

Nonaggressive Central Giant Cell Granuloma: A Case Report.

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Research Article

Received: 08/10/2013

Revised: 22/10/2013

Accepted: 05/11/2013

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Keywords: Central giant cell granuloma, benign jaw tumor, molar, recurrent pericoronitis, Multinucleated giant cells.

ABSTRACT

Central giant cell granuloma (CGCG) is a benign intraosseous lesion that occurs in long bones. It is an uncommon tumor in jaws, its etiology and pathogenesis is unknown. It affects females more often than males, in a 2:1 ratio and is seen most frequently under the age of 30 years. CGCGs can be aggressive or non-aggressive. The reported case is non-aggressive central giant cell granuloma of posterior mandible. The affected patient was a 25 year old Iraqi male who reported to us with recurrent pericoronitis in relation to lower left third molar. The low incidence of the lesion in Arab countries makes it a rare case report.

Introduction

Central giant cell granuloma (CGCG) is a benign intraosseous lesion that occurs in long bones. It is an uncommon tumor in jaws, its etiology and pathogenesis is unknown. It was described first by Jaffe H L as 'Central Giant Cell Reparative Granuloma' in the year 1953 [1]. Females are more commonly affected than males, in a 2:1 ratio and the affected age group is under 30 years. CGCGs can be aggressive or non-aggressive. The nonaggressive form might present as an asymptomatic swelling or might get discovered accidentally during routine radiological investigations. Whereas pain, rapid growth, cortical perforation and root resorption is usually associated with aggressive form of CGCG [2]. Co-existence of central giant cell lesions in patients with both neurofibromatosis (type1) and Noonan-like syndrome have been reported [3].

CASE REPORT

A 25 years old male of Iraqi nationality visiting Gulf dental centre in Ajman, UAE, complained of recurrent pericoronitis in relation to lower left third molar from past 1 year duration (Fig 1). The history revealed that there was pus oozing from beneath the operculum on applying gentle pressure. There was no symptom of pain in any other teeth in the dentition.

On extra oral examination, there was no remarkable facial asymmetry or swelling. Palpation of neck revealed spasm in the sternocleidomastoid muscle on the left side. Mild pain over the left lower border of the mandible and a mild hard swelling in the inner surface of the mandible near the angle were also noted upon palpation. There was sub mandibular lymph node enlargement. Mouth opening was normal.

Intra oral examination revealed good oral hygiene. The left second and third molars showed negative response to vitality test. On applying gentle pressure pus oozed from beneath the operculum of third molar. Panoramic radiograph was taken to examine lower left quadrant.

O.P.G. revealed a well defined, oval, radiolucent, lesion with smooth sclerotic border extending from the tips of second and third molar's root apices to the lower border of the mandible. Radiolucency measured 2X1.5cm in dimension, extending mesially 3mm below the distal root of the lower left first molar (Fig 2).

Figure 1: A 25 years old male visiting our dental centre in Ajman, UAE, complained of recurrent pericoronitis in relation to lower left third molar from past 1 year duration.



Figure 2: O.P.G. revealed a well defined, oval, radiolucent, lesion with smooth sclerotic border extending from the tips of second and third molar's root apices to the lower border of the mandible.



The patient was referred to CT scan by oral surgeon, which revealed an oval, unilocular, osteolytic lesion with no calcifications within and measuring 25X14X10 mm in dimensions with sclerotic borders (Fig 3, 4). Cortical thinning inferiorly and cortical breaching inferio- medially was evident. Tooth erosion was absent and there was no evident soft tissue mass associated. Other investigations done to rule out hyper parathyroid tumor or any chronic inflammation were:

- Serum Calcium was 10.5 mg/dL, normal reference is (8.5 - 10.3 mg/dL).
- Alkaline phosphatase was 84 IU/L, normal reference is (<150 IU/L).
- C-reactive protein was 0.3 mg/L, normal reference is (< 0.8 mg/L).

Based on the interpretation of lab values and CT scan, the surgeon decided to extract the third molar which was fully erupted but non vital. Extraction was done, and to get access to the lesion, extra bone removal was done, and biopsy was taken to differentiate from other jaw lesions like OKC, Ameloblastoma, ameloblastic fibroma etc.

Histopathological examination of the tissue under scanner and higher power showed, numerous multinucleated giant cells dispersed throughout the lesion (Fig 5). Connective tissue was fibro vascular. The inflammatory cell infiltrate was chronic and areas of necrosis were seen within the fibro-vascular connective tissue. Area of hemorrhage and extravasated RBCs were also seen (Fig 6). The clinical, radiographic and histopathological picture was consistent with the diagnosis of Central giant cell granuloma.

One week after the extraction, sutures were removed. On examination the tissue was found to be healed uneventfully. A follow up was done after an interval of 2 months and 6 months. Clinically there were no signs or symptoms. The OPG taken after an interval of 2 months showed a decrease in the size of the lesion and increase in the opacity of the lesion. Radiograph (Fig 7) taken after 6 months showed a further decrease in the size of the lesion and increase in the opacity of the lesion. Patient was advised to report for a radiographic follow up every 6 months.

Figure 3, Figure 4: CT scan revealed an oval, unilocular, osteolytic lesion with no calcifications within and measuring 25X14X10 mm in dimensions with sclerotic borders. Cortical thinning inferiorly and cortical breaching inferior- medially was evident. Tooth erosion was absent and there was no evident soft tissue mass associated.

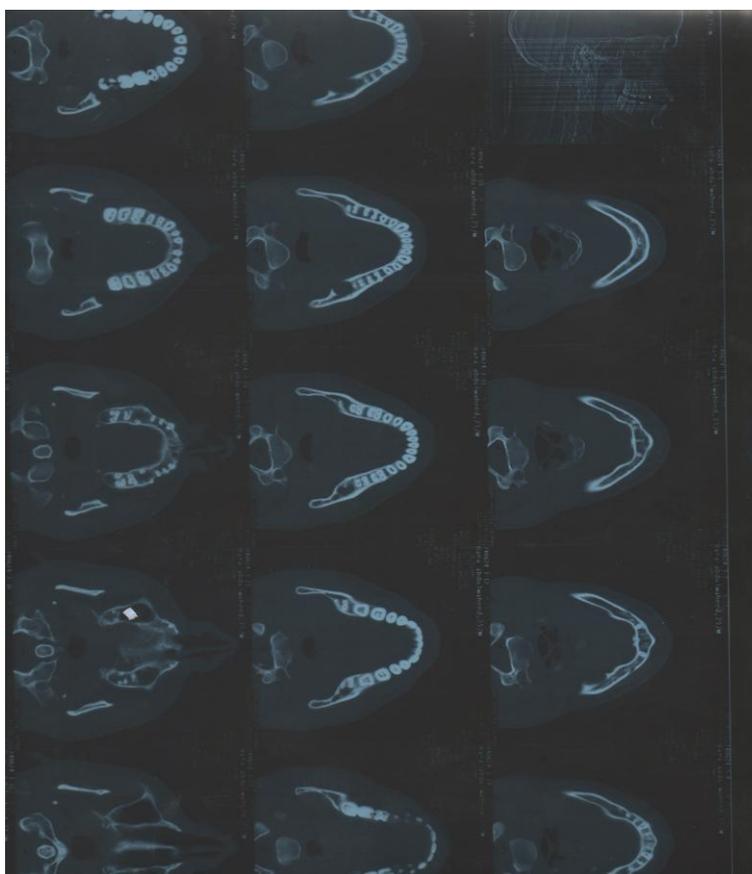
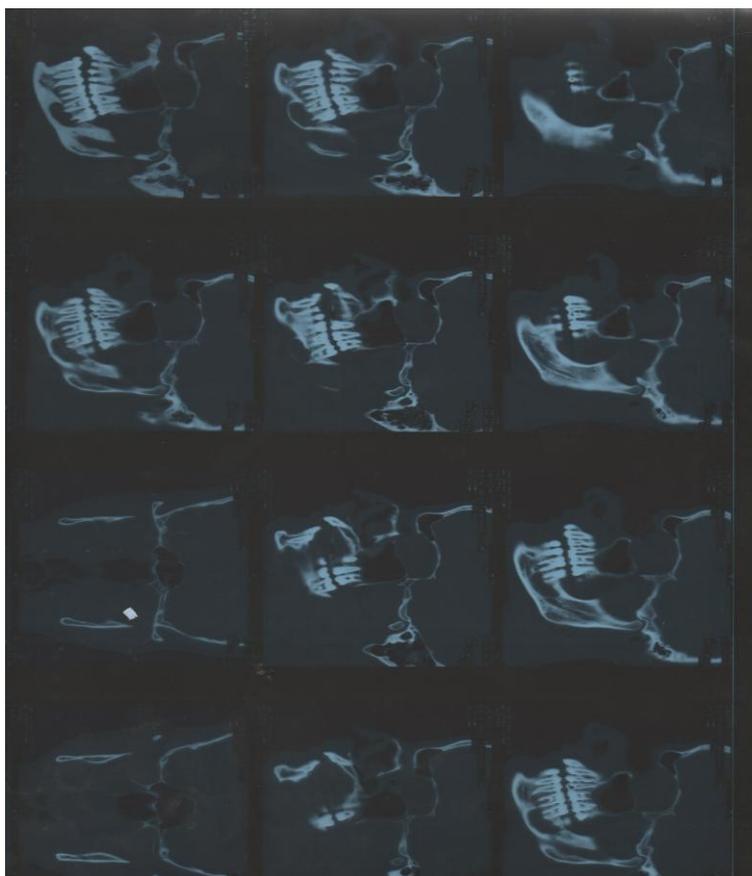


Figure 5: Numerous multinucleated giant cells dispersed throughout the lesion. Area of hemorrhage and extravasated RBCs seen (20X).

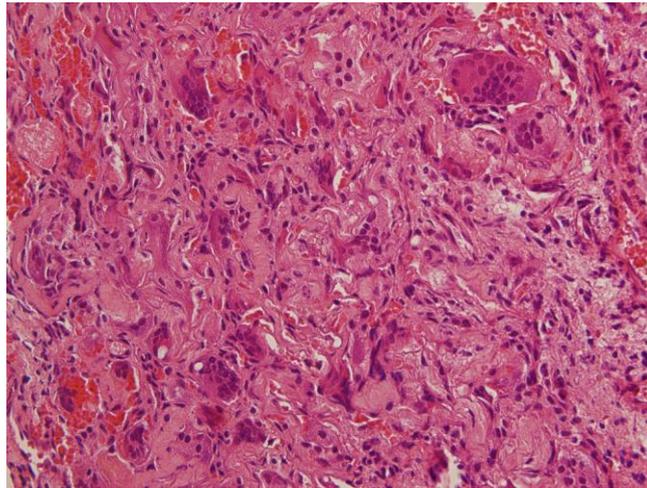


Figure 6: Chronic inflammatory cell infiltrate, multinucleated giant cells and areas of necrosis seen within the fibro-vascular connective tissue (scanner view).

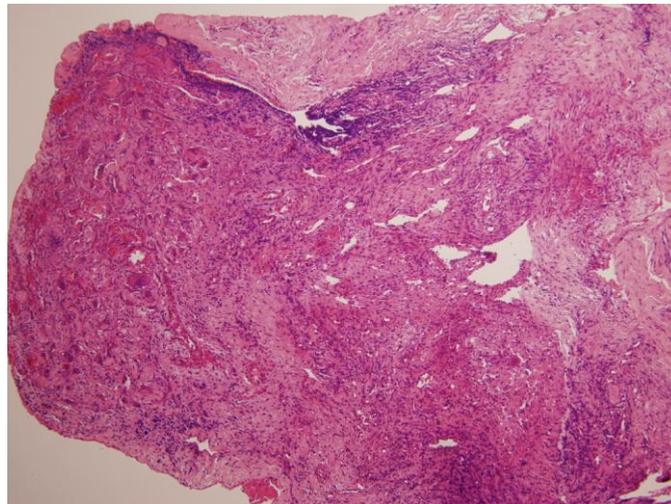


Figure 7: Radiograph taken after 6 months showed a further decrease in the size of the lesion and increase in the opacity of the lesion and the tooth socket.



DISCUSSION

Giant cell granulomas (GCGs) of the jaws arise either centrally in the bone (central GCG) or peripherally from either periodontal ligament or mucoperiosteum (peripheral GCG). Histologically, both central and peripheral

variants of giant cell granuloma are characterized by the presence of numerous multinucleated giant cells (MGCs) in a prominent fibrous stroma [2].

The etiology and pathogenesis of CGCG of jawbones has not been established clearly. However, it has been suggested that it could result as a reactive granulomatous response to local changes in the blood flow to the bone or to previous trauma [4].

CGCG are classified into two types, depending on clinical and radiographic features. The first type of lesion is Non-aggressive type which is slow growing, does not show cortical perforation or root resorption in affected teeth. And it often shows new bone formation. These usually do not recur after treatment. The findings of the case presented in the study correlates with the Non-aggressive type of CGCG and what makes it rare is the low incidence in the Arab countries. The second type is an Aggressive type which grows quickly, shows pain, cortical perforation, and root resorption [2]. Over 60% of the cases occurred before the age of 20 years and have a tendency to recur [5].

The radiological appearance of CGCG is variable. Central giant cell granuloma is essentially a destructive lesion, producing a radiolucent area with either a relatively smooth or a ragged border, and sometimes showing faint trabeculae. The lesion commonly presents as a solitary radiolucency with a multilocular appearance or less commonly, a unilocular appearance and must be differentiated from other jaw lesions like OKC, Ameloblastoma etc [6].

Definite loculations are often present, particularly in larger lesions. It could be well- or ill-defined with variable expansion and destruction of the cortical plate. In slowly growing lesion, borders are usually well defined. It is more common in the anterior than the posterior jaws, often crossing the midline. The mandible is more commonly affected than the maxilla [7]. Displacement of the teeth by the lesion is seen with some frequency. Our case correlates with this finding, though Root and lamina dura resorption, and tooth displacement was not observed. The appearance of the giant cell granuloma is not pathognomic and may be confused with that of many other lesions of the jaw, both neoplastic and non-neoplastic like Ameloblastoma, Odontogenic myxoma, Ameloblastic fibroma, Ossifying fibroma, Hyper parathyroidism, and Cherubism. Since clinical and radiological features are not specific, the final diagnosis eventually rests on histopathology [8].

CGCG is made up of a loose fibrillar connective tissue stroma with many interspersed proliferating fibroblasts and small capillaries. The collagen fibres are not usually collected in bundles; however groups of fibres will often present a whorled appearance. Multinucleated giant cells are prominent throughout connective tissue, but not necessarily abundant. These giant cells vary in size from case to case and may contain only a few or several dozen nuclei. In addition, there are usually numerous foci of old, extravasated blood and associated hemosiderin pigment, some of it phagocytized by macrophages. Foci of new trabeculae of osteoid or bone also are often seen, particularly around the periphery of the lesion.

There is a debate whether fibroblast origin or from monocyte/macrophages. Recent study by Itonaga et al. indicate that the giant cells in CGCG of the jaw are osteoclast like and formed from monocytes/macrophage precursors which differentiate into osteoclast [2].

CGCG is composed of two distinct populations of cells: multinucleated giant cells and spindle shaped stromal cells. The latter are thought to be proliferating tumour cells based on available evidence [9]. Immunohistochemical studies on CGCG have helped to establish the lineage of the cells supporting the theory that the multinucleated giant cells are derived from macrophages. However, statistically significant difference with more expression of Calcitonin receptor has been found in the aggressive type of CGCG [10]. Recently, Kruse-Loser et al also demonstrated that the aggressive variant of CGCG presented a high number of giant cells, an increased mitotic activity, and a high fractional surface area [6]. The present case showed 13-15 giant cells per high power field. The connective tissue showed a moderate cellularity and fibroblast population which correlates with the histopathology of the non-aggressive type.

The management of CGCG depends on the clinical and radiographic findings. The general treatment of the giant cell granuloma opted is curettage or surgical excision. The lesions so treated almost invariably fill in with the new bone and heal with no difficulty. Occasional lesions recur. Curettage of well-defined localized lesions with peripheral Osteotomy is associated with a low rate of recurrence. A more radical excision is mandatory in extensive lesions with radiographic evidence of perforation of cortex. 72% of recurrence is seen in the aggressive forms and 3% of recurrence in the nonaggressive forms [11]. We employed extraction of the offending tooth followed by curettage and peripheral osteotomy to obtain biopsy of the lesion.

In our patient, OPG showed an increased new bone formation 6 months later. Bone density of the newly formed bone after 6 months demonstrated higher density than OPG taken 2 months after the treatment. The patient has been asked to visit every 6 months for a follow up.

CONCLUSION

Despite the fact that the course of CGCG of the jaw is considered benign, there exist some reports in the literature where metastases were observed. Furthermore malignant transformation to osteosarcoma or fibrosarcoma, pleomorphic fibrous histiocytoma has been reported, which mandates a prompt diagnosis.

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