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# Central giant cell granuloma affecting the posterior mandible

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**Type of Publication:** Case Report

**Conflicts of Interest:** Nil

**Abstract**

Central giant cell granuloma (CGCG) is an aggressive, locally destructive but histopathologic ally benign osteolytic lesion having a marked predilection for the craniofacial structures particularly the jaw bones which are encountered occasionally in the daily practise. The lesions are usually solitary affecting mostly the anterior mandible having a unilocular or multi locular radiographic presentation mimicking a honeycomb or soap bubble-like appearance and histopathologic ally being characterised by the presence of numerous multinucleated giant cells. Therefore, the purpose of this report is to present a case of Central Giant Cell Granuloma (CGCG) in an adult female patient affecting the mandibular region along with its clinico-pathological aspects.

**Keywords:** Central Giant Cell Granuloma, intra osseous lesion, multinucleated giant cells, osteoclast. I.

## Introduction

Central giant cell granuloma (CGCG) of the jaw is a benign, non-neoplastic, proliferative intra-osseous, osteolytic giant cell lesion, accounting for up to 7% of Tumors in the head and neck region. It was first described by Jaffe in the year of 1953. The incidence of the disease is estimated to be 0.0001% in general population with 60% of cases occurring before the age of 30. [1,2,3,4] The predisposing factors behind the development of the disease are not yet clearly identified. The clinical manifestations vary considerably depending upon the behaviour of the lesion and thereby, designated either as an aggressive or non-aggressive type. Radiographically, it exhibits unilocular or multilocular radiolucency having a well-defined margin and may cause possible cortical plate expansion and perforation along with root resorption of adjacent teeth in aggressive cases. On histopathological evaluation it demonstrates cellular fibrous connective tissue stroma containing multiple areas of hemorrhage, proliferation of multinucleated giant cells, and occasionally trabeculae of woven bone.[2] It has been classified under the giant cell lesions and bone cysts by World Health Organization under histological classification of odontogenic and maxillofacial bone Tumors (4th edition, 2017). [2] CGCG usually does not present with pathognomonic clinical and radiographical features and thereby relies upon histopathological evaluation to differentiate it from other lesions occurring in the same anatomical location.[2]

## Case report

A 28 years old, female patient from the semi-urban area reported to the Department of Oral & Maxillofacial Pathology, Guru Nanak Institute of Dental Sciences & Research (GNIDSR), Panihati, Kolkata, with the chief complaint of painful swelling involving the right back tooth region for last six to seven months. Extra-orally, there was presence of a large, rapidly enlarging, bony hard, tender swelling causing marked facial asymmetry along with paresthesia of the right side of the face. The overlying skin appeared to be normal. Intra-oral examination revealed the presence of an edentulous area with a saucer shaped depression on the right posterior alveolar ridge and ascending ramus of mandible along with a firm to hard tender swelling measuring about 5 cm x 2.5 cm, extending buccally from 43 to right retromolar region. There was marked swelling in lingual aspect of 46, 47 and 48 regions also and overlying mucosa was relatively normal. Mobility of regional tooth and crowding of lower anteriors were also noted. [Figure 1] Based upon the clinical examination, the case was provisionally diagnosed as an osseous or odontogenic neoplasm.

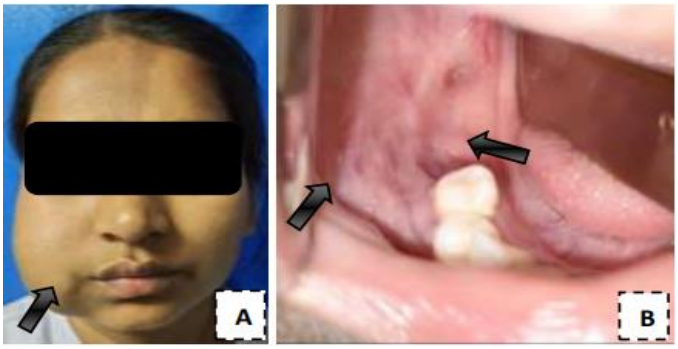


Fig 1: (A) Extra-oral photograph of the patient showing presence of a large well-defined swelling in the right side of face causing marked facial asymmetry (black arrow).

(B) Intra-oral photograph revealed the presence of large, tender, non-pulsatile, non-fluctuating bony hard swelling on the body and ascending ramus of the mandible (black arrow).

Panoramic radiograph (OPG) of the concerned area revealed well-delineated, non-corticated multilocular radiolucencies interspersed with patchy radio-opacities in the body and ascending ramus of mandible having ragged borders and faint trabeculations at places,



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extending from permanent right second premolar region up to posterior coronoid and condylar process region. The second premolar and the first molar showed root resorption along with expansion of right cortical plate. There is also presence of an edentulous area in relation to 47 along with mild displacement of 46 and 48. [Figure 2] Depending upon the clinico-radiological findings, the case had differential diagnosis of osseous tissue or odontogenic neoplasm.

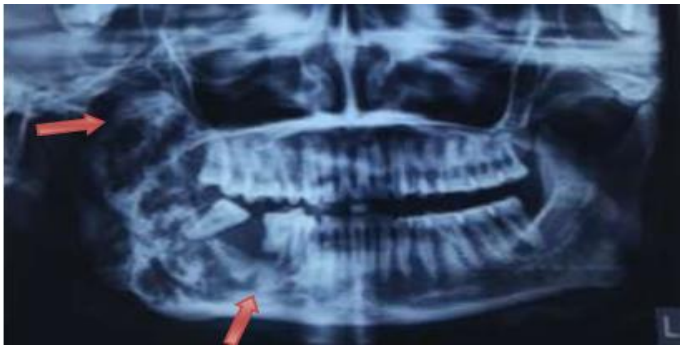

Fig 2: Orthopantomagram (OPG) revealed the presence of multilocular radiolucency interspersed with patchy radio-opacities having non-corticated ragged borders and extending from premolar region up to condylar region of right side of the mandible (red arrow).

Pre-operative routine haematological and biochemical investigations were advised and were within normal ranges. Incisional biopsy was performed under local anaesthesia and the formalin-fixed, paraffin-embedded, Hematoxylin and Eosin-stained sections revealed the presence of a loose, fibrillar, highly cellular fibrovascular connective tissue stroma interspersed with plenty of proliferating plump, spindle-shaped stromal cells, small capillaries along with areas of haemorrhage at places. However, the most striking feature was the presence of multiple, deep purplish, round to ovoid, multinucleated cells of varying sizes resembling the giant cells.

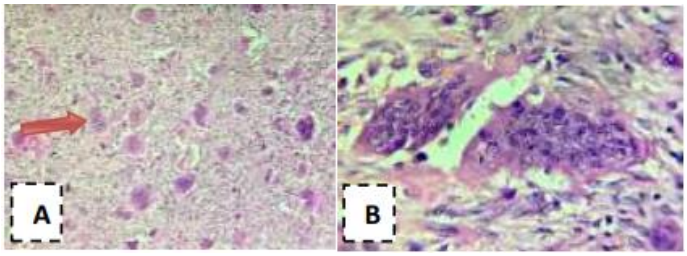


Fig 3: (A) & (B) Photomicrographs depicting H & E-stained sections showing the presence of fibro-vascular, highly cellular connective tissue stroma, consisting of numerous proliferating plump, ovoid and spindle shaped stromal cells along with multiple, multinucleated, round to ovoid giant cells (red arrow) of varying size and chronic inflammatory cell infiltration within it (A=10x, B = 40x).

The differential diagnosis of lesions exhibiting multinucleated giant cells include giant cell tumor, central giant cell granuloma (CGCG), non-ossifying fibroma, peripheral giant cell granuloma, osteoid osteoma, brown tumor of hyperparathyroidism. [5]

The brown tumor of hyperparathyroidism can be differentiated on the basis of biochemical tests, where hypercalcemia, hypophosphatasia and increased level of parathyroid hormone (PTH) will indicate toward the disease. The giant cell tumor of long bones can be sometimes difficult to differentiate from CGCG, especially if CGCG is of aggressive type. But based on its rare occurrence in jawbones, demonstration of larger giant cells, more number of nuclei, generalized distribution of giant cells and absence of osteoid formation, giant cell tumor can be distinguished. Also, cases have been mostly reported in patients already suffering from Paget's disease. The non-ossifying fibroma characteristically will show fibro histiocytic stroma with storiform pattern and prominent xanthogranulomatous reaction. Other giant cells containing lesions include aneurysmal bone cyst and cherubism, where the former exhibit sinusoidal blood



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spaces within the tumor mass, and the latter is diagnosed on clinical basis of bilateral involvement of the jaws in children with a family history. [6]

Therefore, depending upon the overall clinico radiological, biochemical, histopathological findings and after exclusion of the other giant cell lesions the case was finally diagnosed as Central Giant Cell Granuloma (CGCG). The patient was referred to the Department of Oral Surgery for further treatment and management.

**Discussion**

Central giant cell granuloma (CGCG) is a benign lesion of bone with an unknown etiology and can either be locally aggressive (symptomatic) or asymptomatic in nature. [3] The World Health Organisation (WHO) defined it as an intra-osseous lesion having a cellular fibrous stroma containing multiple foci of haemorrhage, collections of multinucleated giant cells and occasional trabeculae of woven bone. [3] It was initially termed as "Reparative Giant Cell Lesion" as it was believed to be the result of a local repair process but sometimes due to its aggressive nature being similar to a neoplasm, the more appropriate terminology was thought to be "Central Giant Cell Granuloma (CGCG)". [5] Though, the origin of this lesion is unclear but some factors such as local trauma, inflammation, intra-osseous haemorrhage and genetic anomalies may be involved. [7]

The disease occurs over a broad age range with more than 60% of cases occurring before the age of 30 years. [8] Women are affected much more often than men, with a ratio of 2:1. [7] The present case too is in accordance to various other studies [7,8] where a female patient was suffering from CGCG having an age of 28 years.

Over 70% of the lesion has a predilection for the mandible whereas less than 30 % cases occur in the maxilla. In the literature, 80% cases are reported in the region anterior to the first premolar and are rarely noted in the posterior segment. [6,7,8] However, in our study the lesion was mainly affecting the posterior segment of the mandible.

The clinical behaviour of CGCG ranges from slow asymptomatic growth to bony perforation and resorption of roots of regional teeth [1]. Based on clinical and radiographic features, it is classified as aggressive or non-aggressive, depending on the intensity of pain, growth rate, cortical plate perforation and the tendency toward recurrence [5]. Chuong et al. described the criteria for aggressive lesions to manifest with pain, paraesthesia and root resorption along with rapid tumor evolution, cortical bone perforation and high rate of post operative relapses. [7]

Table 1: Classification criteria proposed by Chuong, et al. and adapted by Peacock, et al [5]

| Diagnostic criteria | Aggressive type | Non-aggressive type |
|---|---|---|
| Lesion size | ≥ 5 cm | < 5 cm |
| Rapid growth | Yes | No |
| Root resorption | Frequently | No |
| Tooth displacement | Frequently | No |
| Perforation of bone cortex | Frequently | No |
| Recurrence after curettage | Yes | No |

Based on these criteria's (Table 1), the lesion was designated as the aggressive type, as it was growing rapidly having a size greater than 5 cm and exhibited both cortical plate perforation along with root resorption of regional teeth.

Radiographically, CGCG exhibits a radiolucent unilocular or multilocular area with generally



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welldefined margin and possible expansion and perforation of the cortical bone and root resorption of adjacent teeth in aggressive cases [5]. The differential diagnosis may include ameloblastoma and odontogenic myxoma. Ameloblastoma presents with multilocular radiolucencies mimicking either honey-comb or soap bubble appearance. In case of odontogenic myxoma, the radiolucent defect mainly contains thin, wispy trabeculae of residual bone being often arranged at right angles to one another.

Histopathologic ally, CGCG is a benign proliferation of fibroblasts, which are the primary tumor cells and constitutes the proliferative component of the lesion since they express the proliferative protein marker Ki67 that indicates the cells in the proliferative phase. They are believed to be responsible for the recruitment and retention of monocytes which subsequently transform into multinucleated giant cells, which are the secondary cells. The presence of these cells is the most prominent feature of the lesion, distributed haphazardly within the connective tissue stroma forming the clearly recognizable clusters separated by scar-like stromal tissue. The giant cell and their clustering are mostly around the areas of hemorrhage. There may be trabeculae of newly formed reactive bone on the periphery of the lesion. Other accessory cells like macrophages, dendritic cells and endothelial cells are also occasionally found [6].

The present case report also demonstrated similar histopathological picture, although reactive bone was not noted in the sections.

CGCG mainly demonstrates osteoclastic giant cells. Their formation involves the interaction between stromal cells, which express RANKL which is a potent stimulator of osteoclast bone resorbing activity [3, 8, 9].

The common finding of all lesions is that there is an osteoclastic overactivity, but the exact predisposing factor is not clearly identified. One of the factor may be the alteration of the microenvironment of bone leading to the development of giant cell in the lesion. There are also many cytokines involved in bone resorption which may be either stimulator, initiator or inhibitors of the osteoclastic differentiation. The cytokines stimulating the osteoclasts are colony-stimulating factor, interleukin-1 (mediated by prostaglandin), tumor necrosis factor, transforming growth factor and interleukin-6 whereas the cytokines that inhibit osteoclast functions are lymphotoxins, interleukin-4 and interferons. They are produced by macrophages, stromal cells, endothelial cells or T lymphocytes, tumor cells, myeloma cells and sometimes even by the osteoblast themselves. Also, there is evidence that indicate the role of various local factors being generated in the microenvironment of bone-resorbing cells and are much more powerful regulators of osteoclast function than by the hormones like parathyroid hormone, calcitonin secreted and sent in the blood circulation [6].

Recurrence rates range from 3 to 72% in young patients, however, lesions with cortical perforation have a greater tendency toward recurrence [5].

Management of CGCG includes surgical curettage with or without medical management. Medical therapies include intralesional corticosteroids, calcitonin injections, and interferon-alpha therapy. They are alternatives as well as adjuncts to surgical treatment [3].

**Conclusion**

Central giant cell granuloma (CGCG) is a benign, relatively rare, osteolytic lesion having an aggressive nature affecting the cranio-maxillofacial region. It is frequently encountered in the anterior portion of mandible, mainly female individuals of younger age



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whereas posterior sites are considered to be an unusual location for their occurrence and can make the diagnosis difficult. Therefore, a rapid diagnostic assessment, along with an adequate histopathological evaluation, is essential to improve the management and the prognosis of this locally destructive neoplasm.

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