Case Report

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Aggressive Central Giant Cell Lesion Involving Anterior Mandible

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Abstract

Central giant cell granuloma is an uncommon benign intraosseus lesion of jaws. It is benign proliferative lesion having incidence of approximately 7% of all benign tumors of the jaws. It affects females more often than males, in a 2:1 ratio and is seen most frequently under the age of 30 years. It may present as asymptomatic non- aggressive lesion or as aggressive lesion leading to pain, expansion and perforation of the cortex, root resorption and reoccurrence. Here we are reporting a case of aggressive central giant cell lesion involving anterior part of mandible crossing mid line.

Keywords: Aggressive; Multilocular Radiolucency; Reparative; Jaws.

Introduction

Central giant cell granuloma (CGCG) is an uncommon benign proliferative lesion mostly involving jaws. Its incidence is approximately 7% of all benign tumors of the jaws [1]. It affects females more often than males, in a 2:1 ratio and is seen most frequently under the age of 30 years. Mandible is involved more often than maxilla with a ratio of 2:1 to 3:1 [2]. It shows a variable clinical and radiological behavior. It may present as asymptomatic non- aggressive lesion or as aggressive lesion leading to pain, expansion and perforation of the cortex, root resorption and reoccurrence [3]. Cases of CGCG occurring with neurofibromatosis (Type 1), Noonan-like syndrome have been reported. The treatment of CGCG includes simple curettage or resection for lesions. Corticosteroids and calcitonin are used for non-surgical management [4]. Here we are reporting an aggressive form of central giant cell lesion in anterior part of mandible crossing midline.

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Case Report

A 35 year old female came to the department, with a chief complain of swelling in chin region since last 7 months and pain same region 1 month. History of present illness revealed that patient first noticed swelling in chin region was insidious inonset and painless. Swelling progressed slowly from a small size to the present size. There was noaggravating or relieving factors.After 6 months pain started in same region which was mild in intensity used to aggravate on mastication and relived by itself. There was no history of trauma. History of fever orparesthesis was also absent. Past medical history was not significant.

On extraoral examination, facial asymmetry was present due to solitary selling in mental and submental region. Swelling was oval in shape of approximately 5 x6 cm in size having well defined margins. Skin overlyingswelling was of normal color and smooth. Swelling was extending superiorly till 0.5 cm below lower liplaterally till mid of body of mandible on both sides and inferiorly till 3cm below inferior border of mandible (Figure 1,2). On palpation,inspectory findings were confirmed. Temperature over swelling was normal. It was slightly tender and was bony hard in consistency. It was non-compressible, nonfluctuant. Lymph nodes were nonpalpable.

Intraoral examinationrevealed mouth opening

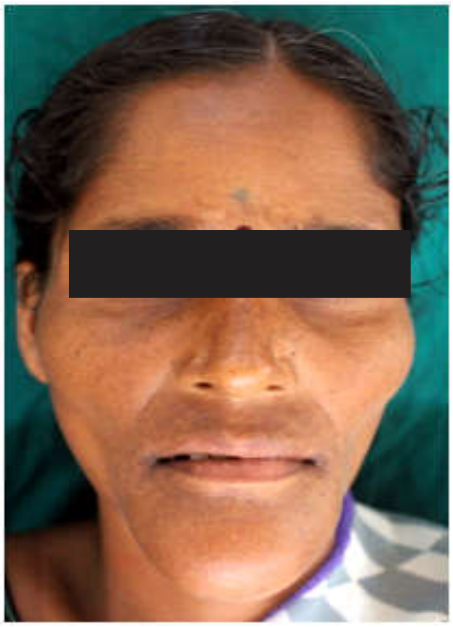

Fig. 1: Asymmetry of face

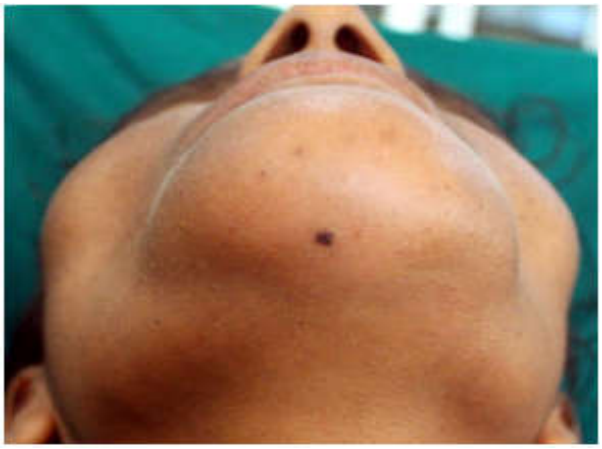

Fig. 2: Solitary swelling in mental and submental region

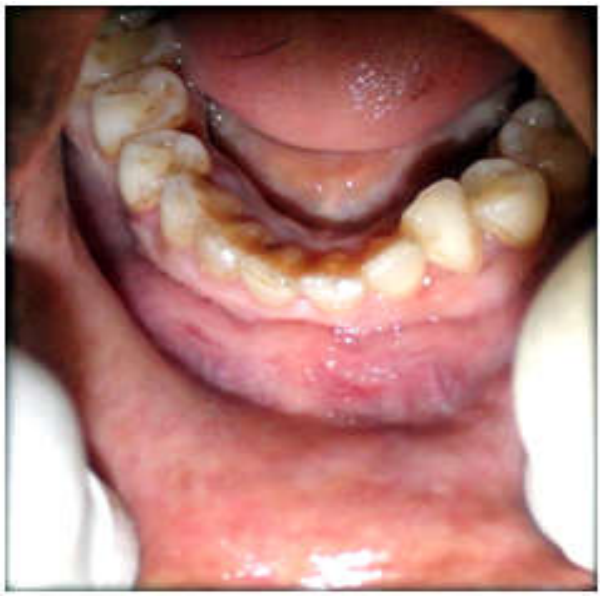

Fig. 3: Vestibular obliteration in relation with lower anterior teeth

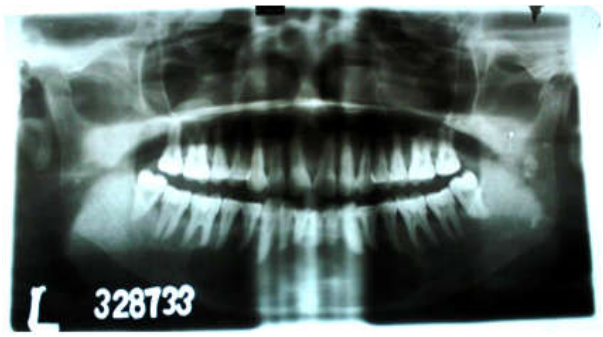

Fig. 4: Orthopantomograph

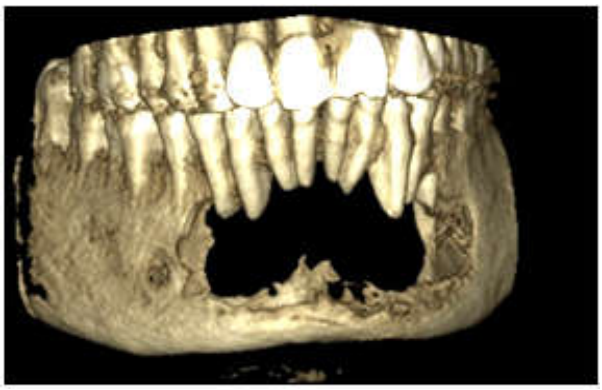

Fig. 5: 3D construction of CBCT scan

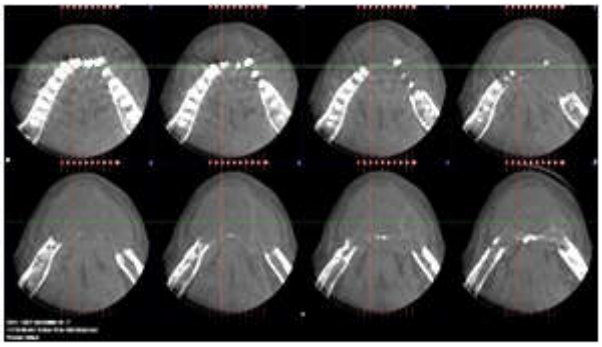

Fig. 6: Axial section

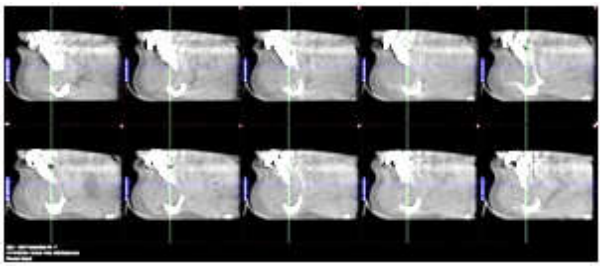

Fig. 7: Coronal section

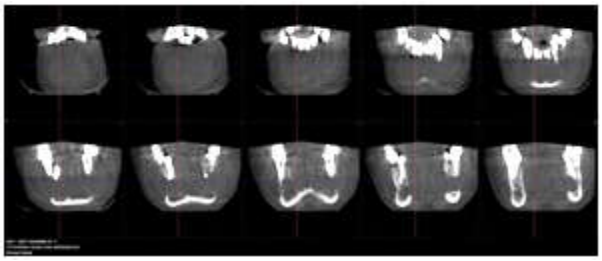

Fig. 8: Sagital section

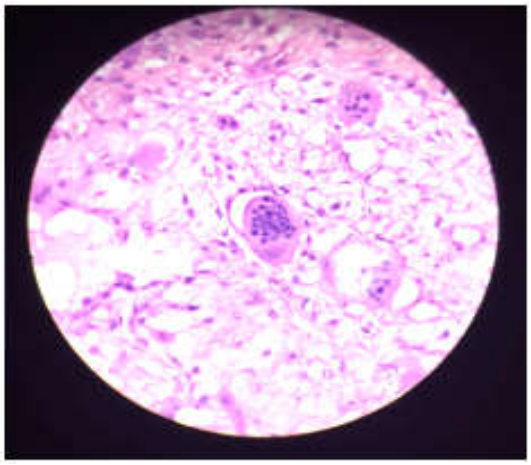

Fig. 9: Multinucleated giant cells under 40X magnification

was normal. Vestibular obliteration was seen in relation with first premolar in right side till first premolar in left side. Mucosa over vestibule was having normal color. On palpation, tenderness was present. Cortical plate expansion was present in both buccal and lingual sides. 33 were tilted lingualy (Figure 3). Other findings were normal.

Based on these findings provisional diagnosis of benign lesion involving anterior mandible was given. Differential diagnosis included Central giant cell granuloma, Ameloblastoma and odontogenic keratocyst. Investigations included orthopantomograph with showed well defined radiolucency in the mandibular anterior region crossing the midline, measuring approximately 6 x 2.5cm in size, extending mediolaterally from mesial root of 46 in left side and till 35 in right side. No evidence of cortication was seen and internal structure was completely radiolucent. Resorption of roots was seen (Figure 4).

Further, CBCT scan was taken which showed extensive osteolytic lesion in anterior mandible crossing mid line. Axial sections showed complete loss of buccal and lingual plates(Figure 5,6,7,8). Incisional biopsy was taken which showed widely spaced multinucleated giant cells separated by variable cellular stroma composed of spindle cells with normal to ovoid nuclei(Figure 9). Thus final diagnosis of central giant cell lesion was given.

Treatment included segmental resection of mandible from 36 to 46 with reconstruction using reconstruction plates.

Discussion

Central giant cell granuloma is a benign lesion affecting the mandible and maxilla that consists of a massive fibrohistiocytic proliferation with numerous heavily hemosiderin laden multinucleated giant cells. It was first described as 'Central Giant Cell Reparative Granuloma' by Jaffe H L in the year 1953. Currently the term 'reparative' is not used for description because of the destructive nature of the giant cell granuloma [5]. Later, World Health Organization has defined it as localized benign but sometimes aggressive osteolytic proliferation consisting of fibrous tissue with hemorrhage and hemosiderin depo-sits, presence of osteoclast-like giant cells and reactive bone formation [6].

Etiopathogenesis

Exact Etiopathogenesis is still clearly not known but etiology is considered to be multifactorial having local, systemic factors as well as possible mutations described in exons 3, 4, 9 and 11 of SH3BP2 gene. But it found that there is association only with exon 4 and the remaining ones would be more related to cherubism, in the study by Teixeiraet al.Local factors comprises of trauma and vascular damage, which produce intramedullary hemorrhageand intraosseous replacement fibrosis. Among the systemic causes, itis associated with neurofibromatosis type I, Noonamsyndrome, Ramon syndrome, Jaffe–Campanacci syndrome, pregnancy and hormonal disorderssuch as hyperparathyroidism [7].

Earlier pathogenesis was thought to represent a reparative response to intrabonyhaemorrhage and inflammation, when it was once as a reactive lesion. Another theory is the vascular hypothesis that suggests that CGCG belongs to the spectrum of mesenchymal proliferative vascular primary jaw lesions in which angiogenesis is modulated by several cytokines and growth factors. Vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) that are produced andreleased from activated monocytes and macrophages are the most potent inducers of angiogenesis [4].

Giant cell lesions may also represent pathologic variations of osteoclastogenesis, though their mechanisms are less well understood. Point mutations in gene SH3BP2 is responsible for an increase in the activity of osteoblasts and osteoclasts. In this process, the gene SH3BP2 influences the regulation of the parathyroid hormone (PTH) and PTH-related protein (PTHrP) receptors. This mediates a reduction inthe expression of osteoprotegerin in dental follicle cells, which promotes osteoclastogenesis. There is also the possibility that the mutation in the gene SH3BP2 may exert some influence on the MSX-1 gene involved in regulating

dental development. Accordingly, the development ofCGCG may be associated with an imbalance of MSX-1, which could lead to a failure in osteoclast differentiation [8].

Clinical Features

It is seen in all age groups ranging from 2 to 80 years, but more than 60% of the cases occur under the age of 30 years. Female predilection is seen, almost twice female are affected more that of males. Either of jaw may be involved but mandible is more common than maxilla also many studies have showed that the lesions are more common in the anterior segments of the jaws and can even cross the midline. Occasionally they may present in the facial bones and small bones ofhand and feet. CGCGs can be aggressive or nonaggressive [9]. According to Chuong et al, aggressive giant cell lesions were defined as exhibiting size greater than 5 cm as well as rapid growth, tooth displacement, root resorption, cortical bone thinning or perforation or recurrence after curettage, equal to or greater than 5 cm and/or that recurred after curettage [10].

The nonaggressive form may present withasymptomatic swelling or may be discovered accidentally during routine radiological investigations. The aggressive form of CGCG presents with pain,rapid growth, cortical perforation and root resorption [11].

Radiological Features

The radiographic appearance of CGCG is not specific as it changes with the size of the lesion. It usually produces well-defined radiographic margins with no evidence of cortication. Small lesions usually appear to be unilocular radiolucent and deprived of internal bone septa. However, large lesions usually appear to be multilocular radiolucent and wispy like bony septae in this area. If these subtle granular septaemanate at right angles from the periphery of the expanded bone, gives characteristic feature of lesion. It often displaces and resorbs teeth [12,13].

Differential Diagnosis

The clinical differential diagnosis for a solitary or multilocular CGCG includes ameloblastoma, odontogenicmyxoma, and odontogenickeratocyst. For patients in the characteristic young age range for CGCG, ameloblastic fibroma, ossifying fibroma, and adenomatoidodontogenictumor can be included. Diagnosis can be confirmed by histopathologic investigation but if the lesion is located anterior to the permanent molars and possibly crossing midline, with a multilocular radiographic pattern with the patient under 30 years of age, a diagnosis of CGCG can be considered [7,14].

Histological Features

Histologically, these lesions are characterized by the presence of numerous multinucleated giant cells embedded in a fibrocellularstroma often found adjacent to blood vessel walls. There is a deposition of hemosiderin, extravasted RBC's, foci of osteoid material dystrophic calcification around the periphery of the lesion.The multinucleated giant cells may be large or small in number, and they may be irregular or round cells that contains more than 20 nuclei which are responsible for bone resorption and local progression of the lesion. Macrophages, mesenchymal cells and fibroblasts are accountable for the growth of the lesion [15,16].

The microscopic appearance of GCGC is almost identical to that of the giant cell lesion associated with hyperparathyroidism. Thus it should be differentiated on the basis of biochemical

tests. Elevated serum levels of parathyroid hormone are indicative of primary hyperparathyroidism [17].

Treatment

The management of CGCG can include conventional surgery treatment including resection in-bloc for the aggressive variant and surgical curettage for non-aggressive lesions. Conservative therapy includesintralesional injection of corticosteroids, calcitonin, bisphosphonates and Interferon-2a [18,19].

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