

Central Giant Cell Granuloma: Case Report with Review of Literature

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Abstract:

Central Giant Cell Granuloma is a non-neoplastic intraosseous lesion and constitutes about 10% of benign jawbone lesions. Etiology of the lesion is not well defined. Approximately one-third of CGCG exhibit local aggressive behaviour with bone destruction and a tendency to recur. Diagnosis of CGCG poses a diagnostic challenge for oral physician as it may mimic many other solitary cysts like radiolucencies which may or may not be contacting teeth. A case of a 26yr old female with CGCG in mandible is presented along with review of literature.

Keywords: Giant Cell Lesion, Nonodontogenic Tumours of Jaws, Central Giant Cell Granuloma, Giant Cell Tumour, Calcitonin, Imatinib, Interferon-Alpha.

Introduction

Central giant cell granuloma (CGCG) is an uncommon, benign proliferative bony lesion. Its etiology is not well defined and its biological behavior is also poorly understood.¹ CGCG is usually present in the jaw bones i.e. mandible and maxilla, in contrast to other giant cell tumors of bone.² The World Health Organization has defined it 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”.³

In 1953, Jaffe described this lesion as a “giant-cell reparative granuloma”. The term 'reparative' has been abandoned due to the differentiation of central giant cell lesions between aggressive and non-aggressive lesions.⁴ Chuong et al defined aggressive giant

cell lesions as exhibiting size greater than 5 cm as well as rapid growth, tooth displacement, root resorption, cortical bone thinning, perforation or recurrence after curettage, equal to or greater than 5cm and/or that recurred after curettage. Nowadays, it is classified as “central giant cell granuloma” or “central giant cell lesion”.^{3,5}

Approximately 70% of CGCG lesions have the biological behaviour of a non-aggressive, asymptomatic, slow-growing lesion, whereas the remaining 30% show an aggressive and increasingly destructive behaviour. The aggressive biological behaviour of some CGCG is reminiscent of that of giant cell tumour of bones (GCTB), and it has been proposed that CGCG and GCTB belong to the same spectrum of lesions.⁶

Case Report

A 26 year old female patient visited

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Department of Oral Medicine & Radiology with a chief complaint of pain & swelling in the right lower back tooth region since two yrs. Patient gave history of extraction with respect to mandibular first molar five months back following which she developed swelling which gradually increased in size & subsided partially on medication.

Extra oral examination revealed a localized swelling on the right side of mandible, approximately [2 x 2] cm in size, hard & tender on palpation.

On intra oral examination a diffuse swelling pink in color was observed in the vestibular aspect extending from mesial aspect of right lower second premolar to distal aspect of right Lower second molar. Swelling was tender on palpation without any associated pus or blood discharge.(Fig. 1)



Fig. 1: Diffuse swelling pink in color at vestibular area w.r.t 46

Based on the history & clinical features a provisional diagnosis of residual cyst was made in relation to missing mandibular first molar.

IOPA & Panoramic radiograph revealed a well-defined tear drop shaped unilocular radiolucency between second premolar and second molar surrounded with a sclerotic border. Slight displacement of roots with loss of lamina dura on the side involved of both teeth was seen along with resorption of the

distal aspect of root of second premolar (Fig. 2 & 3).

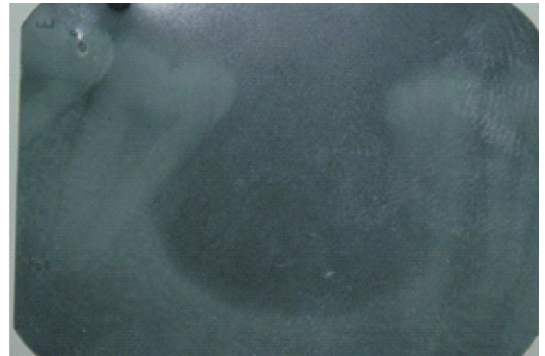


Fig. 2: Intra Oral Periapical Radiograph

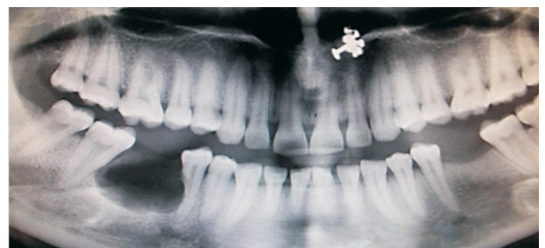


Fig. 3: Orthopantomogram

IOPA & OPG reveals tear drop shaped unilocular radiolucency with sclerotic border & resorption at distal aspect of root of 45

Fine needle Aspiration yielded blood. Routine blood counts revealed all parameters within normal limits.

The lesion was surgically removed under local anaesthesia and the specimen was sent for histopathological examination which revealed loss of fibrous connective tissue stroma with plump fibroblast and multinucleated giant cells of varying size containing upto 20 nuclei. Scattered hemosiderin pigments & extravasated RBCs were also seen. Based on the histopathologic examination a diagnosis of central giant cell granuloma was made.

Patient was recalled for monthly follow up (Fig. 4). Radiopacity at the lesion site suggested adequate bone healing. Healing was observed at the end of sixth months and there was no sign of recurrence (Fig. 5 & 6).



Fig. 4: Postoperative image after removal of 45



Fig. 5 : 1st month follow up



Fig. 6 : 6th month follow up

Discussion

CGCG account for about 10% of all benign lesions of the jawbones (Waldron, 1995).⁷ All age groups can be affected, but most cases are observed in patients below the age of 30 years.⁷ Women are more affected than men (F/M=2.4:1).⁸ In the studies conducted by Stavropoulos and Katz J no correlation was found between the size of the lesions, their

location and the appearance in different age groups, although the size of the lesion was largest in the younger age group (<30 years).⁹ This may be explained by the increased metabolic rate and associated hormonal effects in adolescents. However, scientific evidence to support this hypothesis is not currently available. Lesions occur commonly in the anterior portions of the jaws and the mandibular lesions frequently cross the midline; however in our case lesion was found posterior to molars.¹⁰

Clinical differential diagnosis include post-extraction sockets, residual cysts, traumatic bone cysts, lingual mandibular bone defects, odontogenic keratocysts, primordial cysts, ameloblastomas, primary and secondary hyperparathyroidism, early cement-ossifying fibromas.

The exact process behind pathogenesis of CGCG remains unknown. While the giant cell remains to be the most prominent feature of these lesions, it is actually the mononuclear spindle cell which is the proliferating cell. This is indicated by the expression of the cell cycle protein Ki-67 in CGCGs. It is believed that this spindle cell recruits monocytes from the vascular system and induces them to differentiate into osteoclastic giant cells through release of cytokines. It has been proposed that this spindle cell takes its origin from the mesenchyme of marrow and an epigenetic event signals them to release cytokines and finally the osteoclastic giant cell causes bone resorption making the hallmark feature of CGCG.^{11,12}

Another theory is the vascular hypothesis that suggests that CGCG belongs to the spectrum of mesenchymal proliferative vascular primary jaw lesions. Perhaps the most widely held view is that the initial CGCG is an

endosteal hemorrhage.¹³ El-Labban in the year 1997 studied CGCG and observed that majority of vessels showed intravascular fibrin thrombi and endothelial cell damage with gaps in the cell walls. She also noted that one of the gaps in a vessel had been sealed by a giant cell. The author suggested that the presence of the giant cell closed the gap and stopped haemorrhage and the main purpose for the presence of the stromal cells is the repair not only of the hematoma but also of its contributing vessels.¹⁴

Choung et al. (1986) and Ficarra et al. (1987) defined the lesion into two types, based upon its clinical and radiographic features-¹⁵

1. Non aggressive lesions make up most cases, exhibit few or no symptoms, demonstrate slow growth and do not show cortical perforation or root resorption of teeth involved in the lesion.
2. Aggressive lesions are characterized by pain, rapid growth, cortical perforation, and root resorption. They show a marked tendency to recur after treatment, compared with the nonaggressive types.

In our case, patient had pain, swelling, root resorption, suggestive of aggressive lesion with a tendency to recur and therefore patient was kept on regular follow ups for a period of 6 months.

CGCG occur initially as a unilocular, cystlike radiolucency, but as it grows larger, it frequently develops an architecture that causes a soap-bubble type of multilocular radiolucency.¹⁶ An imaging feature characteristic associated with CGCG, is the presence of subtle granular bone pattern at the periphery of the expanded bone.¹⁷

Generally, if the lesion is located anterior to the permanent molars and possibly crossing

midline, with a multilocular radiographic pattern with the patient under 30 years of age, a provisional diagnosis of CGCG can be considered.¹⁸

Kaffe et al. (1996) in their study on 80 cases found that 51% of the lesions were multilocular, 44% were unilocular, 5% were not loculated, and 68% of all multilocular lesions were seen in Mandible.¹⁹ They also established a statistically significant correlation between the locularity of lesions and their increasing size. Root resorption was observed in 24% male patients and only 6% of female patients.¹⁹

The radiological differential diagnosis can include Ameloblastoma, odontogenic keratocyst and Aneurysmal Bone Cyst, and sometimes also odontogenic myxoma and central haemangioma of bone (the latter two often exhibit more of a honey-combed appearance though). For patients in the young age range for CGCG, ameloblastic fibroma, cemento ossifying fibroma (early stages), and adenomatoid odontogenic tumor.¹⁸

Histologically, CGCG consist of loosely arranged spindle-shaped stromal cells in a fibrous stroma, hemosiderin deposits, macrophages and varying amounts of inflammatory cells.⁷ The hallmark of CGCG is the multinucleated giant cells that are located especially in the hemorrhagic areas. Metaplastic bone formation is also seen, and mitoses might be abundant.⁶

Various conditions 'mimic' the histological presentation of CGCG including peripheral giant cell granuloma, Giant cell tumor, Brown Tumour of hyperparathyroidism, Cherubism, Aneurysmal bone cyst and Fibrous dysplasia.¹⁸

The management of CGCG can include

conventional surgery with or without medical adjunctive treatment or resection en-bloc for the aggressive variant. Radical surgery leads to more aesthetic and functional faults and requires anatomical reconstruction and rehabilitation, which in most cases has a poor functional outcome.¹⁹ A number of studies have reported recurrence rates ranging from 10% to 50%.²⁰ Although most common therapy is surgical curettage but high recurrence rate has raised concern and led to a search for other treatment options.^{21,22}

Jacoway et al were the first to describe the application of intralesional steroids.²³ Intralesional steroid injections into bone cysts result in growth of fibrous connective tissue and reossification by inhibition of lysosomal proteases and the apoptosis in osteoclasts.²⁴ However, the application of Intralesional steroids has controversial findings.²¹ Patients suffering from diabetes, peptic ulcers, infections and immune-compromised and pregnant individuals are not suitable for intralesional treatment. The use of calcitonin was proposed in 1993 by Harris, based on the similarity that exists between CGCG and the tumours of the hyperparathyroidism at histological level.²⁵ Although the calcitonin's mechanism of action remains unclear, it is suggested that it has a direct inhibitory effect of the osseous reabsorption through the osteoclasts, increasing the absorption of calcium of the bones and favouring the osseous cicatrization. Reported disadvantages of calcitonin include the long term treatment with the daily injections, high costs and adverse effects.²² Interferon alpha is known for its inhibition of the angiogenesis in the tumours and its application has recently been instituted in these types of lesions.²⁶ Imatinib was recently suggested as a treatment option

for CGCG. Imatinib is a protein tyrosine kinase inhibitor that specifically inhibits the growth of cells of the monocyte macrophage lineage by abrogating signal transduction through c-fms.²²

Conclusion

The relatively high frequency of CGCGs in the population makes it important for clinicians to understand their clinic-radiologic presentation and clinical behaviour. Classifying these lesions as 'aggressive' or 'nonaggressive' can help in choosing the most appropriate treatment. We suggest that the 'nonaggressive' counterparts can be managed effectively with conservative surgical approach. However, in cases of 'aggressive' lesions seen more often in a younger population, instead of more morbid surgical procedures, an alternative or adjuvant therapy can be relied upon.

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