Intralesional corticosteroid injection for central giant cell granuloma: A case report and review of the literature

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Central giant cell granuloma (CGCG) is a benign intraosseous lesion of the jaws that is found predominantly in children and young adults. Although benign, it may be locally aggressive, causing extensive bone destruction, tooth displacement and root resorption. The common therapy is aggressive curettage, peripheral ostectomy or resection, which may be associated with loss of teeth and, in younger patients, loss of dental germs. A number of alternative non-surgical approaches have been advocated in recent years for the management of CGCGs. These include intralesional corticosteroid injections, calcitonin injections and subcutaneous α-interferon injections.

In this article, an 11-year-old boy with a CGCG is successfully treated with corticosteroid injections and this treatment is discussed within a review of the literature.

Key words: central giant cell granuloma, mandible, treatment, intralesional corticosteroid injection.

Central giant cell granuloma (CGCG) is defined by the World Health Organization as an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of hemorrhage, aggregations of multinucleated giant cells and occasionally trabeculae of woven bone[1]. Its etiology is unknown and its biological behavior poorly understood[2,3]. CGCG is a nonneoplastic lesion that is found exclusively in the maxilla and the mandible[1].

It is an uncommon lesion that accounts for less than 7% of all benign lesions of the jaws in tooth-bearing areas[2,7]. The mandibular/maxillary ratio has been reported as being from 2:1[8] to 3:1[5].

Central giant cell granuloma commonly occurs in children and young adults, with a slight predilection for females. The anterior portion of the mandible has been identified as a more common location for CGCG development, with the lesion frequently crossing the midline[3,9]. There are reports of CGCG behaving like a slow growing neoplasm: expansile and destructive, displacing teeth, enveloping and often eroding dental root ends, perforating the cortex and leading to pathologic fractures[1-12]. When in the maxilla, CGCG can invade the floor of the maxillary sinus or the orbit, as well as the nasal fossae. Mandibular CGCG may expand and even penetrate the cortical bone. The majority of CGCGs (87.5% present as an expansile radiolucency, either unilocular or multilocular, with well-defined or ill-defined margins[3,4,8].

Based on its clinical behavior and radiographic features, CGCG has been classified as one of the following;

1. Non-aggressive, which is characterized by a slow, almost asymptomatic growth that does not perforate the cortical bone or induce root resorption. This variety has a low tendency to recur.
2. Aggressive, which is characterized by pain, rapid growth, expansion and/or perforation of the cortical bone, radicular resorption, and a high tendency to recur. The aggressive lesions are found in younger patients[5,12].

The traditional treatment of CGCG of the jaws has been surgical excision either by curretage[2,3,5,14-16] or en bloc resection[17], depending on the following factors: aggressive versus non-aggressive behavior, location, size and

radiographic appearance[13,18,19]. There are no histologic differences between the aggressive and non-aggressive varieties[12,18-22]. Other treatments have included radiation[10] and systemic injections of calcitonin[18,23-25] and α-interferon[19,21,26].

Many authors have reported cases of CGCG treated with corticosteroids[13,27-32]. This nonsurgical approach is very important in young patients with developing dentition. Investigators reported successful treatment of CGCG with intralesional steroid injections in children[13,29].

The purpose of this case report was to use a less-invasive therapeutic approach for the treatment of CGCG affecting the mandible in an 11-year-old boy.

Case Report

An 11-year-old previously healthy boy was referred with a painless, bony hard swelling of the left side of the jaw. It was first noticed by his parents three months before the consultation and had then slowly increased in size. There was no history of fever, discomfort, pain, sensory disturbance, difficulty in mastication, bad taste, or traumatic injury. Extraoral examination revealed non-tender expansile mass of the left mandibular body; the lesion produced no significant facial asymmetry or marked deformity. There was no skin erythema or apparent cervical or submandibular lymphadenopathy.

Intraoral examination revealed buccal expansion from the mesial side of the left permanent canine to the distal side of the left permanent primary second molar (Fig. 1). The swelling was hard on palpation, consistent with bone, and was covered with normal mucosa. Pressure did not elicit any exudates or any tenderness, and there was no presence of paresthesia. There was minimal swelling of the lingual aspect of the mandible, and dentition was normal; the left mandibular teeth were non-tender and immobile.

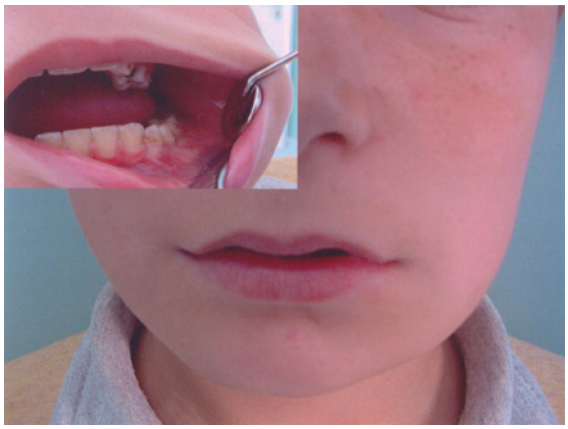


Fig. 1. Osteolytic lesion in the left body in the mandible.

Radiographs of the patient included a panoramic view, occlusal view, cross-sectional tomographies, axial computed tomographies and three-dimensional computerized tomography (CT) scan. These revealed well-circumscribed, unilocular radiolucency (Fig. 2).

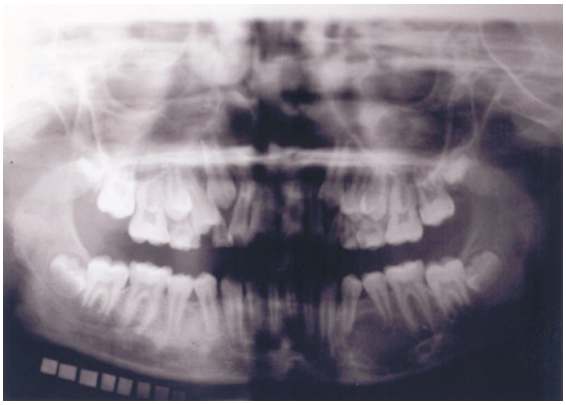
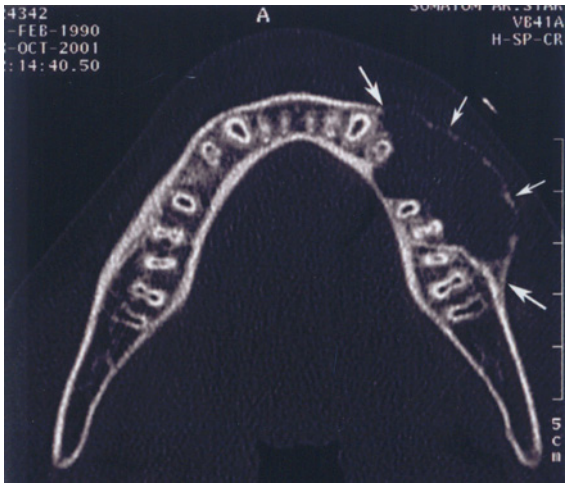


Fig. 2. Panoramic radiograph shows a 3.5x2 cm partially corticated radiolucent lesion extending from mesial area of the left permanent first premolar to mesial area of the left permanent first premolar.

The three-dimensional CT sections showed the outline of the tumor (33x18x23 mm) expanding the bony alveolar cortical plate of the mandible (Figs. 3, 4). The lesion extended from the mesial root surface of the left permanent first premolar to the mesial root surface of the left permanent first molar. The vertical extension was from the gingival third of the mandibular premolar teeth to the basal bone of the mandible, with enveloping but no resorption of the roots of the teeth noted. Moderate buccal expansion was present, with thinning of the cortical plate, and the labial bony cortex was missing in the narrow area between premolars.

Within the radiolucency appeared a radiopaque structure consistent with the calcification. On the basis of the clinical and radiographic findings, the differential diagnoses included odontogenic keratocyst, central giant cell granuloma, aneurysmal bone cyst and ameloblastic fibroma.

Local anesthetic was administered and a needle aspiration of the lesion was performed; no cystic or hemorrhagic fluid was aspirated. An



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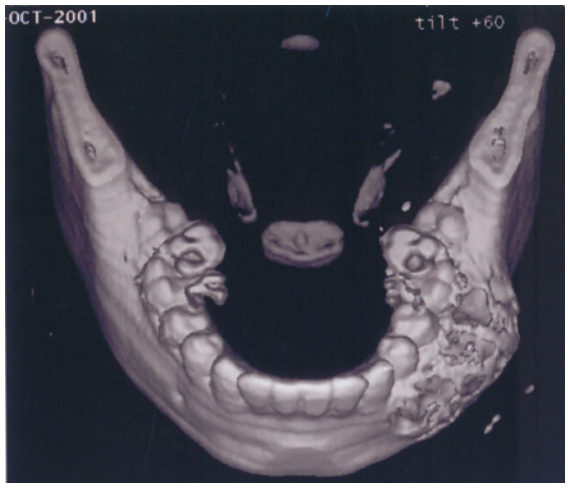


(4)

Fig. 3, 4: CAT scans show expansive radiolucency (arrows) that had partially eroded the buccal cortical plate of the left mandibular body.

incisonal biopsy of the lesion was performed. The cortex was perforated in a small area that fits an area between permanent premolars.

On entering the area, we found the lesion to be a friable, readily bleeding solid mass. Results of the biopsy were consistent with a diagnosis of CGCG. Laboratory values for serum calcium, phosphorus, alkaline phosphates, and parathyroid hormone were within normal limits, as were the blood cell count and differential.

Because of the possible mutilation (defect and deformities) that could arise as a result of surgery, the corticosteroid intralesional injection treatment was proposed to the parents of the patient, with the understanding that surgery was left as an option if the steroid treatment was not fully successful.

Treatment was started with a 5 ml injection of Kenocort-A (10 mg/ml) and lidocaine solution 2% with epinephrine 1:200,000 50% mixture by volume). The solution (4 ml Kenacorte-A and lidocaine) was administered with a 5 cm disposable syringe with a 1 in # 22 G needle and injected by clinically estimating the site where the cortical bone was more expanded and, therefore, the thinnest point. Once inside the lesion, the needle was redirected to inject small amounts into different areas. Identical injections were administered every seven days for a total of six injections.

At monthly intervals, oral and radiographic examinations were performed. Six months later, the patient reported that the lesion appeared to have decreased in size and panoramic radiograph showed increased opacification (Fig. 5).

One year later, radiographs revealed reossification of the area (Fig. 6). Apices of the associated teeth in this region had developed properly. Eighteen months later, CT scan showed complete resolution of the lesion (Figs. 7,8).

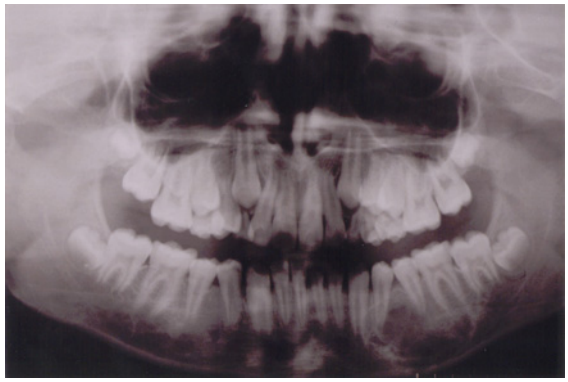


Fig. 5: Panoramic radiograph taken six months after the completion of treatment shows bone healing with increased opacification.

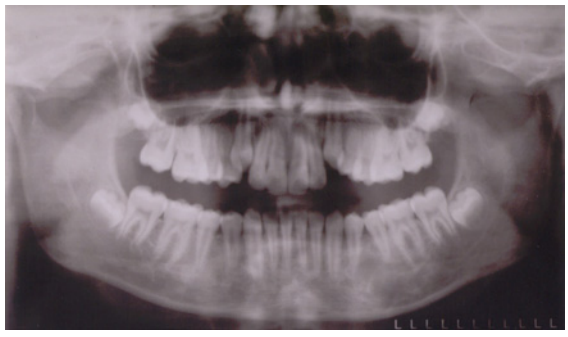
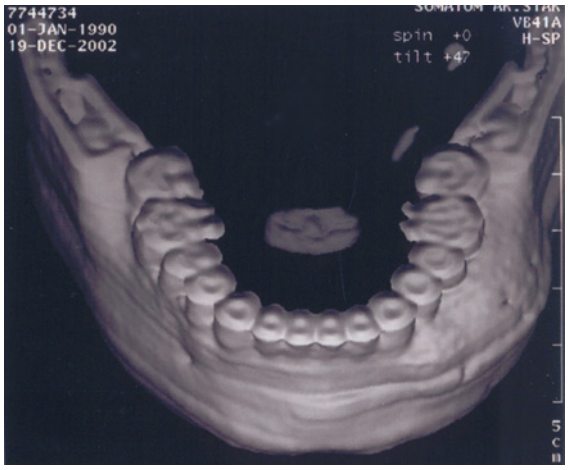


Fig. 6: Panoramic radiograph taken 12 months after the completion of treatment shows almost complete healing of the lesion due to new bone formation.



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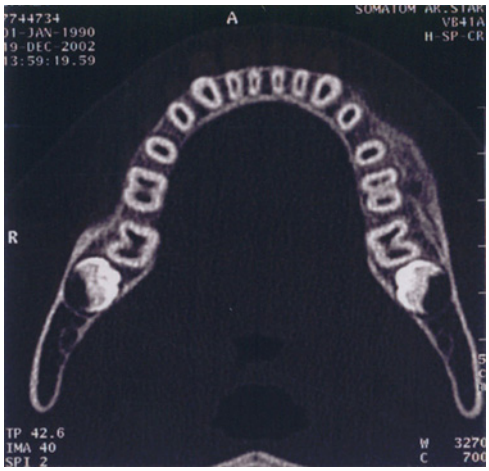

(8)

Fig. 7, 8: CAT scans taken 18 months after the initial infection show a resolution of the lesion with almost complete healing by reossification.

The patient was last seen three years after beginning treatment without evidence of recurrence or side effects associated with the steroid treatment.

Discussion

The conventional therapy of CGCG has been local curettage, and this has been associated with a high success rate and a low recurrence rate[16]. However, some studies have suggested recurrence rates as high as 70% after enucleation or curettage[12,18-21,24,28]. There are no available biologic markers to predict clinical behavior, and standard histologic techniques do not help the clinician determine prognosis[12,13,18,22]. Consequently, a number of different treatment options have been recommended, including aggressive curettage possibly coupled with adjunctive treatment such as liquid nitrogen cryotherapy, Carnoy's solution[3,5,14-15] and (gold standard for therapy en bloc resection with negative histologic margins[17], which result in a major facial deformity. This is of great concern, especially in children and young adults with developing dentition and jaws.

A number of alternative nonsurgical therapies have been described for the management of CGCG. Radiotherapy has not proven to be a statisfactory alternative, because irradiation of giant cells lesions may provoke malignant degradation[33]. Other alternative treatments include pharmacologic therapy with α-interferon or calcitonin, which are administrated via subcutaneous injection over several months[18,19,21,23-26]. Interferon-alpha has been used to treat patients with metastatic or locally advanced, non-resectable, life threatening giant cell lesions of long bones and jaws that have required frequent palliative treatments[19,21,28]. It has been used for these tumors based on the assumption that the lesions are vascular in nature[26]. Calcitonin treatment has also been advocated since it was first suggested in 1993[25]. The original rationale for the use of calcitonin was that the lesion is identical histologically to the brown tumor of hyperparathyroidism, and therefore an as-yet-unidentified parathormone-like hormone may induce this lesion[24,25]. Results of these treatments have been variable[18]. Calcitonin and interferon therapy are complicated owing to the great amount of discomfort, possible side effects and the relatively long duration of treatment, which is not well tolerated by some patients, especially children[3]. Intralesional corticosteroid injection is another alternative nonsurgical method. In 1988, Jacoway et al.[31] treated a case of CGCG with intralesional corticosteroid injections, which produced excellent results.

Jacoway et al.[31], indicating the microscopic similarities between sarcoidosis and CGCGs suggested that similar therapeutic regimens would be of value in treating both conditions[34-36]. This perception has been supported by reports showing that intralesional steroid injections into bone

cysts resulted in growth of fibrous connective tissue and reossification within three years[37].

Studies by Flanagan et al.[38] indicated that multinucleated giant cell granulomas of the jaws are osteoclasts, and that dexamethasone's inhibition of osteoclast-like cells in marrow cultures[31] suports the use of intralesional corticosteroid for CGCGs[27-30].

In addition, it has been shown that the avian osteoclasts and the osteoclast-like multinucleated giant cells of the giant cell tumor of bone respond in vitro to treatment with 17 β glucuronidase (17β-E2) by decreased bone resorption activity[32,39]. Osteoclasts accomplish bone resorption by secreting lysosomal proteases[13]. Kremer et al.[40] demonstrated steroid-dose-dependent decrease in the secreted level of these enzymes and an increase in the intracellular level. The initial decrease was observed between 4 and 18 hours after beginning treatment and a marked decrease was observed after 24 hours. In addition, it has been experimentally shown that steroids induce apoptosis in rat osteoclasts[41-42].

According to Carlos and Sedano[13], intralesional corticosteroid injections may cause cessation of bone resorption via the following two mechanisms:

1. Inhibition of the extracellular production of lysosomal proteases[43].

2. Steroidal apoptotic action on osteoclast-like cells[44-46].

Terry and Jacoway[32] published a protocol derived by Francis Howell for treatment of CGCGs of the jaws. This protocol consists of the intralesional injection of a mixture consisting of equal parts of triamcinolone actinide (Kenalog 10; 10 mg/ml) and local anesthetic (Marcaine 0.5% with epinephrine 1:200,000). The suggested dose is 2 ml/2 cm of radiolucency. The injections are given in multiple locations throughout the lesion in a weekly regimen for at least six weeks[31,32]. In the reported patient, the CGCG responded well to the same intralesional corticosteroid therapy protocol as in this study. Complete calcification occurred two years after beginning treatment. These responses were similar to previous reports of intralesional corticosteroid therapy in children.

Because of no side effect, short duration of treatment and no discomfort, this therapy is a very attractive option, particulary for children and young adults, versus other medical treatments[3,13,29]. Suppression of adrenal hormone production occurs when a sufficient amount of corticosteroid is administered daily; however, these patients receive a weekly low dose of steroid that does not after adrenal gland function[13].

Our case exhibited no side effects related to steroid treatment, which was well tolerated, as in the similar previous reports. In addition, a 2½-year-old girl with CGCG was also reported to have been similarly treated with excellent results and without side effects or recurrence[13].

Generally, the advantages of intralesional corticosteroid therapy in the treatment of selected cases of CGCGs include the following:

1. The less invasive nature of the procedure[29]. Because of the usually expansive growth of the CGCG, the thin bony cortex overlying the lesion may be easily perforated by a thin needle[27,29].

2. The probable lower cost to the patient and lower risk than other alternative treatments[3,27,29].

3. The option to treat the lesion surgically or by other alternative medical treatments in the future if necessary[24,32].

Before the dental professional can start administration of intralesional corticosteroid injections, confirmation of the lesion via biopsy is mandatory. Because the histologic features of CGCG of the jaw are indistinguishable from the brown tumors of hyperparathyroidism, the latter condition should be ruled out by performing the appropriate blood work-up before instituting treatment. In addition, the clinician must perform a careful pretreatment evaluation in all patients to prevent any untoward side effects to therapy. Patients with diabetes mellitus, peptic ulcer, infection and compromised immune systems would probably not benefit from this treatment for obvious reasons.

The treatment of CGCG with intralesional injections of steroids can be used as an alternative to surgery. The technique is simple and inexpensive and, most important, saves the vital structures, thus avoiding a large facial deformity.

We believe that sufficient evidence exists to warrant nonsurgical therapy as the first choice in managing giant-cell lesions in bone, especially in children.

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