2]. It revealed a multiloculated expansile cystic lesion with bony septae within, measuring 2.6 cm × 2.5 cm × 3.7 cm (AP × Tr × CC) in the region of the right angle of the mandible. Overlying cortex was thinned out with breaches of its integrity at places. No calcific foci were noted within the matrix of the lesion. The findings led to a differential diagnosis of an aneurysmal bone cyst, odontogenic myxoma, CGCG, or an arteriovenous malformation.

Magnetic resonance imaging of the lesion showed evidence of a 3.3 cm × 2.5 cm × 3.4 cm well-defined, expansile, mild to moderately enhancing lobulated T1 hypointense and T2 iso to hyperintense lesion in the right angle of the mandible with cortical thinning and cortical breaches [Figures 3 and 4], causing mild compression of the submandibular gland [Figures 4 and 5].

Figure 1: (a-h) Bony hard, nontender swelling with expansion of inferior border as well as the buccal and medial aspects of the right angle region of the mandible. (i) Orthopantomogram revealed a large multilocular radiolucency, with scalloped margins and a soap bubble and honeycomb appearance in the region of the right angle of mandible, with resorption of root tips of the adjacent first molar. (j and k) A sample of tissue was obtained for histopathological examination by removing a small window of bone from the expanded buccal cortical plate and scooping out tissue from within the lesion

Magnetic resonance angiography of the cervical vessels revealed no evidence of abnormal flow voids or abnormal draining channels [Figure 6]. Multiple enlarged right-sided cervical lymph nodes were seen, predominantly in the posterior triangle, the largest measuring 20 mm × 12 mm.

Aspiration biopsy was negative. Tissue biopsy was carried out under LA, by creating a small window through the buccal cortical bone in the retromolar region [Figure 1j and k], through which a representative sample of soft tissue was excavated from within the bony lesion. The tissue was soft and friable and bled readily. Both the cortical bone and soft tissue samples were sent for histopathological examination.

Microscopic evaluation revealed soft tissue fragments of cellular tissue along with lamellar bony trabeculae along the margins [Figure 7]. There were focal areas of hemorrhage and necrosis. There were osteoclast type of giant cells and loose bundles of polygonal to spindle-shaped cells, with small interspersed blood vessels. There were also noted focal collections of lymphocytes and neutrophils and some pigment-laden macrophages. Decalcified sections of the overlying cortical bone showed multiple lamellar bony trabeculae focally lined by rows of osteoblasts and intervening fibrovascular stroma with no evidence of cellular tumor. The findings were suggestive of a giant cell lesion such as CGCG.

Another specimen submitted to a different laboratory revealed an unencapsulated tumor showing numerous osteoclast-type giant cells evenly scattered in a vascular stroma comprising of proliferative fibroblasts and endothelial cells. The stroma showed extravasated red blood cells and hemosiderin deposition along with few scattered mixed inflammatory cells. Mitosis 1–2 per histopathological field was seen in the stroma. There was no cellular atypia noted and no osteoid deposition seen. A diagnosis of GCT was given.

Tests were immediately carried out for assessing the serum calcium, alkaline phosphatase, and serum parathormone levels, to rule out Brown's tumor of hyperparathyroidism, which exhibits similar microscopic findings. Serum calcium level was found to be 10.1 mg/dL (normal range 8.8–10.6 mg/dL); serum parathormone level was found to be 35.5 pg/mL (normal range 12–88 pg/mL); and serum alkaline phosphatase level was found to be 316 U/L (normal range 54–369 U/L). Hyperparathyroidism was hence ruled out.

After routine workup, the child was taken up for surgery under general anesthesia. Enucleation of the lesion followed by aggressive curettage and peripheral ostectomy, through a retromandibular cum submandibular approach was planned.

The incision line was marked 1 cm below the expanded inferior border of the angle region of the mandible and
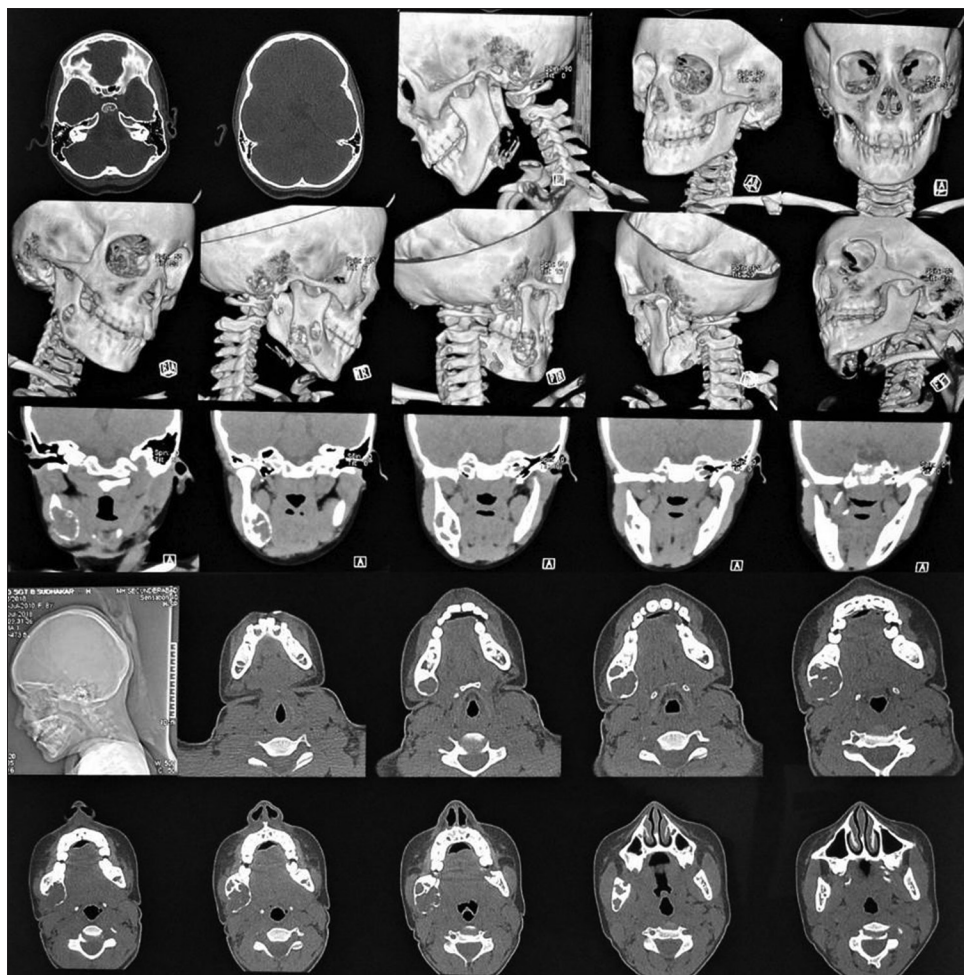
Figure 2: Noncontrast computed tomographic scan revealed a multiloculated expansile cystic lesion with bony septae within, measuring 2.6 cm × 2.5 cm × 3.7 cm (AP × Tr × CC) in the region of the right angle of the mandible. Overlying cortex was thinned out with breaches of its integrity at places

infiltrated with 1: 80,000 adrenaline and 2% lignocaine. The incision was made through the skin and subcutaneous tissue, which was then carefully undermined in all directions to permit ease of retraction and suturing later on. The platysma muscle was sharply incised from one end of the incision to the other. Careful dissection was then carried out through the white glistening investing layer of the deep cervical fascia [Figure 8a]. The marginal mandibular nerve was identified and retracted superiorly; the facial vessels were cut and ligated. The submandibular salivary gland which bulged into the operating site [Figure 8b] was carefully retracted inferiorly using a malleable retractor. The inferior border of the mandible was visualized, which was covered by periosteum anterior to the premasseteric notch and by the avascular portion of the pterygomasseteric sling posterior to the premasseteric notch in the angle region, both of which were incised sharply and stripped from the underlying bone, exposing the tumor mass [Figure 8c]. The mass was covered by a thin shell of bone which was perforated in several areas, exposing the tumor mass within. Once the almost eggshell thin areas of overlying bone were nibbled away with rongeur forceps, the tumor mass

was exposed to view. It appeared chocolatey brown in color, interspersed with hemorrhagic areas welling up with blood. The mass had a soft spongy texture [Figure 8d].

The soft, friable, and vascular tumor mass was enucleated, by scooping it out from the bony cavity underneath. The overlying expanded buccal and medial cortical plates were nibbled away carefully using rongeurs forceps [Figure 8e-g], taking care to avoid any undue pressure of force to prevent an inadvertent fracture of the already weakened mandible. After complete enucleation of the tumorous tissue, vigorous curettage of the residual bony cavity was carried out, followed by peripheral ostectomy using vulcanite trimmers. The oozing from inferior alveolar canal in the far end of the angle was controlled using bone wax. This was thereafter followed by chemical cauterization of the entire tumor bed using cotton pellets soaked with Carnoy's solution [Figure 8h], to ensure prevention of future recurrence. The adjacent tissues were first protected from the caustic chemical, using layers of folded Vaseline gauze [Figure 8h]. After thorough irrigation of the area, hemostasis was ensured and all sharp margins of bone were carefully smoothened using bone files [Figure 8j]. 15 ml of
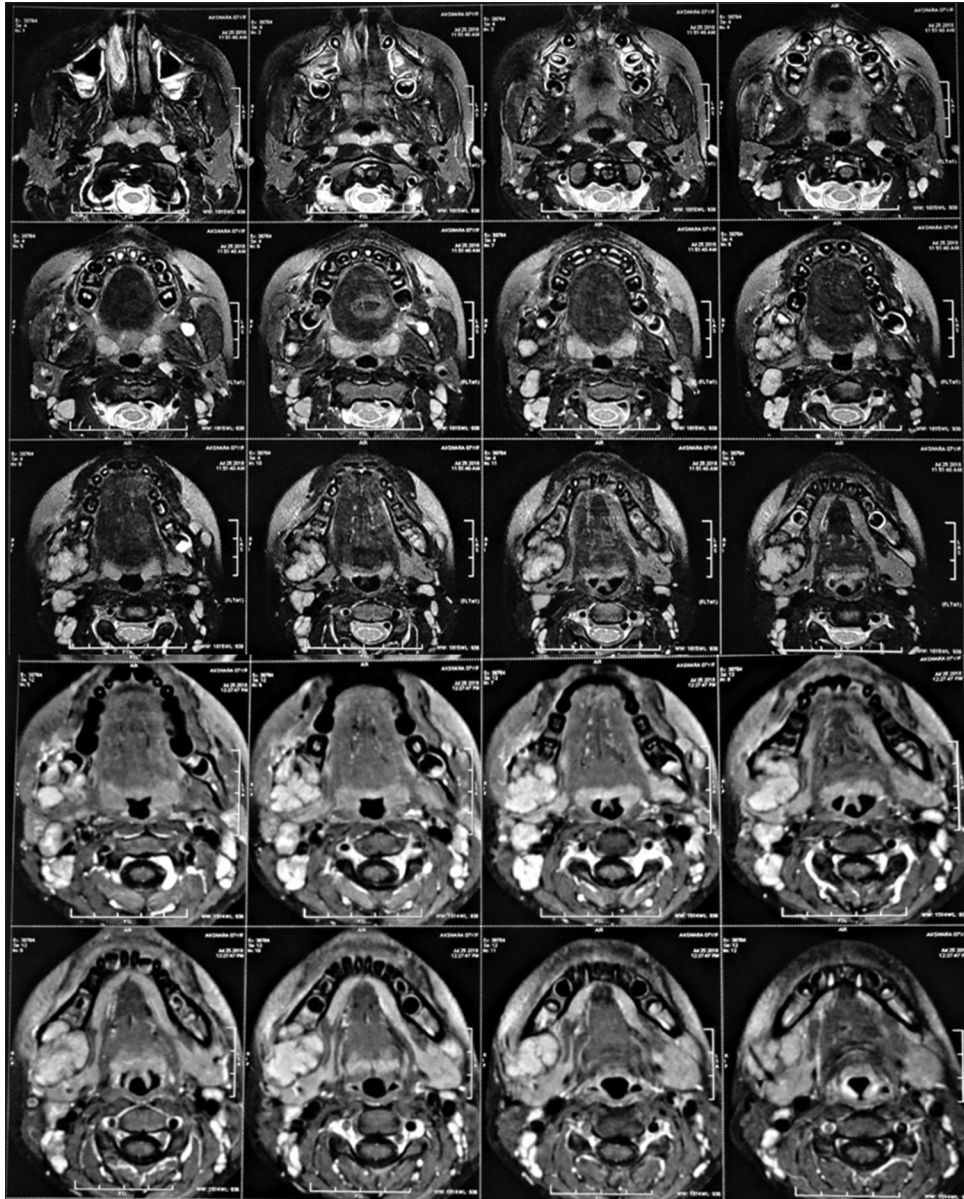
Figure 3: Magnetic resonance imaging of the lesion (axial sections) showed evidence of a 3.3 cm × 2.5 cm × 3.4 cm well-defined, expansile, mild to moderately enhancing lobulated T1 hypointense and T2 iso to hyperintense lesion in the right angle of the mandible with cortical thinning and cortical breaches, causing mild compression of the submandibular gland

blood was drawn from the patient, and autologous platelet-rich fibrin (PRF) was prepared using a tabletop centrifuge. This was placed within the bony defect [Figure 8l-o], which would help in two ways, first by eliminating the dead space and second by providing a host of growth factors such as platelet-derived growth factor (PDGF), insulin-like growth factor, vascular endothelial growth factor (VEGF), and transforming growth factor-β (TGF-β) to hasten soft tissue healing as well as subsequent bone fill in the defect region. This was followed by layerwise closure using resorbable Vicryl sutures for the deeper layers and interrupted Prolene sutures for the skin. An extraoral pressure dressing was applied to prevent formation of a hematoma. Histopathological examination of the excised specimen [Figure 8k] confirmed the prior diagnosis of GCT.

Postoperative recovery of the patient was smooth and uneventful. The mild postoperative pain and edema were controlled with analgesic anti-inflammatory drugs, and the patient was placed on intravenous broad-spectrum antibiotics for 5 days. There were no neurological deficits related to the marginal mandibular nerve. There was noted a mild numbness of the right half of the chin and lip, resulting presumably from removal of the segment of the inferior alveolar nerve involved within the tumor, thus rendering the mental branch nonconductive. Careful placement of the incision line at the time of surgery in the submandibular neck crease had resulted in a fairly inconspicuous and hidden resultant scar [Figure 9]. Postoperative NCCT of the region [Figure 10] revealed smooth residual margins, walls, and floor of the residual bony defect. Histopathological examination of samples of
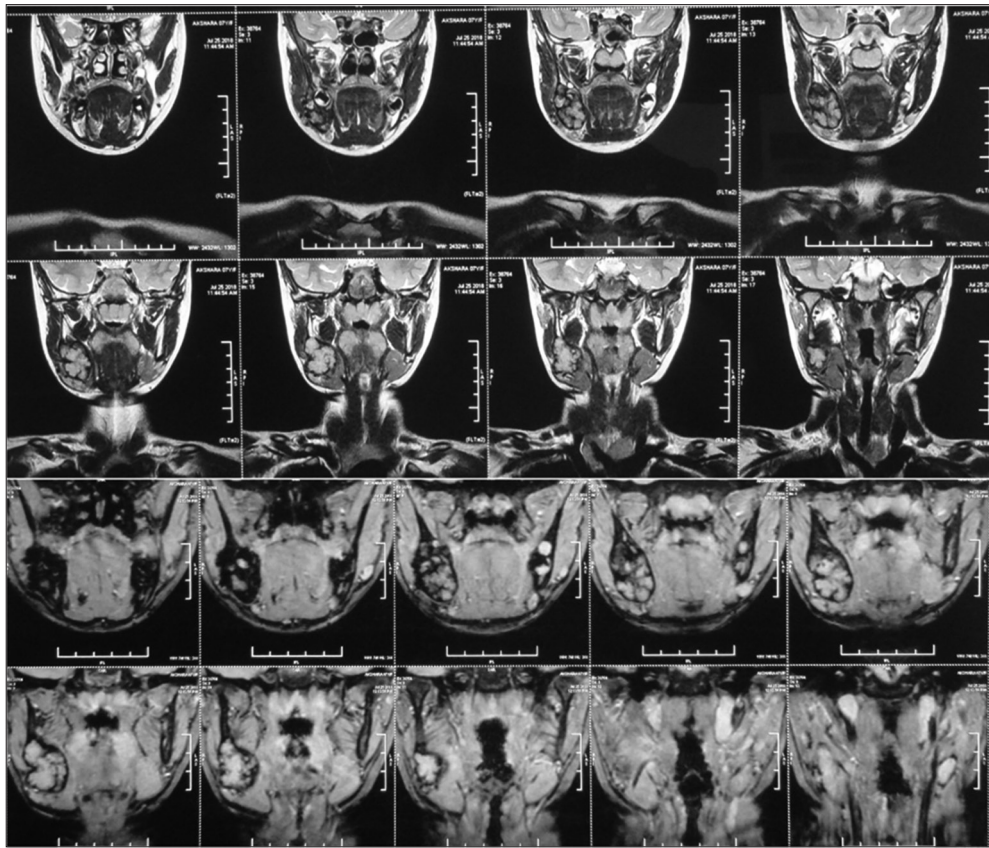
Figure 4: Magnetic resonance imaging of the lesion (coronal sections) revealing mild compression of the right submandibular gland by the expanding lesion of the right angle of the mandible
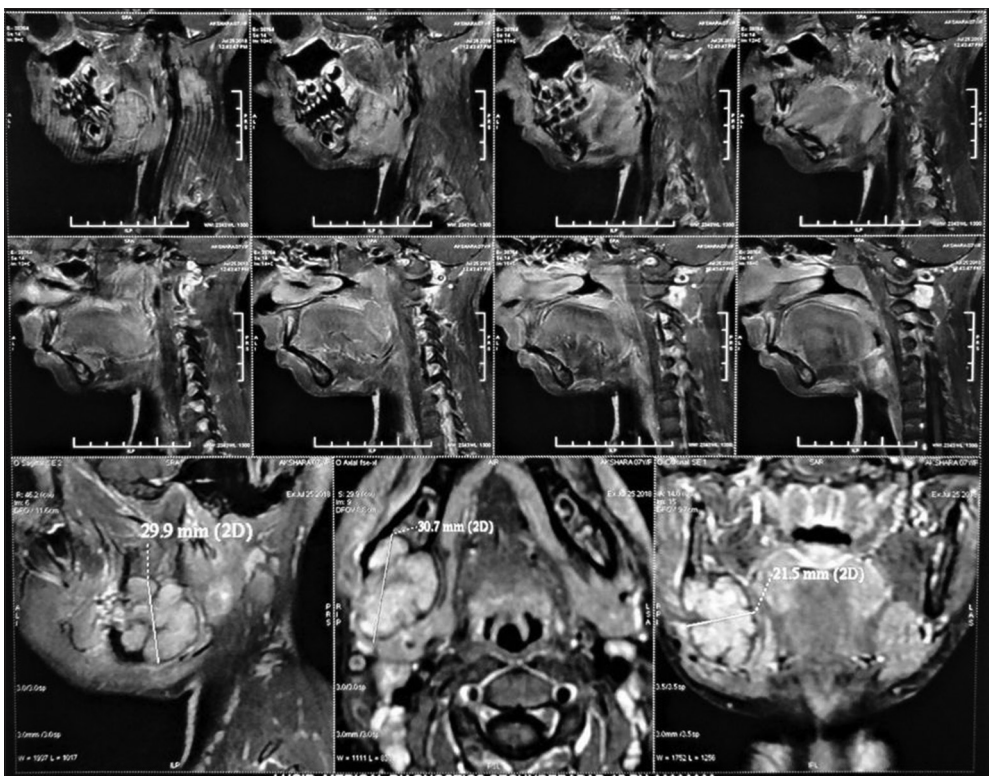

Figure 5: Magnetic resonance imaging of the lesion (sagittal and axial sections) revealing multiple enlarged submandibular and cervical lymph nodes, especially in the posterior triangle

tissue from the excised specimen confirmed the diagnosis of CGCG [Figure 11].

The patient was followed up for 1 year, and there was no clinical or radiographic evidence of recurrence of the lesion.

DISCUSSION

Correct identification and diagnosis of bone tumors of the craniomaxillofacial region can be quite challenging. Numerous bone tumors such as the CGCG, aneurysmal bone cyst, ameloblastoma, ossifying fibroma, odontogenic myxoma, sarcomas, and arteriovenous malformations present with a seemingly similar soap bubble or honeycomb appearance with scalloped margins, radiographically.[8]

Figure 6: Magnetic resonance angiography of the cervical vessels revealed no evidence of abnormal flow voids or abnormal draining channels, ruling out an arteriovenous malformation

Lymphoid neoplasias such as non-Hodgkin's lymphomas may on rare occasions manifest themselves in intraoral locations,[14] including the jaw bones, and hence justify their inclusion in the differential diagnosis of CGCG. These malignant neoplasms arise from hematopoietic and lymphoid tissues which at times may develop in oral and maxillofacial locations such as the tonsils (55% of oral cases), palate (30% of cases), and genial mucosa (2% of cases). There are also extranodal sporadic manifestations affecting the tongue (2% of cases), buccal floor (2% of cases), jaw bones (1% of cases), and retromolar trigone (2% of cases).[14]

Infectious granulomas affecting the oral and maxillofacial region[15] must also be considered in the differential diagnosis of expansile lesions of the mandible. The common aspect of all granulomatous diseases is the typical form of chronic inflammatory response with distinct microscopic granulomas that are formed secondary to either definitive etiologic agents, such as bacteria, fungal, or parasitic, or due to unknown etiologic agents, such as trauma, autoimmune, or even neoplastic processes.[16] Two types of granulomas are typically encountered: foreign body granulomas and immune granulomas, the differences between them lying in their pathogenesis. The absence of any infective element or inflammatory component in our case as evidenced both by general clinical examination and blood investigations as well as microscopic evaluation of the biopsy specimen, ruled out the above. Further, the presence of distinct multinucleated giant cells with evenly distributed nuclei was suggestive of CGCG rather than a foreign body or immune granuloma.

Many bone tumors also have multinucleated giant cells, that must be distinguished from the conventional CGCG. These range from benign lesions such as ossifying fibromas, locally aggressive lesions such as aneurysmal bone cysts, to malignant lesions such as high-grade sarcomas. Certain metabolic disorders such as hyperparathyroidism are also characterized by masses of reactive osteoclast-like giant cells, which histopathologically mimic GCTs of bone.[16]

The normal serum calcium and alkaline phosphatase levels found in this case ruled out hyperparathyroidism. In aneurysmal bone cyst and other such lesions, giant cells are found close to areas of hemorrhage;[16,17] whereas in this
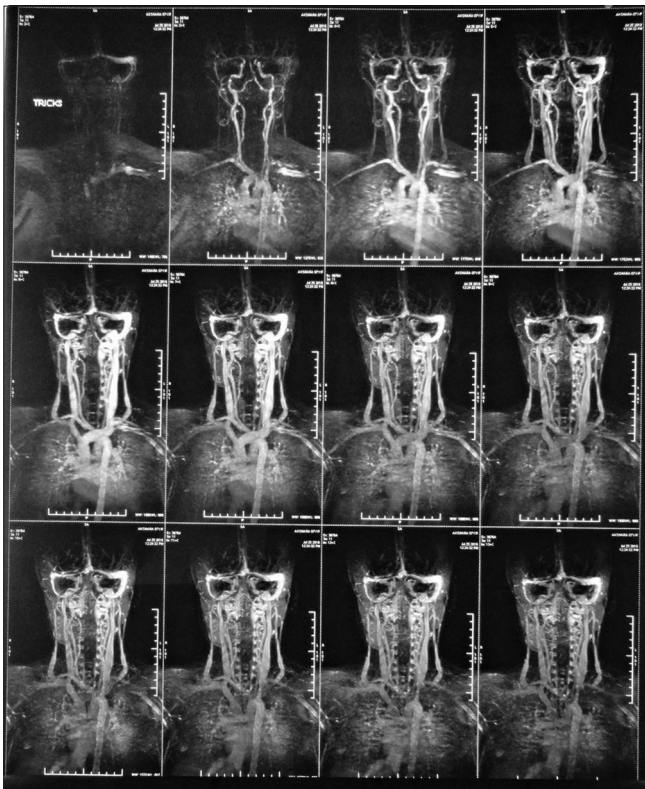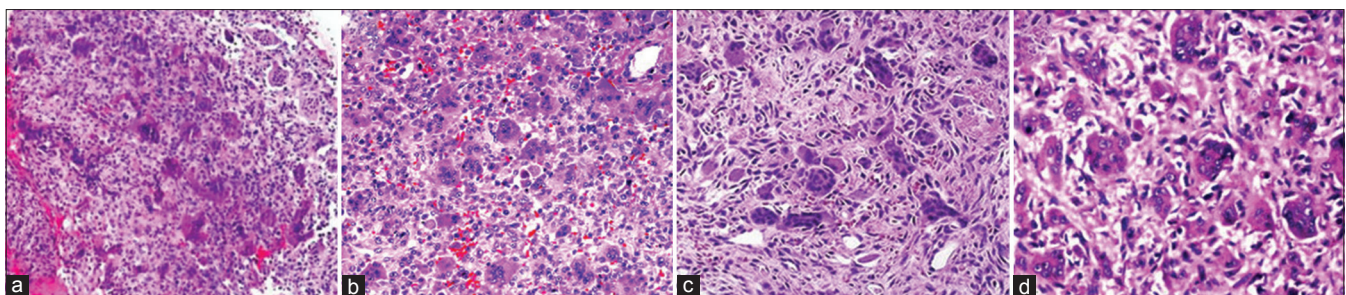

Figure 7: (a-c) H and E section × 10 and × 20 showed unencapsulated tumor containing multiple osteoclast-type giant cells evenly scattered in a vascular stoma comprising of proliferating fibroblasts arranged in a whorled pattern. (d) H and E section ×40 showing giant cells scattered in the stroma which contained areas of hemorrhage and hemosiderin deposition along with few scattered mixed inflammatory cells. No necrosis or atypia was noted
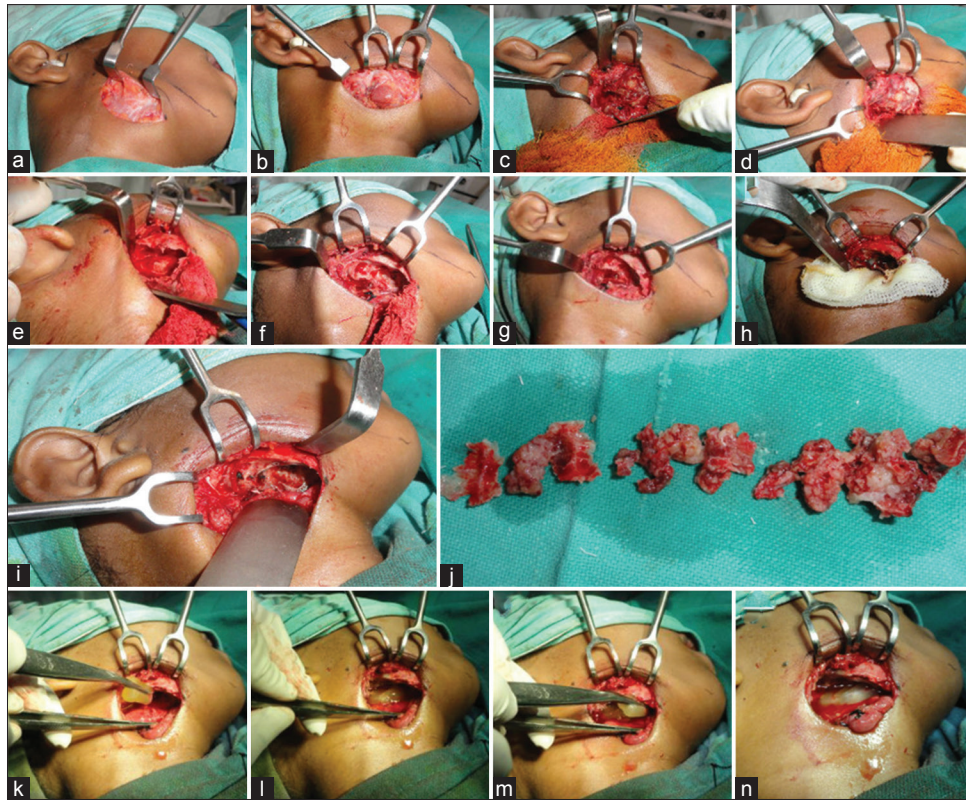
Figure 8: (a-d) Submandibular approach exposing the expanded and bulbous right angle of mandible. Thin shell of overlying cortical bone, nibbled using rongeurs, exposing the soft spongy, vascular tumor mass, which was carefully excavated. (e-g) Vigorous curettage followed by trimming of bony edges and peripheral ostectomy of the base of the residual defect. (h and i) Chemical cauterization of the defect using Carnoy's solution. (j) Extirpated tumor mass. (k-n) Autologous platelet-rich fibrin prepared intraoperatively and place into the bony defect before closure of operated site

Figure 9: (a-d) Postoperative photographs showing good healing of the operated site with esthetic positioning of the incision line and an inconspicuous resultant scar

case, the giant cells were evenly distributed throughout the lesion. Histopathologically, the even distribution of giant cells throughout the cellular stroma composed of nonreactive, spindle-shaped fibroblastic stromal cells, the giant cells with evenly distributed nuclei close to 25–50, fresh regions of hemorrhage with hemosiderin deposits, inflammatory cell aggregates, and areas of fibrosis and reactive bone formation, all led to the final diagnosis being made in favor of CGCG of the mandible.

Greater than 90% of oral malignancies arise from the epithelium;[18] a vast majority is associated with tobacco habit. Use of tobacco in smoked and smokeless forms is widely prevalent in all parts of the world and reaches epidemic proportions in the Asian subcontinent. Tobacco may be smoked or used alone/mixed with additives and chewed/kept in the buccal/labial sulcus. On a critical appraisal of available literature on a possible relation between the use of tobacco in smoked and smokeless forms and development of GCTs of the jaws, no direct or indirect correlation between the two could be found. Neither could an etiopathological basis nor correlation be drawn between these tumors and the use of electronic cigarette, which have been proposed as a product able to aid to stop smoking by simulating the act of tobacco smoking by vaporizing a mixture of propylene glycol, nicotine, and flavoring agents.[19]
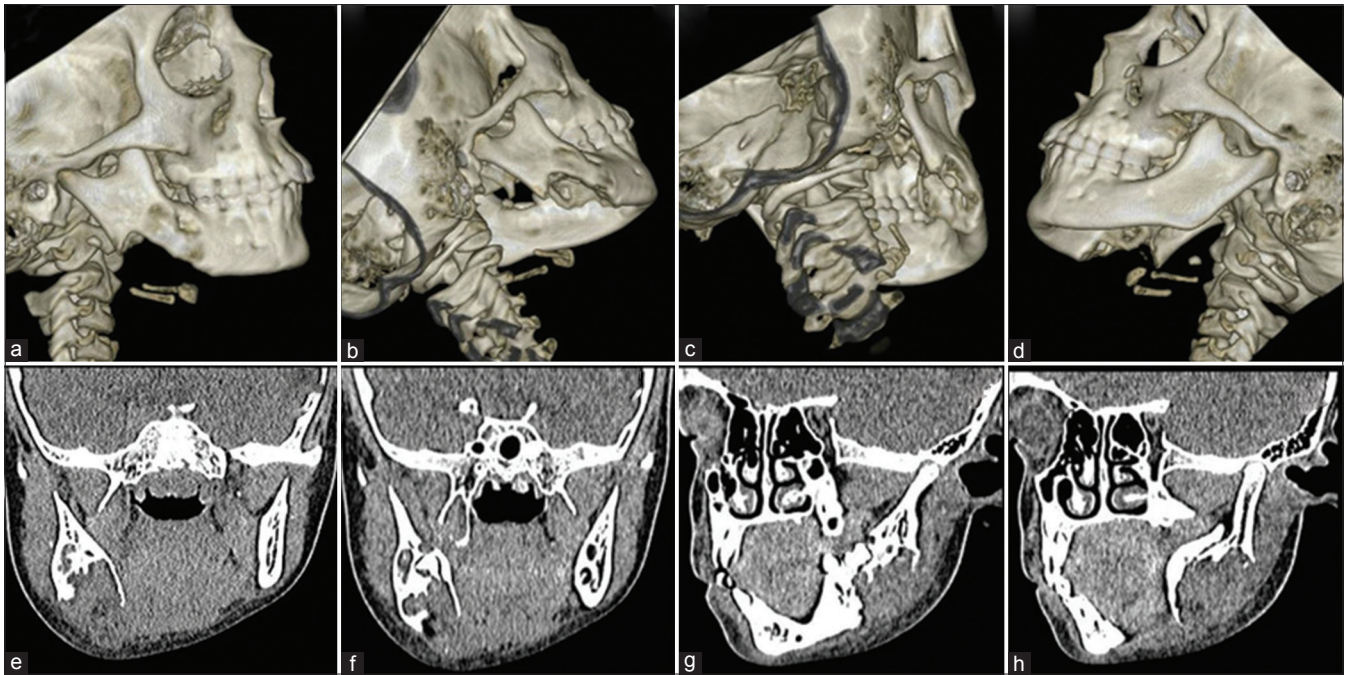
Figure 10: (a-h) Postoperative non contrast computed tomographic revealed smooth residual margins, walls, and floor of residual bony defect
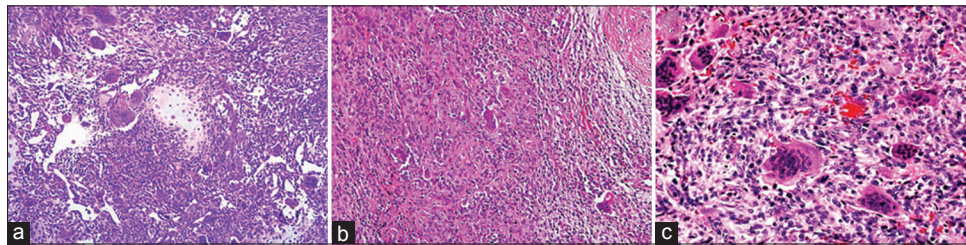

Figure 11: (a-c) Histopathological examination of excised specimen confirming the diagnosis of central giant cell granuloma

Innovative technologies such as "Bioimpedance assays" can serve as valuable diagnostic aids in tumoral tissues.[20] Bioimpedance is a measure of the electrical properties of biological tissues. It has been demonstrated that tumoral tissues often show lower bioimpedance values than healthy tissues. Bioimpedance is a valid aid in the early detection and clinical monitoring of the suspicious lesions which could lead to a potentially malignant evolution. In this way, in the case presented, they could help in reaching a conclusive diagnosis by helping in ruling out malignant lesions.

The biologic behavior of CGCG of the jaws ranges from a quiescent, indolent asymptomatic lesion with slow growth and low recurrence rate, to an aggressive pathological process, characterized by pain, rapid growth, root resorption, cortical perforation, and a high recurrence rate.[21]

The gold standard of treatment of CGCG is surgical enucleation and curettage, and this was used in the case presented. Curettage used in combination with cryotherapy may reduce the rate of recurrence in nonfacial bones, which has been reported to be >50% when curettage alone is used. Radiation has been used as a therapeutic modality, but the subsequent development of sarcoma has been reported. Segmental resection is advocated only in case of multiple recurrences or extension to overlying tissues.[3]

In the case presented, enucleation was accompanied by thorough and aggressive curettage and peripheral ostectomy using vulcanite trimmers to remove a 1 mm thick layer of bone all along the walls, floor, and margins of the residual bony cavity. This was followed by chemical cauterization using Carnoy's solution (a tissue fixative) to fix and destroy any residual tumor cell remnants. The use of Carnoy's solution has hitherto not been described or reported in literature in the management protocol of this lesion, and it is proposed that it may serve as a valuable adjunctive measure to minimize the chances of possible recurrence by serving as a physicochemical means to penetrate bone and kill any organic matter within the bone matrix around the lesion, thus eliminating any residual tumor cells from the peripheral bone, a rationale similar to its use for other locally invasive and aggressive tumors such as keratocystic odontogenic tumor and ameloblastoma. It has a strong penetration power of 1.54 mm into bone after application with a cotton-tipped applicator for just 5 min.[22]

Further, incorporation of PRF within the large residual bony cavity could aid soft as well as hard tissue recovery, healing, and regeneration, resulting in a quicker and more efficient bone fill and reossification, thus reducing chances of pathological fracture of the weakened, hollowed out mandible.

Tissue engineering is a combination of three key elements: scaffolds (collagen, bone mineral), signaling molecules (growth factors), and cells (osteoblasts, fibroblasts). PRF belongs to a new generation of an immune and platelet concentrate collecting on a single fibrin membrane, isolated from peripheral blood. It is a rich autologous source of growth factors delivered in high concentrations to the site of bone defect or a region requiring augmentation.[23] Khiste and Tari have shown that PRF is a suitable scaffold for breeding human periosteal cells *in vitro*, which may be suitable for bone tissue engineering applications.[23] This platelet gel greatly aids and hastens wound healing, bone growth and maturation, graft stabilization, wound sealing, and hemostasis. This is as pertinent in the young child as it is in the adult.[24]

The growth factors present in platelets are important to guide the regenerating cells to the area of healing. The proteins derived from α-granules of platelets include PDGF, TGF-β, VEGF, and epidermal growth factor.[23] PRF holds on to these growth factors enmeshed in its fibrin network, resulting in their sustained release over a period of time that can accelerate the wound healing process. PRF also stimulates the chemotactic migration of human mesenchymal stem cells to the injury site. These growth factors are considered to have the ability to accelerate chemotaxis, mitogenesis, angiogenesis, and synthesis of collagen matrix and favor tissue repair when applied on bone wounds.[23] There is also an important link between growth factors and tissue oxygenation. Oxygenation enhances the phagocytic and bactericidal ability of the immune system of the host cells; also, it helps in supporting the protein as well as collagen synthesis. In this way, PRF is equally useful and valuable in the pediatric age group just as it is in the adults.[24] This serves to hasten bone fill and reossification of bony defects, resulting in clinically as well as radiographically appreciable postoperative results, in terms of soft as well as hard tissue recovery, healing, and regeneration.[23]

Literature studies have revealed other innovative methods to restore the lost tissues with autologous matrices. Native extracellular matrix (ECM) scaffold is an emerging tool in tissue engineering for the reconstruction of three-dimensional (3D) tissues and organs, respecting their structural and functional features.[25] It has been hypothesized in a recent study on an experimental model[25] that the scaffold is able to guide migration and differentiation of stem cells which can derive from skeletal muscle, bone, cartilage, or circulation; however, the presence of other soluble factors specific of the tissue at the interface with the scaffold (i.e., muscle or bone) is necessary to guide stem cell differentiation toward the specific features of that tissue. Skeletal muscle acellular scaffolds (MAS) implanted at the interface of tibialis anterior/tibial bone

and masseter muscle/mandible bone in a murine model were colonized by muscle cells near the host muscle and by bone-cartilaginous tissues near the host bone, thus highlighting the importance of the environment in directing cell homing and differentiation. These results unveil the multipotency of MAS and point to the potential of this new technique as a valuable tool in musculoskeletal tissue regeneration.[26]

Another study has proposed that the ECM of decellularized organs possesses the characteristics of the ideal tissue-engineering scaffold (i.e., histocompatibility, porosity, degradability, and nontoxicity).[27] The microenvironment (including the stem cell niche) is determined by three major components: the ECM, cells, and local growth factors. MAS was demonstrated to be a suitable environment for muscle and nonmuscle 3D constructs characterized by a highly organized structure whose relative stability promotes integration with the surrounding tissues. This study highlighted the plasticity of MAS, suggesting that it may be possible to consider MAS for a wider range of tissue engineering applications than the mere replacement of volumetric muscle loss, including osteogenic replacement of lost bone.[27]

Additional adjunctive measures which could probably supplement and enhance results of surgical management include incorporation of natural antioxidants which are bioactive compounds that can improve mitochondrial functionality and regulate apoptosis, thus having the potential to eliminate rapidly multiplying residual tumoral cells. Studies have been carried out on tumoral cells treated with the polyphenolic extracts derived from crude extracts of wastewater generated from brewing industries[28] and have shown an enhanced mitochondrial oxidative function, which is likely related to a decrease in oxidative stress and an increase in mitochondrial biogenesis.

Conclusion

A multidisciplinary approach in the diagnosis and treatment of giant cell granulomas involving the maxillofacial skeleton is vital to its appropriate and complete management, with an ideal functional and esthetic outcome and rehabilitation. This includes, first, establishing a prompt, early, and accurate diagnosis with the help of various diagnostic tools and aids such as intra- and extraoral radiographs, computed tomographic scans with accurate interpretation by an experienced radiologist as to extent and involvement of the lesion, blood and urine investigations to rule out metabolic disorders producing radiographically similar lesions of the bone, and histopathological and if possible, immunohistochemical examination of biopsy specimens from the lesion by an experienced pathologist to reach a conclusive and confirmatory diagnosis.

A complete elimination of the neoplasm is the next step and is the key to successful management of the CGCG, which can otherwise lead to extensive bone destruction, resulting in considerable cosmetic deformity as well as functional debility.

The size, extent, involvement, and clinical behavior of the tumor will dictate the treatment modality to be employed. As children and young adults are usually affected, early definitive management would help reducing the chances of recurrence requiring further ablative surgical procedures.

In the case reported, removal of the lesion was followed by aggressive curettage and peripheral ostectomy of the tumor bed. This was further supplemented by two additional and adjunctive measures, which we recommend for all such lesions. The first is chemical cauterization using Carnoy's solution of the floor and walls of the residual bony cavity, which could serve to reduce the chances of possible recurrence, especially in cases of aggressive lesions. The second was the placement of fresh autologous PRF within the residual bony defect to hasten bone fill and reossification, so as to eliminate the need for bone graft in the region and its associated donor site morbidity. A quicker bone fill of the defect would help reduce the chances of a residual bony deformity or a pathological fracture of the weakened mandible.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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