Case Report

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# Central Giant Cell Granuloma in a 2 Year Old Child: Report of a Case and Review of Literature

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## ABSTRACT

**Background**: Central giant cell granuloma (CGCG) formerly called giant cell reparative granuloma is a non-neoplastic proliferative lesion of unknown etiology. It occurs most commonly in the mandible. The case reported here resembled a wide variety of conditions that led to a misdiagnosis both on clinical and radiographic examination but was histopathologically diagnosed as CGCG. We describe a case of central giant cell granuloma arising from the anterior maxilla in a 2 year old boy to highlight the importance of histopathology, radiology and management of this lesion.

**Keywords:** Central giant cell granuloma, multinucleated giant cells, hyperparathyroidism.

## INTRODUCTION

Giant cell lesions (GCLs) are benign primary bone tumors. The central giant cell granuloma (CGCG) of the jaws is a clinically well characterized lesion, but one that is still poorly understood from a biologic and behavioral point of view.[1]The lesion is generally accepted as being a benign, nonaggressive process that occurs in the tooth bearing areas of the jaws. They are mesenchymal in origin and consist of a stroma with fibroblast-like spindle cells, multinucleated giant cells, and a dense vascular network composed of endothelial cell–lined capillaries. There may be multiple areas of hemorrhage within the tumors and mitoses in the spindle shaped cells.[2]

According to the World Health Organization, central giant cell granuloma (CGCG) is an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of hemorrhage, multinucleated giant cells, and trabeculae of woven bone.[3]This lesion accounts for less than 7% of all benign jaw tumors and was considered by Jaffe as a locally reparative reaction of bone possibly due to either an inflammatory response, hemorrhage, or local trauma. CGCG of the jaws, occurs over a wide age range.[1, 4] The giant cell lesion originates either peripherally (gingival mucosa) or centrally (in the bone), affecting the adjacent tissues (by direct spread) as it grows.

CGCG has a predilection for women at any age, although most occur before the age of 30 years. The lesion produces a firm, painless expansion of the involved area, and the cortical plates are thinned, but usually not perforated. CGCG may be differentiated based on their clinical behavior into aggressive and nonaggressive types. They behave as single lesions, and, the appearance of multiple lesions should alert the possibility of an associated hyperparathyroidism or cherubism (the central giant cell lesion can be associated to both these entities).[5]

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The radiographic features consist initially of a unilocular radiolucency and as the lesion enlarges, a multilocular radiolucency with well-defined borders may appear which displaces or resorbs tooth root.[6] Histologically, the lesion is composed of a proliferation of fibroblasts within a collagenous connective tissue stroma containing many small vascular spaces with hemosiderin-laden macrophages. Multinucleated giant cells, which frequently aggregate around the vascular channels, are present and foci of ossification may occur.[7]The presentation of this lesion outside the jawbone is very rare. Many authors believe that when it occurs in locations other than the jaws, it is considered a giant cell tumor.[8]

## CASE REPORT

A 2 year old boy reported to the Department of Oral and Maxillofacial Surgery, Kannur Dental College with a swelling on the right upper anterior region. Patient had a fall when he was one year old which caused fracture of 51 and 52 causing intrusion of the latter with slight bleeding and pain at that time. This persisted for one week and subsided with antibiotics. After nine months, patient again had a history of fall and injury to the same site causing the same symptoms and within a weeks' time a small swelling was noted and it started to increase in size and reached the present level. On examination size of the swelling was 1.5 cm x 2cm. 52was intruded and it was totally covered by the swelling. (Fig 1)

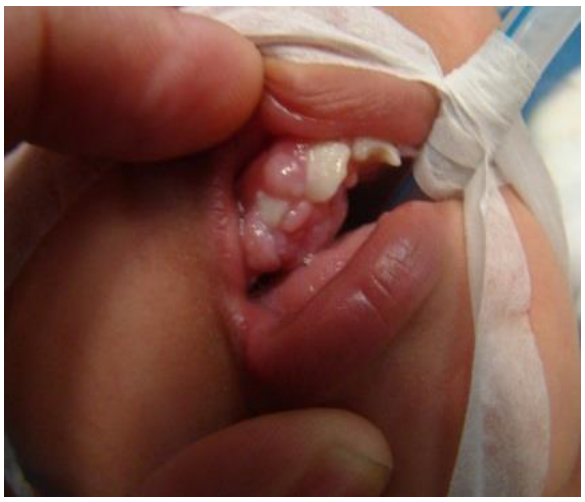

Fig 1: Preoperative photograph

The swelling extended on the buccal aspect, with inflammation of the papilla. It extended from the incisal edge of 53 and extended palatally to 51 on the same side. Swelling was round and firm. There was bleeding on probing. There was no pus discharge. The swelling exhibited blanching. The swelling was firm, fluctuant and was not uniform. The papillae were enlarged. The patient did not have any co morbidities. He was otherwise healthy and moderately nourished. Radiographic examination of the area revealed a unilocular lesion with resorption of roots. (Fig2)

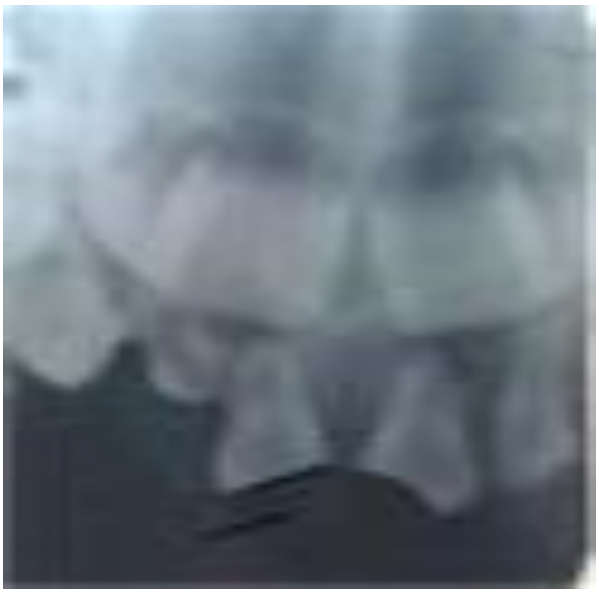

Fig 2: Radiograph

Since the patient was uncooperative an incisional biopsy could not be done. So the case was planned under general anesthesia. After oral intubation, the lesion was aspirated with a wide bore needle; since the nature of the lesion was unknown and it yielded a negative result. The area was infiltrated with lignocaine with 1:200000 adrenaline. A crevicular incision was placed from 51to 53. The mucoperiosteal flap was reflected. The whole exophytic mass was removed along with the mobile 52.Since there was bone involvement, the bone was debrided and curetted with peripheral ostectomy. The mass was sent for histopathologic examination. The tissues included the soft as well as the debrided bone too. The wound was closed with a 3/0 vicryl. (Fig 3,4and 5)

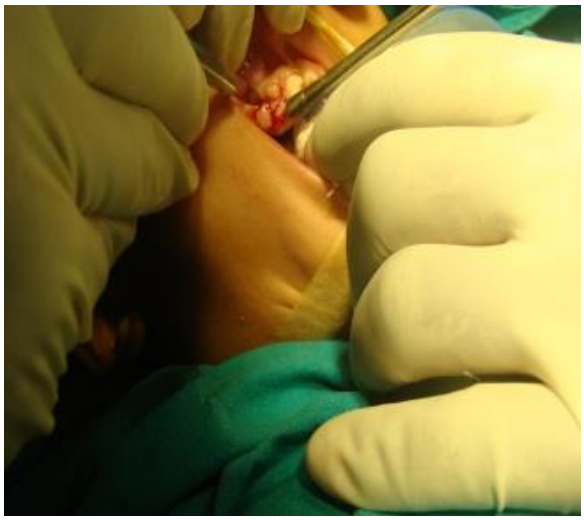

Fig 3: Intraoperative photograph.

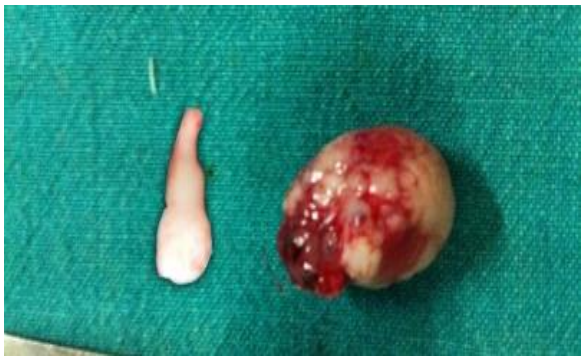

Fig 4: Specimen removed intoto with tooth.

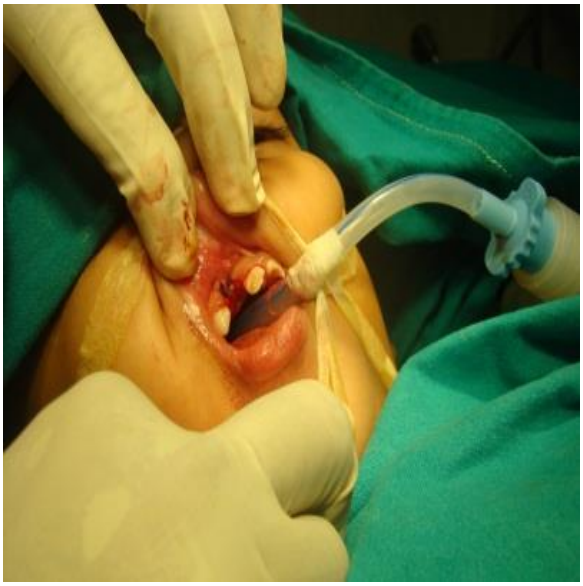

Fig 5: Wound closure.

The patient was revived. The patient is being followed up every six months and so far hasn't reported with any recurrence. (Fig6)

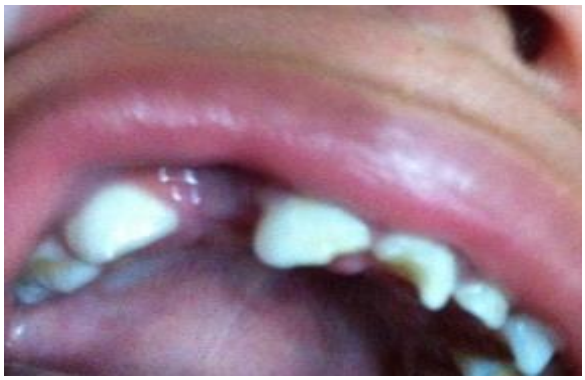

Fig 6: Post operative photograph.

When considering the differential diagnosis of a multilocular radiolucency, odontogenic keratocyst, ameloblastoma, odontogenic myxoma, aneurysmal bone cyst, and other lesions of the jaws must be ruled out.HPE revealed proliferation of fibroblasts within a collagenous connective tissue stroma containing many small vascular spaces with hemosiderin-laden macrophages. Multinucleated giant cells, around the vascular channels, are present throughout the stroma(Fig7), Since histological features of CGCG are identical to the brown tumor of hyperthyroidism, serum levels of calcium, phosphorus and alkaline phosphatase were advised which were found to be in normal limits (Calcium → 9.3 mg/dl, Phosphorus → 4.1 mg/dl and Alkaline phosphatase → 92 U L).Brown tumor of hyperparathyroidism was excluded by demonstrating normal levels of serum calcium, phosphorus and alkaline phosphatase levels, thus establishing the diagnosis of central giant cell granuloma of the anterior maxilla.

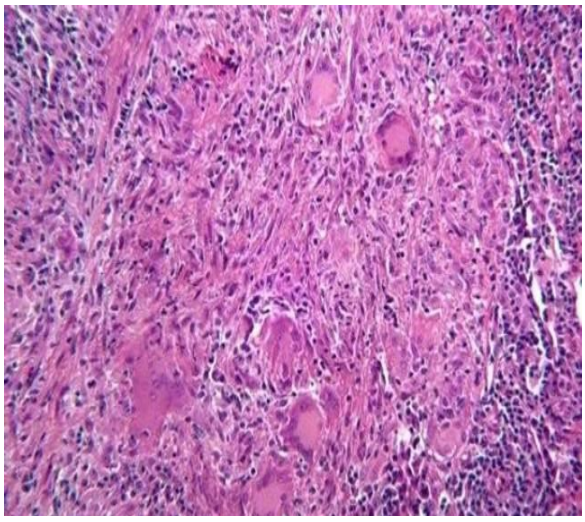

Fig 7: photomicrograph.

## DISCUSSION

There is much confusion and conflicting information regarding the cause, incidence, and behavior of giant cell granulomas. The cause of the CGCG remains elusive. Its histological appearance, behavioral characteristics, and clinical presentation share similarities with several lesions. Patients with CGCG present with asymptomatic localized swelling of the affected area and 20% or more have pain or paresthesia. The clinical behavior of these types of lesion is distinctly variable, and sometimes difficult to predict. The fundamental clinical sign is swelling, with or without tooth mobility, and growth that ranges between silent and aggressive. Patients with highly aggressive lesions (generally younger patients with larger tumors) usually have associated pain, bleeding, and local bone destruction with tooth displacement and radicular resorption, as with the case herein described.[3]

Giant cell granulomas of the jaw bones may be peripheral or central. Peripheral lesions present as pedunculated or sessile lesions on the gingiva while central lesions are endosteal.[9,10] 44% to 50% of CGCGs appear as a unilocular radiolucency and 50% to 60% present as multilocular radiolucency.[9] CGCGs may thin, perforate or, less commonly, expand cortical bone. Radiographically, they appear with equal frequency as unilocular and multilocular radiolucencies. The radiographic border may be well or poorly defined, with the tumor frequently extending beyond the radiographic margins. The lesion is often associated radiographically with tipping of the associated tooth roots. The lesions also may appear as periapical radiolucencies associated with vital teeth, sometimes causing blunting and resorption of the root apices. The clinical behavior of these lesions is quite variable and difficult to predict.

The light microscopic appearance of central giant cell granuloma is identical to that of the brown tumor of hyperparathyroidism, and must be differentiated based on serum chemistries. Hyperparathyroidism is associated with increased calcium, alkaline phosphatase, and parathyroid hormone levels, and a decreased phosphorus level, as opposed to normal levels in uncomplicated central giant cell granuloma.[10]. The CGCG also histologically resembles bone lesions such as the aneurysmal bone cyst, fibrous dysplasia, and cherubism.

The CGCG, and these bone lesions, all show the presence of numerous multinucleated giant cells in a hyper cellular stroma of fibroblasts and collagen. This matrix can contain large sinusoidal spaces and frequent extravasated red blood cells. These multinucleate giant cells are osteoclastic in nature. The cells were found to excavate cortical bone and this bone resorption was inhibited by the addition of calcitonin to the culture.[11]It is unclear whether this represents an infiltrative repair process or deregulated tumorogenic growth.

Histologically, this granuloma is characterized by the appearance of abundant benign giant cells, each with 5-10 nuclei, and high mitotic activity, with proliferation of cells in bone without atypia and with osteoclastic. Abundant hemorrhagic foci were evident. Increased osteoblastic activity with development of reactive bone is also characteristic feature of this entity.

The histological, radiographic and clinical diagnosis is particularly difficult in these types of lesions. In spite of this, the combination of a radiographic examination (unilocular or multilocular radiolucency), histological findings (giant cells contained within the fibroblastic matrix), serum levels of parathyroid hormone (compatible with normal levels) and the clinical characteristics, confer the diagnosis of CGCG ,against the various differential diagnoses and allows the surgical treatment correctly. However, the histological and clinical similarities continue to convince some authors that the CGCG of the jaws may even represent more than one type of lesion, with some being true tumors and others merely reparative lesions. [12]

The recurrence rate is consistently reported to be between 13% and 22%.[13] There has been considerable interest in predicting the aggressiveness of these lesions. The lesions are usually treated with aspiration followed by curettage and conservative peripheral ostectomy. In lesions with associated teeth, promising results have been reported when root canal therapy is performed although most authors recommend extraction of involved teeth.[14, 15] The standard treatment for preoperatively diagnosed CGCG was

resection without a continuity defect and peripheral ostectomy, via an intraoral approach under general anesthesia. Chuong et al suggested that aggressive tumors that present with pain, rapid growth, facial swelling, or cortical perforation be treated with en bloc resection.[5]

The giant cell tumor in a slightly older age group, radiographically shows indistinct borders, usually is painful, has a higher recurrence rate, dominated by multinucleated giant cells with larger, more rounded nuclei, and is treated more aggressively than the central giant cell granuloma. However, this remains an area of controversy because many pathologists are of opinion that a true giant cell tumor of the jaws does not exist. If a giant cell tumor does occur in the jaws, it is likely to be more aggressive than the giant cell granuloma.[16]

In this mentioned case, it seems possible that CGCG is a disease associated with an intraosseous hemorrhage, caused by continuous trauma, to the particular region, followed by unbalanced osteoclastic activity, leading to progressive bone resorption. CGCGs generally do not show perineural invasion.[14] Recent limited clinical trials have reported successful nonsurgical treatment of CGCGs using intralesional corticosteroid injections and long-term subcutaneous calcitonin injections.[17]While the initial nonsurgical results are promising, only a few cases have been documented, and no long-term data available. Based on these findings, it is possible that CGCG is a disease associated with an intraosseous hemorrhagic condition followed by unbalanced osteoclastic activity, leading to progressive bone resorption. This blood will stimulate new bone-healing, reducing osteoclastic activity and allowing for the osteoblastic activity to occur, as in extraction socket healing. Thus these lesions can be treated by simple exploratory surgery that induces new intraosseous bleeding followed by new bone-healing.

## CONCLUSION

CGCG is considered as a benign intraosseous jaw lesion of undefined etiology. Whether it is caused by a reactive, inflammatory, infective, or neoplastic process remains a matter of debate. Although CGCG is expansive in its growth, it does not grow around or invade nerve trunks. It also does not invade perineural sheaths or spread via perineural spaces. Nonsurgical treatment of CGCG is probably a good treatment option for small slowly enlarging lesions. Successful treatment of painful, large, and rapidly growing lesions is more likely achieved by surgical removal.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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