Central Giant Cell Granuloma : Case Report of a Rare Presentation

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Abstrcat

Central giant cell granuloma is a non neoplsatic lesion which exhibits a spectrum of clinical behavior ranging from non aggressive to aggressive variants. It is defined as an intraosseous lesion consisting of cellular fibrous tissue containing multiple foci of hemorrhage and aggregation of multi nucleated giant cells. These lesions may sometimes lead to a confusion in their diagnosis as many pathologists report them taking in to consideration one of the prominent histopathologic feature. These confusions may be because of the smaller number of cases reported in the literature with uncertain clinical radiographic and histopathologic features of these lesions. The case reported here resembled a wide variety of conditions that led to a misdiagnosis on clinical and radiographic examination but was histopathologically diagnosed as CGCG. This paper presents a case of CGCG involving the anterior mandible in a young male patient with clinical, radiological, histopathological and surgical aspect of the lesion. The striking feature of the present case is its aggressive nature and the presence of an impacted canine in the lesion which led to misdiagnosis of the pathology.

Key words: Central giant cell granuloma, multinucleated giant cells, spindle shaped cells, curettage.

Key Message: The central giant cell granuloma is a relatively uncommon pathological condition accounting for less than 7% of all benign lesions of the jaws. The clinical behavior of CGCG of the jaws is variable and difficult to predict. We describe a case of central giant cell granuloma to highlight the importance of histopathology in the diagnosis of this enigmatic lesion.

Introduction

The central giant cell granuloma is considered to be a benign intraosseous jaw lesion of unknown etiology. Recently the World Health Organization has defined it as localized benign but sometimes aggressive osteolytic proliferation consisting of fibrous tissue with haemorrhage and haemosiderin deposits, presence of osteoclast- like giant cells and reactive bone formation.[1]

The central giant cell granuloma occurs predominantly in children or young adults according to nearly all reported series, is somewhat more common in females than in males the ratio being approximately 2:1.[2] Either jaw may be involved, but the mandible is affected more often and lesions often cross the midline.[2,3,4] CGCG usually is an asymptomatic lesion, which may become evident during routine radiographic examination or as a result of painless but visible expansion of the affected jaw. Cortical plates are thinned but perforation in to the surrounding soft tissue is rare. Radiogrphiclly central giant cell lesions present as radiolucent defects, which may be unilocular or multilocular. [5] The defect usually is well circumscribed and, in some cases, displacement of teeth can be found. The appearance of giant cell granuloma is not pathognomonic and small radiolucent lesions can be confused with periapical cysts and multilocular giant cell lesions cannot be distinguished radiographically from amelolastomas or other multilocular lesions.[2,6,7] Central giant cell lesions of the jaws are categorized on the basis of radiographic and clinical features. Aggressive and nonaggressive lesions have been described, with the likelihood of recurrence a feature of aggressive lesions.[6,7] In addition, the aggressive lesions are found in younger patients, grow quickly, cause pain and induce root resorption and bone perforation.[8] Studies have failed to identify any biochemical or histologic differences between the aggressive and nonaggressive variants.[9,10] Giant cell lesions of the jaw exhibit a variety of histopathological features. Common to all lesions is the presence of multinucleated giant cells in a background of collagenous stromacontaining spindle cells. The giant cells are frequently aggregated around numerous vascular channels with in the lesion.[7] A patchy distribution of cellular elements is one feature that helps differentiate CGCG from true giant cell tumors, which are more homogeneous. The histopathologic findings closely resemble, and may be identical with, those seen in cherubism, the aneurysmal bone cyst and the brown tumor of hyperparathyroidism.

The traditional treatment of CGCG has been local curettage. However aggressive subtypes of CGCG show a tendency to recur and necessitate bone resection that may determine extensive defects in jaws.[11] This is particularly mutilating in a growing child or young adult. Intralesional corticosteroid injections are good alternative to surgery in the treatment of CGCGs.[12] A case of central giant cell granuloma is reported in which the clinical and radiographic features were misleading, diagnosis being made, based on the histopathology.

Case Report

A 20 year old male presented to the oral surgery unit of the dental department of VCSGGMS& RI in September 2009 with the complaint of swelling in the front lower jaw since one year. One year before the patient had felt mobility in lower right canine, which he got extracted at a local dentist. The swelling was insidious in onset, slow growing, hard and associated with intermittent pain. There was no history of trauma, neurological deficit, fever, loss of apetite, loss of weight. There were no similar swelling present in any other parts of the body. Medical history and family history were non contributory. The patient did not report of any deleterious oral habits. On extra oral examination a single diffuse swelling

was seen on the anterior mandible involving the entire chin. The lesion was 4×4 cms and hard on palpation covered with normal skin. The swelling was firm in consistency, showed no secondary changes and was slightly tender on palpation. Intra oral examination revealed fair oral hygiene with expansion of buccal cortical plate extending from right lower second premolar region to left first premolar region, obliterating the buccal sulcus and mucosa covering the swelling was intact. The lower border continuity of the mandible was maintained with a mild bulge in the symphysis region. 42, 41, 31, 32, 33 were displaced towards the right side. There was no discoloration of teeth and were non tender to percussion. Mouth opening was 40 mm. Based on the history and clinical examination AOT, fibrous dysplasia, Calcifying epithelial odontogenic cyst (CEOC) were considered in the differential diagnosis.

Radiographic examination revealed a well defined unilocular radilolucency extending from right second premolar region to left first premolar region. The striking feature was the presence of an embedded canine like tooth in the left parasymphysis region, for which dentigerous cyst and ameloblastoma were also considered in the differential diagnosis. Displacement of the roots of the involved teeth was also seen. Intra oral aspiration was attempted with a wide gauge needle under local anaesthesia but it did not yield any aspirate.

After the investigations were carried out, CEOC and fibrous dysplasia were ruled out. An unproductive aspirate ruled out cystic lesions like CEOC and dentigerous cyst. The absence of characteristic ground glass appearance in the radiograph and the presence of a radiolucent lesion eliminated fibrous dysplasia from the diagnosis. Negative aspiration did not rule out AOT because the lesion may or may not be associated with aspirate. AOT was still considered in diagnosis based on the fact that lesion may appear completely radiolucent or a mixed radiolucent radiopaque radiographically.

Routine haemogram and urine examination were normal. Serum levels of calcium, phosphorous and alkaline phosphatase were advised which were found to be within normal limits, thereby excluding the possibility of hyperparathyroidism. Biopsy was planned under local anaesthesia. The cortex was intact but thinned out completely. On entering the area, we found the lesion to be a friable, readily bleeding solid mass. The whole lesion was removed in one piece along with the impacted tooth. The specimen was sent for histopathological examination, which revealed numerous multinucleated giant cells which were distributed in a stroma that was highly cellular comprising both spindle shaped and round cells and were found mostly in the areas of haemorrhages. The giant cells were numerous and distributed randomly, the nuclei mainly confined to the center of the cells leaving a clear zone of cytoplasm at the periphery. These findings were consistent with the diagnosis of central giant cell granuloma.

Discussion

Central giant cell granuloma was first described by Jaffe in 1953. [13] He described the lesion as a response to injury and designated it as central giant cell reparative granuloma. In recent years the word reparative has been deleted from the term, since it is realized that many of these lesions are more destructive than reparative.The etiopathogenesis of CGCG of jaw bones has not been clearly established but it has been suggested that it is the result of an exacerbated reparative process related to previous trauma and intraossous haemorrghage that triggers the reactive granulomatous process.[14,15] Donoff and Rosenberg discussed a case report of an uncomplicated extraction because of pericoronitis in the area of the lesion and claimed the local changes in the blood flow throughout the bone and local bone dysplasia could be probable etiologic factors.[16] Unal et al presented a 12 year old girl CGCG in the mandible caused by a molar tooth extraction and explained the pathogenesis by a traumatic etiology.[17] In our case, we can assume that the tooth extraction was probable inciting injury since the lesion was evident and grew rapidly only after the tooth extraction.

When those giant cell- containing lesions of bone such as hyperparathyroidism, fibrous dysplasia, the giant cell granuloma and a related lesion, the aneurysmal bone cyst are properly categorized there still remains a very aggressive group of lesions, and it is these which have been classified as true giant cell tumors of bone with both a benign and malignant form being recognized. [2] Jaw lesions of CGCG are frequently compared with giant cell tumors of other tissues due to the similarity in histologic appearances of these lesions.[18]

Giant cell tumor, giant cell granuloma and brown tumor of hyperparathyroidism have different histological features and clinical entities. The histologic criteria are that the number of stromal nuclei distribution of giant cells is somewhat helpful in differentiating between the GCT and GCG.[5] Histologically, CGCG have a hemorrhagic background with presence of plump bland fibroblasts, haemosiderin and fewer giant cells with smaller number of nuclei which are less uniformly distributed. While in case of GCT, giant cells are uniformly scattered and have a larger number of nuclei and absence of fibroblasts and haemorrhage. Diffuse sheets of large giant cells and polygonal mononuclear cells seen in GCT are lacking in CGCG. Differentiation from brown tumor is based mainly on laboratory and clinical data as well as differences in the age of onset and multiplicity of lesions.

Unlike osteoblastoma and giant cell lesions of hyperparathyroidism, a great majority of cases with CGCG are found under 20 years of age and this may be helpful in differential diagnosis.[19] If the internal structure of the CGCG contains septa, the differential diagnosis may include ameloblastoma, odontogenic myxoma and aneurysmal bone cyst. If a granular internal structure is present, cemento ossifying fibroma may be considered. However, ameloblastoma tend to occur in an older age group and more often in posterior mandible and ameloblastomas have coarse, curved, well defined trabeculae, whereas giant cell granulomas have wispy, ill defined trabeculae, some of which are at right angles to the periphery. Odontogenic myxomas occur in older age group, may have sharper and straighter septa and do not have the same propensity to expand as do giant cell granulomas. Aneurysmal bone cysts are comparatively rare lesions that occur more often in the posterior aspect of the jaws and usually cause profound expansion. Evidence of displacement or resorption of the adjacent teeth or expansion of the outer cortical bone differentiates it from simple bone cysts.[3]

Although CGCG is a benign osseous lesion, some authors separate CGCG in to two types, referring to its clinical and radiographic features: (a) Nonaggressive lesion is usually slow growing and asymptomatic; does not show cortical resorption by the lesion or root perforation in teeth affected, and it is significantly less likely to recur than the aggressive type [8] ; and (b) Aggressive lesions, is usually found in younger patients and is painful, grows rapidly, is larger overall, often causes cortical perforation and root resorption and has a tendency to recur. [5] Prediction of the behavior of CGCG that will exhibit a higher risk of recurrence after treatment has been problematic. The most reliable factors related to an increased risk of recurrence include clinical activity of lesions (72% of recurrence in the aggressive forms, 3% of recurrence in the nonaggressive forms), younger patients, demonstrated perforation of cortical bone and tumour size.[20,21] Chuong and colleagues compared the nonaggressive and aggressive variants and discovered a greater fractional surface area occupied by giant cells and larger relative size of giant cells in aggressive lesions. [5] An attempt to differentiate between aggressive and non naggressive lesions via nuclear DNA analysis has failed.[9]

The radiographic appearance of CGCG is variable. Usually the lesion appears as a unilocular or multilocular radiolucency. It may be well defined or ill defined and shows variable expansion and destruction of the cortical plate. The radiologic appearance of the lesion is not pathognomic and may be

confused with that of many other lesions of the jaws. The final diagnosis eventually rests on histopathology because the clinical and radiologic features are not specific.

The management of CGCG traditionally has been accomplished via surgical removal of the lesion. Some authors recommend en bloc resection including uninvolved bone; others, however, prefer conservative surgical treatment via simple curettage or curettage with peripheral ostectomy[8], because these lesions lack the characterstic of malignant tumors. Unal et al recommended microdrill with diamond burr to obtain margins of security after removing the lesion and filled the cavity with iliac crest chips.[17] Becelli et al described a case treated by means of excision of a mandibular CGCG, reconstruction using autogenous iliac crest graft, dental implants and overdenture prosthesis.[22] Resection of CGCG results in a major defect to the patient. This is of great concern especially in children and young adults with developing dentition and jaws. Non surgical approaches have been introduced, as administration of intralesional corticoids[23] or systemic calcitonins that inhibit the osteoclastic activity[24]. Other non surgical treatments include interferon- alpha or bifosphonates. [20] In our case curettage and enucleation has been applied and no signs of recurrence have been seen at the end of two years follow up.

Conclusion

Because of the lesser number of cases reported in the literature and no specific clinical and radiological features, histopathologic examination remains the main stay of diagnosis of these lesions. Clarity to this entity with respect to terminology, behavior and its adjunctive nature to other similar lesions of the jaws still remain doubtful. The present case highlights the difficulty in diagnosing CGCG just on the basis of clinical and radiographic features and emphasizes the histopathology as the main diagnostic tool.

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Legends

Fig. 1 : Patient showing mandibular swelling.
Fig. 2 : Radiograph showing radiolucent lesion with impacted tooth.
Fig. 3 : Mass removed from oral cavity.
Fig. 4. : Lesion removed in toto.
Fig. 5 : Cavity formed after removal of the lesion.
Fig. 6 : Photomicrograph showing multinucleated giant cells with spindle round cells and blood vessels. 10X.
Fig. 7 : Photomicrograph showing multinucleated giant cell 40X.

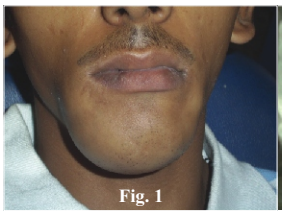
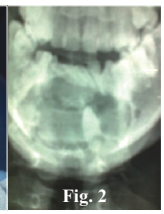


Fig. 1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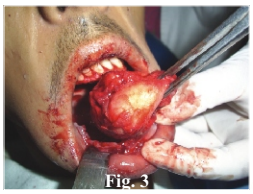
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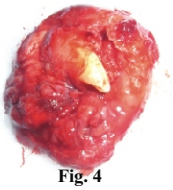
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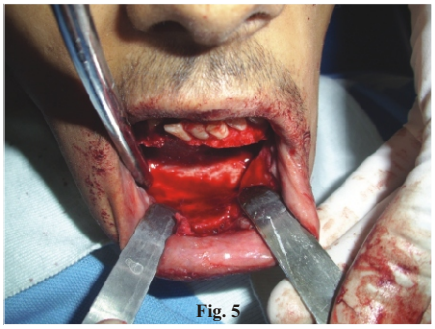
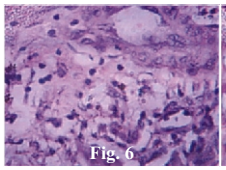


Fig. 5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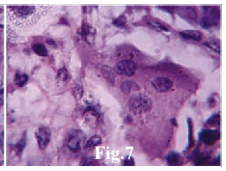
Fig. 7