Central giant cell granuloma of posterior mandible: Report of a case

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Abstract
Central giant cell granuloma (CGCG) is a benign intraosseous lesion of the jaws. The lesion is considered to be a reactive phenomenon, a developmental anomaly, or a benign neoplasm. The clinical behavior of the lesion varies from an asymptomatic osteolytic lesion that grows slowly without expansion (non-aggressive), to an aggressive, painful process. Radiographically, the lesions appear as unilocular or multilocular radiolucencies with well-delineated borders. The occurrence of CGCG in the posterior mandible is a rare incidence. The present case is that of a 28-year-old female patient with a complaint of slow growing posterior mandibular swelling. The rarity of CGCG in the mandibular body-ramus area creates a diagnostic challenge as ameloblastoma, aneurysmal bone cyst, and odontogenic myxoma present commonly in the posterior mandibular region. Diagnosis is critical as a conservative line of management can be followed in case of CGCG as compared to radical treatment required in other lesions. This report describes the unusual presentation, the differential diagnosis, radiographic features, and management of this lesion.

Keywords: Aggressive, central giant cell granuloma, intraosseous, mandible

Introduction
Central giant cell granuloma (CGCG) is a benign intraosseous lesion first described by Jaffe in 1953. The lesion is considered to be a reactive phenomenon, a developmental anomaly or a benign neoplasm.1 Neville et al. considered this entity to be a non-neoplastic lesion. Formerly designated as giant cell reparative granuloma, there is little evidence that the lesion represents a reparative response.2 The World Health Organization has defined CGCG as localized benign but sometimes aggressive osteolytic proliferation consisting of fibrous tissue with hemorrhage and hemosiderin deposits with the presence of osteoclast-like giant cells and reactive bone formation.3 The WHO classifies it as a bone-related lesion and not a tumor. However, most of the times, its clinical and radiographic features mimic a benign tumor.1

Giant cell granulomas may be encountered in younger age group, 60% of cases occurring before the age of 30. A majority of the lesions occur in females.1 70% of the lesions occur in the mandible, anterior to the first molar in young patients. After the first two decades of life, there is a predilection for the posterior aspect of the jaws. In the maxilla, lesions occur more commonly anterior to the canine. Mandibular lesions frequently cross the midline. Occasionally, maxillary lesions have some malignant-type characteristics.4

CGCG is categorized into the aggressive and non-aggressive types based on their clinical and radiographic characteristics. Non-aggressive lesions usually present clinically as a slow growing, painless swelling.1 Radiographically, they appear as well-defined uni/multilocular radiolucencies with undulating borders.4

Aggressive lesions are encountered in a younger patient population, tend to grow faster and recur more often. Aggressive lesions demonstrate ill-defined borders with variable amounts of cortical destruction on radiographs. This is especially true for lesions involving the maxilla.4,5 The radiographic appearance of CGCG is not pathognomonic and may be confused with several other lesions of the jaws such as brown’s tumor of hyperparathyroidism, aneurysmal bone cyst, and odontogenic myxoma.5

The most common presentation of CGCG is in the anterior mandible. The occurrence of CGCG in the posterior aspect of the mandible is a rare phenomenon. The present case is that of a 28-year-old female patient with a complaint of slow growing posterior mandibular swelling. The present case can pose a diagnostic challenge due to its presentation in the posterior mandible mimicking lesions such as ameloblastoma, traumatic bone cyst, aneurysmal bone cyst, and odontogenic myxoma. Diagnosis is critical as a conservative line of management can
be followed in case of CGCG as compared to radical treatment required in other conditions.

This report is to describe an unusual presentation of CGCG in the mandibular body and to discuss the differential diagnosis, radiographic presentation, and management of this lesion.

**Case Report**

A 28-year-old female patient reported with a complaint of pain in the lower left back teeth region since 1 week. The patient gave history of discomfort and pain since 6 months following which she noticed a swelling in the left cheek. The pain was gradual in onset, intermittent, mild in intensity, localized, and non-radiating. The swelling was of gradual onset. The swelling had not progressed in size since the patient first noticed it. The patient had been prescribed antibiotics at a private clinic, but pain and swelling did not subside.

On extraoral examination, inspection revealed a diffuse swelling measuring 4 cm × 5 cm in relation to lower left body of the mandible extending antero posteriorly from the corner of the mouth, 4 cm posteriorly and supero inferiorly from the line joining the corner of the mouth to the lobule of the ear till 2 cm beneath the lower border of the mandible. The skin overlying the swelling appeared stretched and erythematous. No ulceration, bleeding or discharge was evident from the surface of the swelling. There was no local rise in temperature. On palpation, inspectory findings were confirmed with respect to size, shape, and extent. The swelling was hard in consistency, non-tender on palpation, non-compressible, and non-reducible. The lower border of the mandible was not palpable, and the swelling was soft in consistency in this region. Intraoral hard tissue examination revealed restorations with respect to 36 and 37. Periodontal pockets were noted with respect to 36 and 37 with Grade I mobility. No tenderness on percussion was evident with respect to 35, 36, 37, and 38. Soft tissue examination revealed vestibular obliteration extending distally from 36 region, the posterior extent of which was not well-delineated. On palpation, vestibular obliteration was evident extending from distal aspect of 36 to the anterior border of ramus [Figure 1]. Buccal and lingual expansion of cortical plates was evident. The lingual expansion was evident from 37 to 38 region. The swelling was hard in consistency, non-tender on palpation, non-compressible, and non-reducible.

On radiographic investigation, an intraoral periapical radiograph of 36, 37 region showed an ill-defined radiolucency extending posteriorly from the distal root of 36 [Figure 2]. The posterior extent could not be appreciated. Panoramic radiography revealed a well-defined unilocular radiolucency extending from the mesial aspect of the distal root of 36-38 region. The periphery showed no evidence of cortication. Erosion of the lower border of the mandible was evident. The internal structure showed evidence of wispy and ill-defined internal septae. The distal root of 36 and roots of 37 and 38 was seen within the radiolucency. No root resorption was noted [Figure 3].

Correlating the history, clinical, and radiographic findings, a differential diagnosis of ameloblastoma, aneurysmal bone cyst, odontogenic myxoma, and CGCG was given.

On further investigation, computed tomography (CT) scan revealed a well-defined expansile lytic lesion [Figures 4 and 5].
measuring 30 mm × 21 mm × 30 mm in the left side of the mandible, at the junction of the ramus and the body. Few septations were noted within. The roots of 2nd and 3rd molars were seen within the lesion. The 1st molar root was partially seen within the lesion. There was evidence of thinning and perforation of both buccal and lingual cortical plates. No obvious periosteal reaction was noted. There was no evidence of any associated soft tissue involvement. A differential diagnosis of ameloblastoma, dentigerous cyst, and odontogenic keratocyst were given.

Incisional biopsy revealed the presence of a syncytium of spindly stromal cells and osteoclast-like giant cells involving the bone. The congested vasculature was evident. Features were highly suggestive of CGCG.

The patient underwent enucleation with curettage followed by bone grafting of the defect with synthetic bone granules. The surgical specimen on subsequent histopathologic examination revealed predominantly spindle cells along with oval cells. Numerous multinucleated giant cells were seen dispersed throughout the stroma. Numerous blood vessels and areas of hemorrhage were also noted. The peripheral reactive bone formation was evident [Figure 6]. A final diagnosis of central giant cell lesion was given. The patient is on follow-up, and there are no clinical signs of recurrence.

**Discussion**

CGCG is an intraosseous lesion consisting of cellular fibrous tissue that contains foci of hemorrhage, multinucleated giant cells, and trabeculae of woven bone. The etiopathogenesis of the CGCG of jawbones has been suggested as an exacerbated reactive process following previous trauma or vascular insult causing intramedullary hemorrhage. Partial maintenance of blood supply following trauma may predispose to the development of CGCG. CGCG begins as a single resorption lacuna that enlarges by the association with adjacent resorption lacunae.[6] Local changes in the blood flow throughout the bone and local bone dysplasia had also been suggested as a probable etiologic factor.[7]

The incidence of CGCG in the general population is estimated to be 0.0001%. Giant cell granulomas may be encountered in patients ranging from 2 to 80 years of age, 60% of cases occurring before the age of 30.[2] In a systematic review on CGCG, 60% of the patients were younger than 30 years, and 35% were younger than 19 years.[5] The present case favored the younger age group predilection.

A majority of the lesions occur in females with a female: male ratio of approximately 2:1. It has been noted that the development of CGCG occasionally coincides with the onset of pregnancy or menarche. Pregnancy may alter the progression of CGCG but is very unlikely to initiate a new lesion.[6] The present lesion was seen in a young female patient.

CGCG is classified into the aggressive and non-aggressive types based on clinical and radiologic features. The non-aggressive lesion tends to be asymptomatic, slow growing with intact cortices, absence of root resorption, and smaller size (diameter <2 cm) with only 20% of patients complaining of pain or paresthesia. In contrast, aggressive lesions demonstrate pain, rapid growth, cortical perforation, root resorption, and a larger size (diameter exceeding 2 cm).[6] In the present case, the lesion was slow growing, but demonstrated features of aggressiveness such as size >2 cm (4 cm × 5 cm), pain and discomfort, cortical expansion, and perforation. There were no signs of root resorption.

The mandible is commonly affected than the maxilla, with a mandible/maxilla incidence ratio of 2:1.[5] In the mandible, the most common site is anterior to the first molars. After the first two decades of life, there is a tendency for the involvement of the posterior aspect of the jaws. The maxillary lesions tend to occur anterior to the canines. Mandibular lesions frequently cross the midline. Occasionally, maxillary lesions have some malignant-
type characteristics.[4] In a systematic review on CGCG, the majority of the lesions, 17 (85%) occurred in the mandible. In 81% of the cases, the lesion was anterior to the molar region.[5] In another study, lesions showed a maxillary predilection (69.6%) which was in contrast to the proved thesis. Moreover, most lesions were located in the posterior region of the jaws (65%). The author attributed these discrepancies to specific ethnicity or small sample size.[6]. In the present case, however, posterior mandibular body-ramus area was involved.

The radiological features of CGCG described in the literature are variable. Initially, CGCG appears as a unilocular, radiolucent cyst-like lesion, and later may appear multilocular. CGCG is reported to have a low growth index; therefore, their borders appear to be distinct and non-diffuse.[12] A systematic review of 232 well-established cases depicted ill-defined borders in 66%, multilocularity in 54%, displacement of teeth and anatomic structures in 43%, cortical bone expansion in 51%, and cortical perforation in 38% of the cases. Paresthesia was reported in 6% of the cases.[5]

In the present case, well-defined unilocular radiolucency with internal structure showing evidence of wispy, ill-defined internal septae were evident. Expansion of the cortical plates with perforation and erosion of the lower border of the mandible was also present. Loss of lamina dura with respect to the involved teeth was noted. However, there was no resorption of the roots of the involved teeth. The presence of a subtle granular bone pattern at the periphery of the expanded bone and in some of the internal septa is an imaging feature of CGCG in CT scans.[1] However, in contrast, CT image of the present case did not show any evidence of granular bone pattern.

Microscopic examination of giant cell granulomas shows numerous multinucleated giant cells and mononuclear cells (fibroblast and histiocyte-like cells and monocyte-macrophages) within a prominent fibrous stroma. The size and number of giant cells correspond to their aggressiveness. It has been suggested that the aggressive variant of CGCG shows the presence of a high number of giant cells, an increased mitotic activity, and a high fractional surface area.[3] The present case demonstrated osteoclast-like multinucleated giant cells with large, numerous nuclei in a spindle cell stroma, along with areas of hemorrhage. There was no evidence of cellular atypia or increased mitosis.

The radiographic appearance of CGCG is not pathognomonic. Therefore, a differential diagnosis of ameloblastoma, aneurysmal bone cyst, odontogenic myxoma, traumatic bone cyst, odontogenic cysts, and brown tumors of hyperparathyroidism may be suggested. Since the present case involved the posterior mandible with cortical expansion and perforation, the suspicion of ameloblastoma was high. Ameloblastoma is usually seen in older age group and presents as a unilocular radiolucency with coarse, curved internal septae. A younger age group and the presence of wispy ill-defined internal septae in the present case were not in favor of ameloblastoma.

Aneurysmal bone cyst usually presents in the posterior mandible as a multilocular radiolucency with ill-defined filamentous septae and shows a greater degree of cortical expansion. It has comparatively a rare incidence. Odontogenic myxoma usually is multiloculated with sharper and straighter septae. In addition, usually a missing or an impacted tooth is associated with myxoma, which was not a finding in the present case.

Traumatic bone cyst presents as a well-defined unilocular radiolucency with smooth borders. The internal structure is totally radiolucent without any true septae. The lamina dura of the involved tooth remains intact, and the lesion shows only minimal cortical expansion. Odontogenic cysts may be ruled out since they produce a smooth cortical bone expansion and shows no presence of internal bony septae. Brown tumors of hyperparathyroidism usually present as multiple radioluencies within a single bone. They have well-defined margins with very subtle and ill-defined internal septa and produce cortical expansion. Estimation of serum calcium, parathyroid hormone, and alkaline phosphatase levels was necessary to rule out hyperparathyroidism.

These differentiations were critical as a conservative line of management can be followed in CGCG due to its less aggressive nature and low recurrence rates as compared to ameloblastoma, aneurysmal bone cyst, and odontogenic myxoma, where a radical line of management is preferred.

The treatment of CGCG ranges from curettage to resection. In patients with aggressive tumors, alternatives to surgery include intralesional injection of corticosteroids, calcitonin, bisphosphonates, and interferon alfa-2a.[12] In the present case, a conservative approach with enucleation and curettage followed by bone grafting of the defect was performed.

Recurrence is a feature of the aggressive type of CGCG. Recurrence rates in CGCG have been reported to range between 11% and 49%. An increased risk of recurrence is attributed to the clinical activity of the lesion, younger patients, demonstrated perforation of cortical bone and tumor size.[3] In the present case, as some features of aggressive behavior were evident, the chances
of recurrence cannot be ignored. Hence, a regular follow-up was necessary in this case.

**Conclusion**

CGCG in the posterior aspect of the mandible is a rare incidence. Considering the aggressive clinical progression and high recurrence potential, a prompt diagnosis and proper management with regular follow-up is necessary.

**References**