Combination of Surgery Followed by Intralesional Steroids in Treatment of Aggressive Mandibular Giant Cell Granuloma: A Case Report

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Abstract

Central Giant Cell Granuloma (CGCG) is an intraosseous lesion consisting of cellular fibrous tissue that present clinically as an expansile lesion affecting the jaws, which may severely thin the cortices, including the inferior border of the mandible, displace teeth, resorb interradicular bone, and has a relatively high rate of reccurrence. The combination of surgical debulking followed by injection of intralesional corticosteroids is employed to treat a case of aggressive CGCG of the left posterior mandible in a 15 year old female as an alternative for radical surgery, which is the recommended treatment in conditions with such behaviour. The lesion was treated successfully by 2 courses of intralesional corticosteroids injections with a follow up of 3 years with no evidence of recurrence. We found that the use of intralesional corticosteroids following debulking to treat the presented aggressive variant of CGCG is a safe, minimally invasive and reversible option that spares patients the high morbidity associated with radical surgical treatment and can be repeated in large CGCG lesions if satisfactory regression was not evident following the primary treatment.

Keywords: Central Giant Cell Granuloma, mandible, intralesional steroids.

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Introduction

Central Giant Cell Granuloma (CGCG) is a unique lesion that almost exclusively affects the jaws. It was first described by Jaffe in 1953 as being a reparative process in response to trauma.[1] The World Health Organization defined CGCG as an intraosseous lesion consisting of cellular fibrous tissue containing multiple foci of hemorrhage, aggregations of multinucleated giant cells, and occasionally trabeculae of woven bone. [2] It is one of the giant cell lesions which include CGCG, peripheral giant cell granuloma, Cherubism, Aneurysmal bone cyst, Brown Tumors of hyperparathyroidism and Giant Cell Tumor.

The aetiology of this lesion is still unknown but seems to represent benign tumors of osteoclastic origin. The incidence was reported to be 1.1 per million, occurring more frequently in females than in males, with an age range from 10 to 25 years. The mandible is affected twice as often as the maxilla, with a tendency to involve the anterior region. The lesion occasionally crosses the midline. [3]

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In general, CGCG presents as a painless clinically expansile lesion, but rapid expansion may occasionally stretch the periosteum causing pain. Radiographically, this lesion classically presents as a multilocular radiolucent lesion (soap bubble appearance) but can have unilocular presentation. Those lesions range from well- to ill-defined radiolucencies that may severely thin the cortices, including the inferior border. It is also known to scallop the inferior border, displace teeth, and resorb interradicular bone. It may also resorb tooth roots to some degree. Recurrence rate is relatively high and the treatment of this lesion has been controversial with surgery being the gold standard, but shifting to simpler modalities is a major concern in the current treatment approach for benign lesions like CGCG. In this paper, we report the use of a combination of surgery followed by intralesional steroid injections to treat an aggressive CGCG of the posterior mandible.

Case Presentation

A 15-year-old female patient was referred to our maxillofacial clinic in Jordan University Hospital from the orthodontics department at the same hospital in March 2005, as the orthodontist noticed a swelling in the left retromolar area in the posterior mandible that was rapidly enlarging and associated with severe pain.

On examination, an expansile hard lesion in the posterior part of left mandible was found causing an extraoral swelling on the left side and an intra-oral lump with a diameter of 2 cm's in the left retromolar area. The lesion was painlful with red overlying mucosa. There was no parasthesia of lower lip, the lesion was not palsatile, and there was no cervical lymphadenopathy.

On the Orthopantomogram, a 6×3 cm ill-defined multilocular radiolucency was found in the left mandible that extends from the left lower second molar tooth up to the ascending ramus just below the sigmoid notch, the impacted lower left third molar tooth was anteriorly displaced and overlapping the second molar tooth without a radiographic evidence of root resorption (Figure 1) .

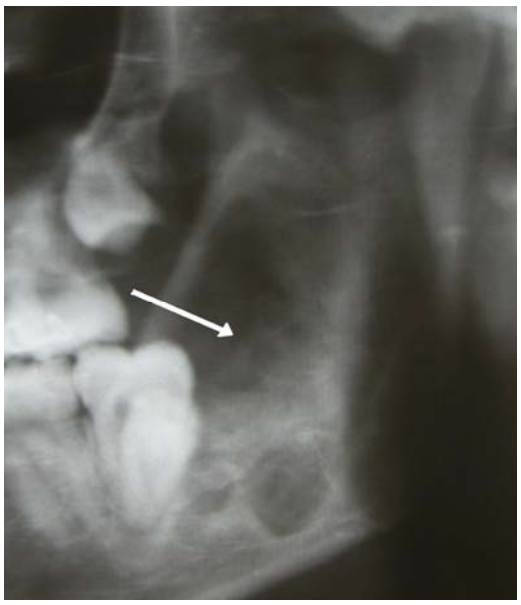

Figure (1): Part of an OPG showing a multilocular radiolucency of left posterior mandible with anterior displacement of the wisdom tooth.

The diagnostic protocol was discussed with the patient and family. A fine needle aspiration was done using a 22-gauge needle from 2 different sites, which yielded 4 mL of blood. Also, a facial C.T scan was performed which confirmed the presence of this multilocular lesion with both buccal and lingual expansion and cortical thinning (Figure 2) with a small buccal cortical perforation.

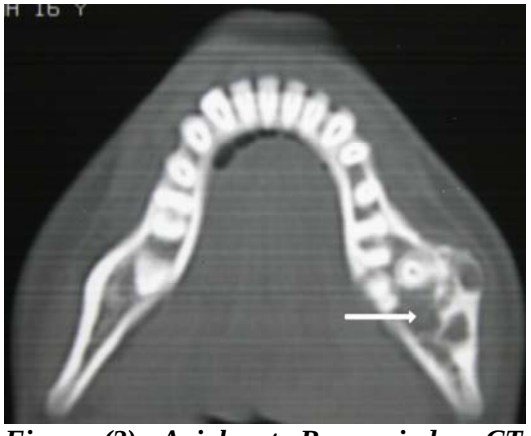

Figure (2): Axial cut, Bone window CT scan showing a multilocular radiolucency of posterior left mandible with buccal expansion, cortical thinning and anteriorly displaced lower left wisdom tooth.

The impacted lower left wisdom tooth was planned to be removed as part of the treatment plan. The surgical exposure of the lesion during the extraction procedure allowed for debulking of the lower part of the lesion, which was performed without taking an osseous safety margin to avoid sacrificing the inferior dental nerve. This part was sent as an incisional biopsy. Following buccal bone removal, the wisdom tooth was carefully removed to avoid injury to the inferior dental nerve. During the follow-up visit, patient examination revealed that inferior dental nerve function was intact with no neurosensory deficit

Intraoperatively, thinning and perforation of the lingual buccal cortises was found. The lesion was considered to be aggressive according to Chuong et al. [4] classification with a large lesion size of 6x3 cm, severe pain, evidence of buccal and lingual cortical bone perforation and teeth displacement. Blood testing was normal for Calcium, Phosphorous and PTH, thus hyperparathyroidism was excluded.

Histopathological examination of Haematoxylin and Eosin (H&E) stained sections of the biopsied lesion showed the typical histological appearance of central giant cell granulomas (Figure 3).

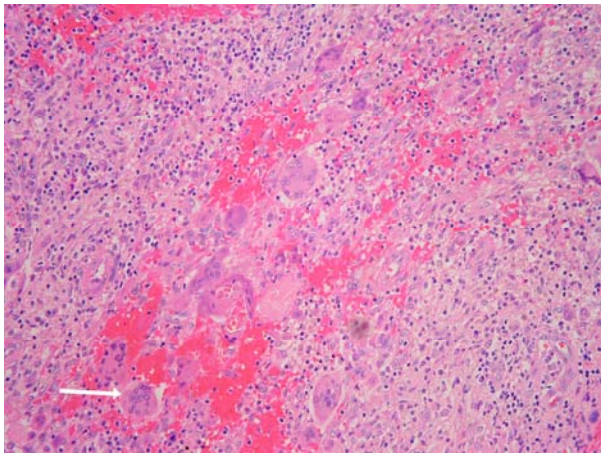

Figure (3): H&E stained section at x20 magnification showing the typical histopathological appearance of central giant cell granuloma. Note the aggregation of giant cells around a blood vessel and the abundance of extravasated erythrocytes (arrow).

Large numbers of multinucleate giant cells containing 5-20 nuclei were found within a vascular fibrous tissue stroma. The stroma showed many spindle shaped small cells, in addition to fibroblasts and endothelial cells.

The giant cells were mainly found in focal aggregates and were separated by vast areas of fibrous stroma. Many giant cells were at close proximity to blood vessels.

Extravasated erythrocytes were also seen in the lesion while osteoid and bony trabeculae were lacking.

Treatment options were explained to the patient. The conventional surgical excision of the lesion that involves a large part of the mandibular ramus and its posterior border with possibly scarifying the inferior dental nerve was abandoned in favor of the conservative medical treatment approach. The patient was started on a regimen of intralesional steroids as described by Terry and Jacoway,[5] this protocol consists of intralesional injection of a mixture consisting of equal parts of Triamcinolone Acetinide and Marcain 0.5% with epinephrine 1/200,000, the dose used was 2 ml/ 2cm of radiolucency. The injections were given in multiple locations throughout the lesion once a week for 6 weeks. The patient was followed up during the next 6 months. At that point, partial regression of the lesion was noticed but no complete resolution. We elected to start the patient on another 6 weeks course, after which the patient was followed closely both clinically and radiographically for 3 years. The lesion responded to treatment with a reminant 1×0.5 cm lesion which was stable radiographically and considered to be a scar tissue (Figure 4, 5); a finding that was described by Terry and Jacoway,[5] who had some residual radiolucencies after the steroid treatment. Those radiolucencies were surgically curetted, and the histology revealed "moderately collagenized fibrous connective tissue containing no multinucleated giant cells."

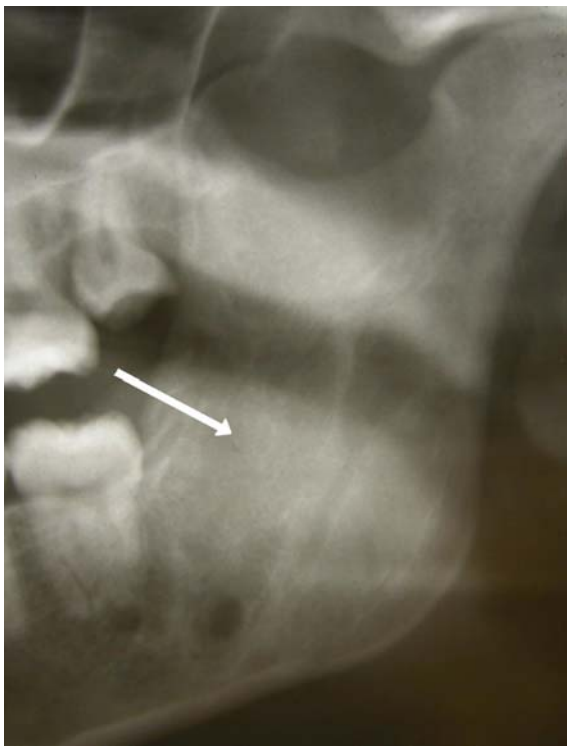

Figure (4): Part of an OPG showing adequate calcification at the site of the lesion taken 3 years post treatment by intralesional steroids with a remnant small radiolucency that was persistent and considered to be a scar tissue.

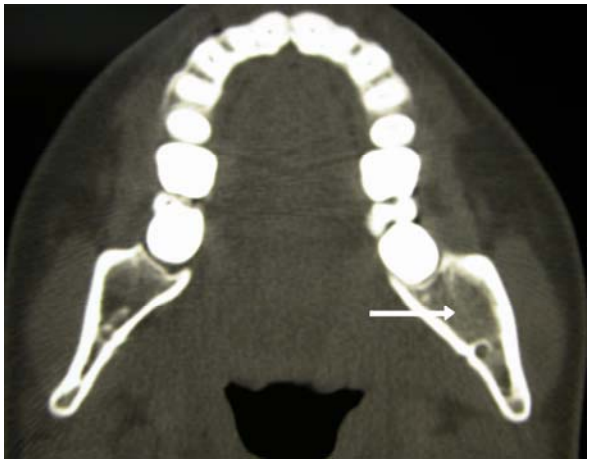

Figure (5): Axial cut, Bone window CT scan taken 3 years post-treatment by intralesional steroids, showing marked regression and good calcification at the site of the lesion with no cortical thinning.

Discussion

Several modalities have been described in management of CGCG, but the most common treatment is a thorough curettage of the lesion and its bony cavity by peripheral osteoctomy.[3] The high recurrence associated with simple curettage may reach 72%,[4] which renders this modality inadequate, particularly in larger lesions and those that involve a significant number of teeth.

Multiple recurrent lesions or lesions with significant destructive bone resorption to the point of near pathologic fracture may require resection. A recurrence rate of 6% or less have been reported in association with surgical resection (including 0.5-1 cm safety margin).[7] Such an extensive radical surgical therapy, however effective in these aggressive lesions, resulted inevitably in the loss of teeth and tooth germs and in disturbances in the function of the inferior alveolar nerve. It is therefore questionable whether this form of therapy should be considered in the treatment of a benign lesion such as CGCG.[3] Thus, seeking a simpler and a pharmacological alternative increased in the last few decades.

Radiotherapy was not proven to be a satisfactory alternative, because irradiation of giant cells lesions may provoke malignant degradation. Calcitonin therapy was another non-surgical option of treatment firstly reported by Harris [8] in a study on 4 patients, where a total remission of the lesions was obtained. Moreover, it has been demonstrated that giant cells express calcitonin receptors, [9] it was therefore assumed that giant cells –which are osteoclasts- are directly inhibited in their function by calcitonin. However, the therapeutic response to calcitonin is variable, and is influenced by the mode of administration, which can be in the form of subcutaneous injections or as a nasal spray.[3]

Interferon (IFN), which is an antiviral and anti-angiogenic agent that is used in a variety of conditions, was used in the treatment of CGCG. The rationale to use it was related to the presumed vascular nature of CGCG.[10]

IFN administered as a mono-therapy for aggressive CGCG seems capable of terminating the rapid growth of lesions and consolidating or even diminishing their size, but it is probably still necessary to apply additional surgery to eliminate the lesion. The reason that total remission of the lesions cannot be achieved, in spite of the high doses of IFN, is probably because IFN has no direct inhibiting effect on the proliferating tumor cells,[3] since immunohistochemical staining of CGCG shows that the mononuclear tumor cells are fibroblasts, not endothelial cells. [11]

In 1988, Jacoway et al. [12] first reported the use of Corticosteroids in the treatment of CGCG, and in 1994, Terry and Jacoway[5] presented 4 patients treated with steroids with a success rate of 75%. Marx and Stern[6] reported that 65% of the lesions will resolve completely, and 35% become more aggressive or don't respond at all to treatment by Corticosteroids. The Mode of action is not fully understood, it was shown that dexamethasone in vitro, stimulates the proliferation and differentiation of osteoclast precursors, but also inhibits lacunar resorption by mature osteoclasts isolated from giant cells tumors of the bone. [13] it is hypothesized that the extracellular production of bone resorption mediating lysosomal proteases by the giant cells is inhibited and steroids induce apoptosis of osteoclast like cells.[14] The expression of glucocorticoid receptors has been evaluated on 41 specimens of CGCG, all 41 CGCG showed positive staining for glucocorticoid receptors but with a variable intensity. [15]

Marx and Stern [6] stated that most cases of central giant cell tumor are initially treated with the series of intralesional corticosteroid injections. The potential value of resolving these tumors without invasive surgery is compelling. Because the treatment sequence is associated with minimal morbidity and does not preclude further therapy should it be unsuccessful, it is a reasonable first choice. If the tumor fails to respond or accelerate growth results, a population of altered osteoclasts that do not have cell membrane receptors for corticosteroids is implied. Such tumors are then treated with either curettage or a resection with 0.5 to 1.0 cm margins if they are sufficiently large.

In our case, the lesion was found to be of the aggressive type according to Chuong et al. [4] classification, with a diameter of 50 mm, evidence of buccal and lingual cortical bone perforation severe pain, and tooth displacement (common findings in aggressive CGCG lesions). The use of 2 courses of intralesional corticosteroid alone to treat this patient was successful and no recurrences were found for 3 years after the completion of treatment, recurrence in such lesions is usually reported 12-18 months post treatment. [6]

No side effects related to steroid treatment were observed in our patient, as was shown in similar previous reports. Suppression of adrenal hormone production occurs when a sufficient amount of corticosteroid is administered daily; however, these patients receive a weekly low dose that doesn't affect adrenal gland function[16]. Our patient was also saved from the morbidity of surgery that can lead to profound esthetic and functional impairment. No adverse effect of treatment was evident on the inferior alveolar nerve.

Although there are no controlled studies published on this therapy, there are advantages for the intralesional corticosteroid therapy in the treatment of CGCG that include the following:

1. The less invasive nature of the procedure. Because of the usually expansive growth of the CGCG, the thin bony cortex overlying the lesion may be easily perforated by a thin needle.
2. The probable lower cost to the patient and lower risk than other alternative treatments. [7]
3. The reversibility and the option to treat the lesion surgically or by other alternative medical treatments in the future if necessary.

Conclusion

We recommend the use of a combination of surgical debulking and intralesional corticosteroid for CGCG treatment as a first

choice because it is safe, minimally invasive, reversible option with a high success rate.

The 6-week course of intralesional corticosteroid can be repeated in large CGCG lesions if satisfactory regression was not evident following the primary treatment.

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معالجة ورم حبيبي مركزي للخلايا العرطلية في الجزء الخلفي من الفك السفلي باستخدام الجراحة والحقن الستيروئدية ضمن الآفة

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الملخص

الورم الحبيبي المركزي للخلايا العرطلية هو عبارة عن آفة داخل عظم الفك تتكون من نسيج ليفي، حيث تظهرسريريا على شكل آفة موسعة للفكين، التي قد تسبب ترققاً شديداً في القشرة قد يتضمن الحافة السفلية للفك السفلي، كما قد تسبب تزحزحاً في الأسنان المجاورة وامتصاصاً في العظم البين الجدري. ويعتبر معدل الانتكاس لهذه الآفة مرتفعاً.

تم استخدام العلاج بالجراحة لتصغير الحجم، ثم بالحقن الستيروئدية ضمن الآفة؛ وذلك لعلاج ورم حبيبي مركزي للخلايا العرطلية من النوع العدواني، الذي أصاب الجزء الخلفي من الجهة اليسرى للفك السفلي لفتاة تبلغ الخامسة عشرة عاما كبديل للجراحة الجذرية الموصى بها في الحالات المماثلة من ناحية السلوك. وقد تمت المعالجة بوساطة دورتين من الحقن الستيروئدية ضمن الآفة مع متابعة الحالة مدّة ثلاث سنوات من غير حدوث أي انتكاس، حيث وجد أن علاج هذه الآفة ذات السلوك العدواني بوساطة الحقن الستيروئدية ضمن الآفة بعد تصغير الحجم هي طريقة آمنة وفعالة ويمكن الاعتماد عليها، مما يوفر على المريض المضاعفات الناتجة عن العلاجات الجراحية التقليدية، كذلك يمكن معاودة إعطاء الحقن في الآفات الكبيرة إذا لم يكن انحسار الآفة كاملاً بعد العلاج الأولي.

الكلمات الدالة: الورم الحبيبي المركزي للخلايا العرطلية، الفك السفلي، الحقن الستيروئدية.