Case Report

Nonsyndromic Synchronous Multifocal Central Giant Cell Granulomas of the Maxillofacial Region: Report of a Case

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Abstract

Central giant cell granuloma (CGCG) is a benign proliferation of fibroblasts and multinucleated giant cells that almost exclusively occurs in the jaws. It commonly occurs in young adults showing a female predilection in the anterior mandible. Multifocal CGCGs in maxillofacial region are very rare and suggestive of systemic diseases such as hyperparathyroidism, an inherited syndrome such as Noonan-like multiple giant cell lesion syndrome or other disorders. Only 10 cases of multifocal CGCGs in the maxillofacial region without any concomitant systemic disease have been reported in the English literature. Here, we report an unusual case of 36 year-old female presented with non-syndromic synchronous, multifocal CGCGs in the left posterior mandible and left posterior maxilla without any concomitant systemic disease. Relevant literature is reviewed and the incidence, clinical features, radiological features, differential diagnosis and management of CGCGs are discussed.

Keywords: Central giant cell granuloma; Multifocal; Mandible; Maxilla

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INTRODUCTION

Central giant cell granuloma (CGCG) is a benign neoplasm occuring exclusively in the jaws. It commonly occurs in young adults with a female predominance. This tumour comprises of fibroblastic proliferation with multinucleated giant cells [1]. The mandible is the most common site of occurrence, followed by the maxilla and other facial bones with lower frequencies. The maxilla/mandible ratio is reported from 2:1 to 3:1 [2,3]. For this lesion, the term reparative giant cell granuloma was widely accepted at one time, as it was considered primarily to be a local reparative reaction of bone, possibly due to intramedullary haemorrhage or trauma. As this lesion has a destructive process, the term reparative is not used anymore [4]. The presence of multiple central giant cell granulomas in the maxillofacial region is rare and is suggestive of hyperparathyroidism, Noonan-like multiple giant cell lesion syndrome, Giant cell tumour, Cherubism or Paget's disease [5].

Multifocal, synchronous CGCGs without any concomitant systemic disease are extremely rare. To the best of our knowledge, only 10 such cases have been reported to date in English literature. We report nonsyndromic synchronous multiple central giant cell granulomas in the maxillofacial region of a 36 year-old female with no concomitant systemic disease.

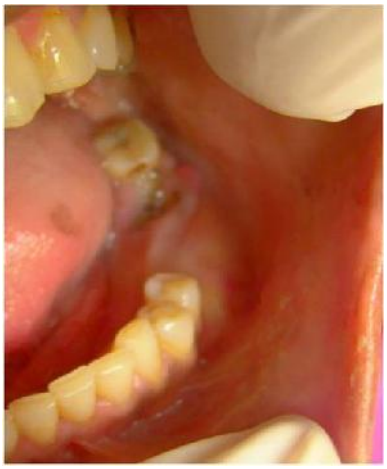

Fig 1. Clinical photograph showing swelling with left mandibular posterior region

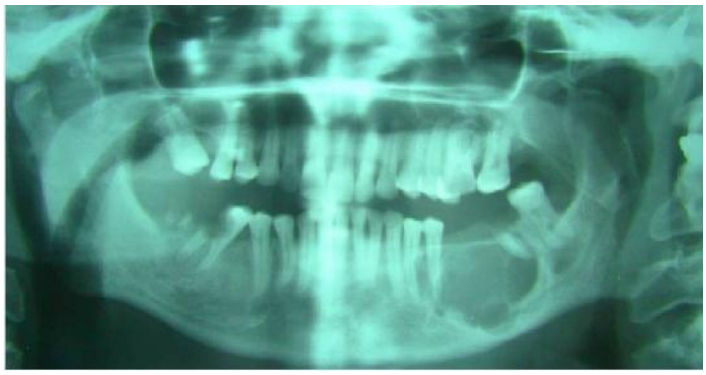

Fig 2a. Panoromic radiograph showing well defined multilocular radiolucent lesion in left posterior mandible and maxilla

CASE REPORT

A 36 year-old female patient was referred to our department with the chief complaint of swelling in the left posterior region of the lower jaw since eight months earlier. No other symptoms were associated with the swelling. Medical and family histories were noncontributory. The patient was of normal stature, appearance and intelligence. Extraorally, a diffuse swelling was present at the left lower one third of the face. It was firm and nontender on palpation and there was no paraesthesia. Intraoral examination revealed a diffuse swelling extending from the lower left first premolar to second molar, obliterating the buccal sulcus. The overlying mucosa was of normal color, smooth and intact with expansion of buccal and lingual cortical plates [Fig 1]. The swelling was hard in consistency and nontender on palpation. The mandibular first premolar and third molar had Grade II and Grade I mobility, respectively and the lower left first molar was missing.

A careful examination of the mouth revealed a second asymptomatic lesion at the left posterior maxilla. Expansion of the posterior maxilla was evident on buccal aspect, which was hard and nontender on palpation.

Radiographic examination [Fig 2 (a,b)] revealed a large, multilocular radiolucency extending from the mandibular left first premolar to the third molar with well-defined corticated margins, causing thinning and expansion of buccal and lingual cortical plates. There was no displacement of teeth or root resorption.

A large, well corticated, expansile radiolucent lesion was seen in the left posterior maxilla.

CT scan showed a well corticated, expansible, heterogeneously enhancing, lytic lesion measuring 3.5 X 2.5 cm and involving left alveolar process of the maxilla, lateral wall of the maxillary sinus and lateral pterygoid plate, causing an inward bulge in the left maxillary sinus. A multiloculated lesion causing expansion of cortices was also seen involving the left side of the mandible measuirng 2.9 X 2.8 [Fig 3 (a,b)]. Odontogenic keratocyst, CGCG, ameloblastoma, odontogenic myxoma and aneurysmal bone cyst were included in differential diagnosis. An incisional biopsy was performed. Histopathological evaluation revealed connective tissue with collagen fibers, proliferating fibroblasts, numerous blood vessels and extravasated red blood cells. Numerous gaint cells of varying sizes were randomly scattered throughout the connective tissue. Newly developing osteoid tissue was noticed at the periphery [Fig 4]. The histopathological diagnosis of CGCG was made. Since the patient had multiple lesions, to rule out hyperparathyroidism, serum calcium, alkaline phosphatase,

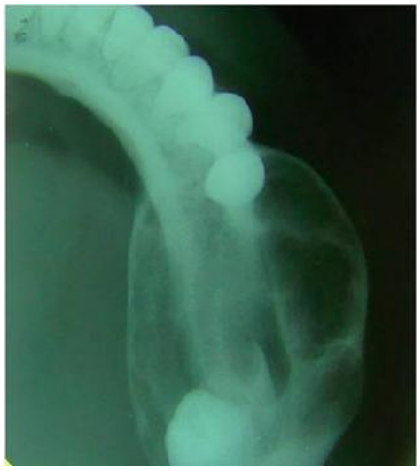

Fig 2b. Mandibular occlusal radiograph showing thinning and expansion of buccal and lingual cortical plates

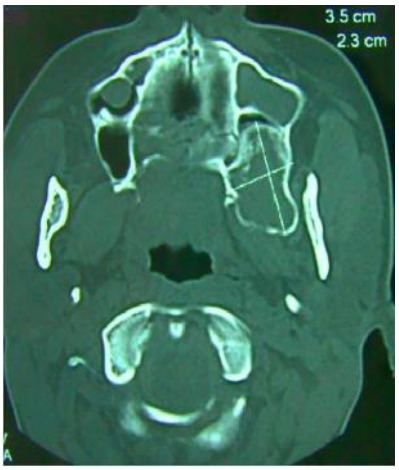

Fig 3a. Axial CT scan showing a lesion in the left posterior maxilla involving pterygoid plates and maxillary sinus

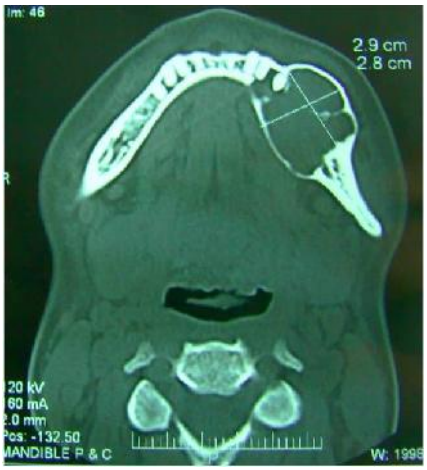

Fig 3b. Axial CT scan showing the mandibular lesion.

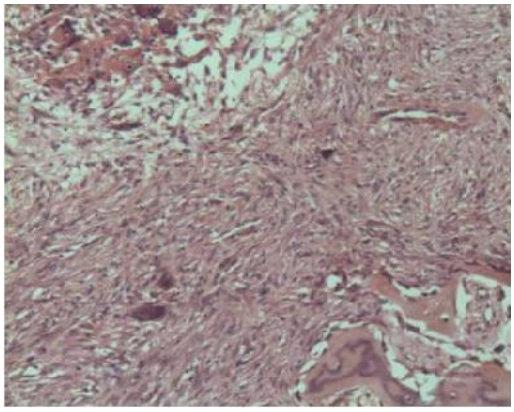

Fig 4. Photomicrograph of a specimen from the lesion showing multilocular gaint cells and areas of reactive bone formation in a fibrovascular connective tissue. stroma (hematoxylin- eosin stain, original magnification X 40)

phosphorus and parathyroid hormone levels were tested, which were found to be within the normal limits (Table 1).

Table 1. Results of preoperative workup

Serum Chemistries	Test results	Normal Range
Parathyroid hormone (PTH)	17.2 pg/mL	12-75 pg/mL
Calcium level	9.2 mg/dl	8.5-11 mg/dl
Phosphorus	2.0 mg/dl	2.0-4.5 mg/dl
Alkaline phosphatase	154.6 IU/L	108-306 IU/L

A skeletal survey was also performed, which was normal.

As the patient was 36 years old, Paget's disease and cherubism were ruled out. Noonan-like multiple giant cell lesion syndrome was ruled out as the patient was of normal stature, intelligence and appearence.

Later, successful surgical enucleation of both lesions was done. Histopathological diagnosis of the enucleated lesions was confirmed to be CGCG.

The patient did well postoperatively and is on regular follow up. There were no signs of recurrence one year after the surgery.

DISCUSSION

CGCG is a benign intraosseous lesion occuring in the jaws. Much controversy surrounds the CGCG. Initially, it was not distinguished from the giant cell tumor (GCTs) of the extragnathic skeleton, but later it was described as a distinct entity by Jaffe (1953) [6].

Some authors suggest the use of the term central giant cell lesion while others use it as CGCG. The lesion has been proposed to be both a reactive response to hemorrhage or trauma and a neoplasm [3,7]. However, others considered CGCG and GCTs of the extragnathic skeleton as seperate entities [6]. CGCGs may be differentiated into aggressive and nonaggressive types based on their clinical behaviour. The aggressive type is large and rapidly growing and may cause local bone desrruction, tooth mobility or displacement, root resorption and cortical expansion or perforation; it also has high recurrence rate [3]. CGCG occurs more commonly in the mandible, anterior to the first molar and often crosses the midline. Occasionally, they may occur in the facial bones, the maxillary sinus, ethmoidal sinus, temporal bone, cranial vault and small bones of hands and feet [1].

Radiologically, the lesion appears as a unilocular or multilocular radiolucency with well-defined or ill-defined borders and shows variable expansion and destruction of the cortical plates [4]. Mineralization, although uncommon, may be seen in these lesions, and is usually limited in extent as seen in the maxillary lesion of our present case. The occurence of multiple CGCGs is rare. They may be synchronous or metachronous. Synchronous involvement would strongly support a concept of multifocality, while metachronous occurence may potentially represent recurrences due to seeding or incomplete surgical excision [8]. There is a strong association between multiple lesions and disorders such as hyperparathyroidism, Noonan like multiple giant cell lesion syndrome, GCT, cherubism and Paget's disease. The occurence of synchronous, multifocal CGCGs without systemic involvement or family history is extremely rare. To date, there are only 10 such cases reported in the English literature (Table 2)[8-17].

The light microscopic appearance of CGCG is identical to that of brown tumor of hyperparathyroidism, and must be differentiated based on serum chemistries.

Table 2. The reported cases of multifocal central gaint cell granulomas of the maxillofacial region

Study	Age/ Gender	Location	Type (Metachronous(M)/ Synchronous(S)
Davis and Tideman[9], 1977	31/F	Right mandibular body, left maxilla	M
Cassatly et al[10], 1988	27/F	Parasymphysis and mandibular body	S
Smith et al[11], 1990	41/F	Right mandibular ramus, left maxillary sinus, nasal bone, orbit and right maxillary sinus	M
RA. Loukota[12], 1991	25/F	Maxillary and mandibular body	M
Wise and Bridbord[13], 1993	23/M	Left mandibular body; left and right nasomaxillary areas	S
Milora and Quinn[8] PD 1995	37/F	Left posterior maxilla and anterior mandible	S
Cutis and Walker[14] 2005	62/M	Right maxilla, right body of mandible and left angle of mandible	M
Martin WD[15] 2007	35/F	Left maxilla and right mandible	S
E. Bilodean, Khalid Chaudhary [16] 2009	42/F	Maxillary sinus , ethmoidal sinus	M
MS Kang[17] 2010	17/M	Bilateral posterior mandible and right maxilla	S
Our case 2012	36/F	Left posterior mandible and left posterior maxilla	S

Hyperparathyroidism is associated with increased levels of calcium, alkaline phosphatase, and parathyroid hormone, and a decreased level of phosphorous, as opposed to normal level in uncomplicated CGCG. With regard to the giant cell tumor, similar clinical and histopathological pictures may be encountered. A careful examination will usually allow adequate differentiation [18].

The giant cell tumor is rare and large and occurs in a slightly older age group. It is usually painful and has radiographically indistinct borders. It has a higher recurrence rate that CGCG and is dominated by evenly distributed multinucleated giant cells with larger, more rounded nuclei and less fibrous tissue without osteoid formation [8,18].

In Noonan-like multiple giant cell lesion syndrome other features include a short stature, webbed neck, cubitus vulgus, pulmonary stenosis, multiple lentigenes, low intilligence, occular hypertelorism and posteriorly angulated ears. Cherubism is characterisied by bilateral multilocular lesions in the posterior mandible and maxilla in a young age group (between the ages of 1 and 4 yrs.) with progressive and symmetrical enlargement of the jaws [14,17].

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It is usually inherited as an autosomal dominant condition and the gene has been mapped recently to chromosone 4p16:3. Paget's disease is usually seen in old age groups with complete bone involvement and occurs in the jaws, facial bones, skull and extragnathic skeleton [17]. Radiographically, cotton wool appearence is noted and serum alkaline phosphatase level is increased.

The management of CGCG depends on the clinical and radiological findings. Surgical management, which is the treatment of choice, includes curettage with or without peripheral osteoctomy and en bloc resection.

The medical management as an adjunct to surgery consists of treatment with steroids and calcitonin, which inhibits osteoclastic activity [19].

Interferon alpha is reported to be useful for the treatment of agressive CGCG due to its anti-angiogenic action. Bisphosphonates have been administered intravenously in CGCG with promising results [4,20].

Recurrence rates are high, ranging from 11-72% in different studies and are mainly due to incomplete removal of the lesion. Therefore, a careful follow up over a long period is essential. Regular standardised radiographic follow up is the most sensitive and useful measure for determining the growth rate and diagnosing recurrence in these lesions.

In conclusion, multifocal CGCGs in the maxillofacial region are suggestive of a systemic disease such as hyperparathyroidism or an inherited syndrome such as Noonan-like multiple giant cell lesion syndrome. Our paper presents a case of multifocal, nonsyndromic, synchronous CGCGs in the left posterior mandible and left posterior maxilla without any concomitant systemic disease, which is rare.

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