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ORIGINAL RESEARCH

Central Giant Cell Granuloma of the Jaws: A Short Series and Review of Literature

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ABSTRACT

Introduction: Central giant cell granuloma (CGCG) accounts for less than 7% of all lesions of the jaw. It occurs more commonly in the anterior mandible compared to the maxilla. Females have 2 to 3 times higher incidence. Children and young adults are affected the most.

Materials and methods: The present series reviews 10 cases of CGCG suspected on clinical and radiologic basis and confirmed by histopathologic examination.

Results: The age of 10 cases ranged from 7 to 32 years (mean age 19.8); there were six females and four males; six had lesion in the lower jaw and the remaining four in the upper jaw. After radiologic evaluation, the treatment involved surgical curettage which was subjected to histopathologic examination and diagnosed as CGCG.

Conclusions: CGCG is diagnosed by a combination of clinical and radiologic findings and confirmed by histopathology. The condition needs to be distinguished from other giant cell containing lesions. The early and precise diagnosis of CGCG allows conservative management with minimal risk to the adjacent tooth or bone.

Keywords: Central giant cell granuloma, Peripheral giant cell granuloma, Reparative granuloma, Mandible, Maxilla, Jaw.

INTRODUCTION

Giant cell granuloma (GCG) as an entity was first introduced by Jaffé[1] in 1953 to distinguish it from giant cell tumor (GCT) of the bone. He established two pathological entities in this regards, the central giant cell granuloma (CGCG) arising within the bone and the peripheral giant cell granuloma (PGCG) arising in the soft tissues. CGCG, also termed as reparative giant cell granuloma, is an uncommon benign intraosseus lesion that occurs most often in the jaws—more so in the mandible than the maxilla, and much less often at extragnathic sites.[2,3] Etiopathogenesis of these lesions has remained unclear—some consider them as reparative response rather than neoplastic condition while others consider them as neoplastic with potential to progress sometimes.[4-6] However, their histology and clinical behavior have been studied in depth.

The CGCG of the jaw accounts for approximately 7% of all tumors of the jaw.[5] It may occur at any age but is more commonly seen in the first three decades of life.[6] The usual clinical presenting feature is of a painful or painless red purple nodule located in the region of gums or edentulous alveolar margins. Approximately one-third of the CGCGs are located in the anterior mandible in the incisor, canine and premolar regions.[5] CGCG of the jaw is usually unifocal and has traditionally been treated surgically, the common therapy being curettage or resection.[7] The clinical behavior of CGCG varies from a slow-growing asymptomatic swelling to an aggressive lesion that manifests with pain, cortical perforation and root resorption.[8]

The present short series of CGCG highlights the clinico-radiologic aspects and emphasizes the role of histopathology in its differential diagnosis from other morphologically similar conditions and in determining its clinical behavior.

MATERIALS AND METHODS

The study was conducted jointly by the Department of Pathology, Pt BD Sharma PGIMS, and Department of Oral and Maxillofacial Surgery, Government Dental College and Hospital, Rohtak, by retrieving archival case records and histopathologic slides of all cases diagnosed as CGCG of the upper or lower jaw during the preceding 2 years. A total of 10 cases were accessioned during this period. Their clinical features were compiled and radiologic/CT findings recorded. Slides of biopsies submitted in each case were reviewed and special stains (such as Perl's stain for iron, Masson's trichrome and Van Gieson for collagen, Verhoeff's for elastic fibers) were done, wherever required.

RESULTS

The clinical profile and radioimaging features of the patients are given in Table 1. The age of patients ranged from 7 to 32 years (mean age 19.8 years) with male: female ratio of 2:3. In six cases, the lesion was located in the mandibular region while maxilla was

Table 1: Clinical profile and radiological features of cases of CGCG (n = 10)

Case no.	Age/sex	*Location of lesion*	*Duration*	*Clinical features*	*Clinical diagnosis*	*Imaging features*
1	30/F	Left maxillary anterior region	4-5 months	Painless, soft, pedunculated swelling, recent increase in size	Odontogenic cyst	IOPA: Periapical pathology wrt tooth number 23
2	18/M	Left mandibular anterior region	5 months	Painless, pedunculated, soft tissue overgrowth, size 1 × 2 cm	Ameloblastoma	IOPA: Involvement of tooth number 123
3	20/F	Right maxillary palatal region	4 months	Diffuse, nontender hard swelling, causing expansion of bone	Benign odontogenic tumor	Occlusal view: Multilocular lesions on right side of palate in 7-4 region
4	19/F	Right maxillary gingival region	1-1.5 months	Painless, nontender swelling	Giant cell granuloma	IOPA: Multilocular lesion with bony trabeculae in right maxilla with bony expansion
5	32/F	Left posterior mandibular region	6 months	Bony hard swelling, slightly tender on palpation	Ameloblastoma	OPG: A radiolucent lesion with slight radiopacity in center of the lesion extending from region 5-8
6	7/M	Right mandibular posterior region	1 month	Firm, hard swelling, subsides on taking medication; nontender on palpation	Neoplastic lesion	OPG: Radiolucent lesion with irregular margins in right mandibular posterior region
7	25/M	Left mandibular buccal vestibule	6 months	Nontender, pedunculated, erythematous mass, not fixed to the underlying structures	Fibroma	OPG: Mass 3 x 3.6 cm wrt 345
8	10/F	Right mandibular region	2 months	Pain and swelling	Myxofibroma	OPG: Radiolucent lesion with irregular margins
9	15/M	Maxillary anterior region	3 months	Pain, swelling in upper front teeth	Fibro-osseous lesion	CT: A fibro-osseous lesion present as swelling in the labial vestibule
10	22/F	Right mandibular vestibule from premolar to molar region	20 Days	Pain, swelling	Giant cell tumor	OPG: Multilocular well-defined noncorticated radiolucent lesion

IOPA: Intraoral periapical X-ray; OPG: Orthopantogram; CT: Computed tomography

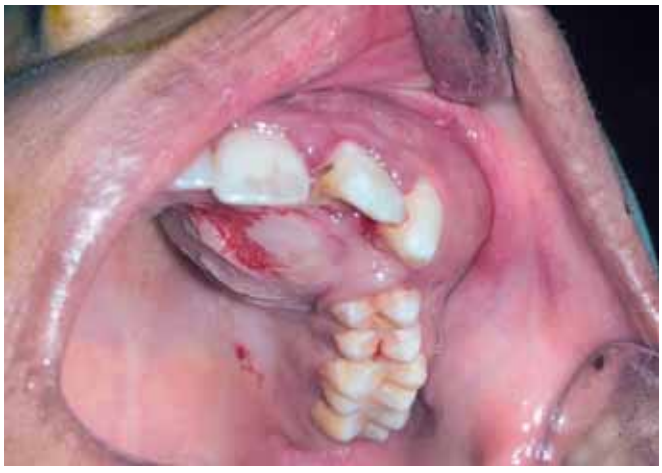


Fig. 1: Clinical appearance of lesion on left side of the palate in maxillary anterior region

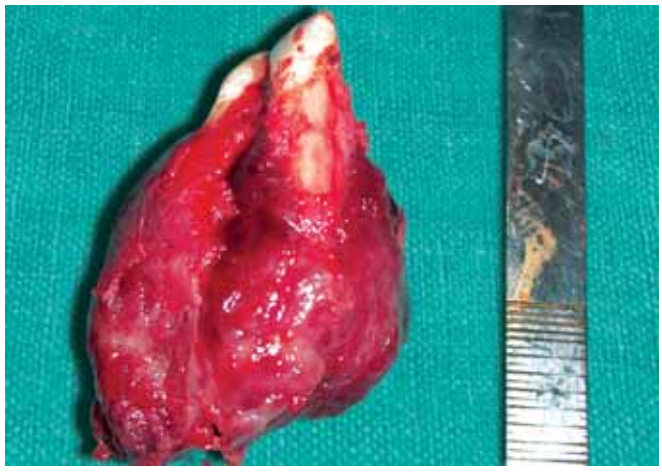


Fig. 3: Gross appearance of excised lesion, posterior view. The lesion measured 2 x 1 cm in size and was grayish-white and hemorrhagic

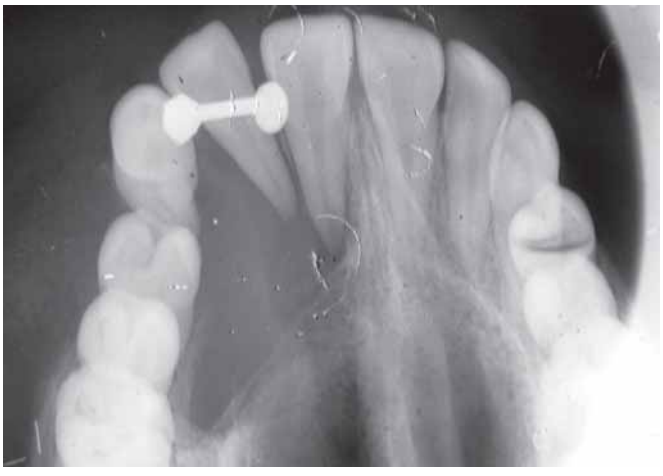


Fig. 2: Postoperative radiograph showing radiopacity in region after enucleation of lesion

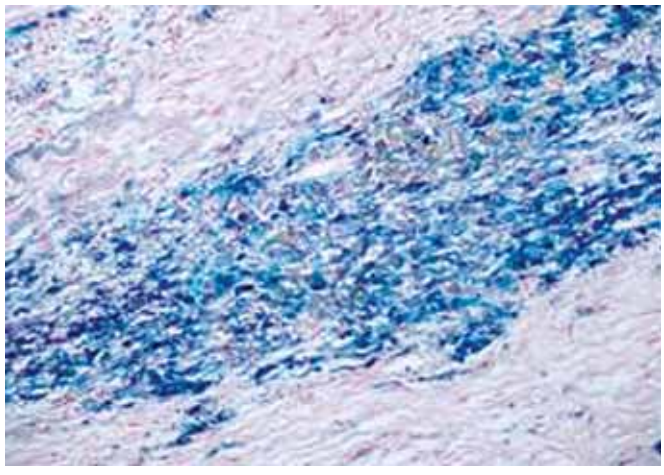


Fig. 4: Perl's stain to demonstrate hemosiderin pigment as Prussian blue color (×200)

Table 2: Detailed histopathologic features of cases of CGCG (n = 10)

Case no.	Stromal cells	Giant cells	Vascularity	Hemorrhage	Hemosiderin-histiocytes	Mitosis
1	Bland fibroblasts	+++	Moderate	Present	++	–
2	Plump fibroblasts	++	Moderate	Present	++	–
3	Bland fibroblasts	++	Moderate	Present	++	–
4	Young fibroblasts	++	Moderate	Present	++	–
5	Collagen	+	Less	Little	+++	–
6	Plump fibroblasts	++	Rich	Present	++	+
7	Collagen	+	Less	Absent	+++	+
8	Plump fibroblasts	++	Moderate	Present	++	–
9	Bland fibroblasts	+++	Moderate	Present	++	–
10	Young fibroblasts	++	Rich	Present	+	–

the site of involvement in remaining four cases. Most of the patients presented with painless swelling (60%) in the upper or lower jaw, insidiously growing over a period ranging from 20 days to 6 months (Fig. 1). There was no history of trauma or any systemic or local infection in any case. Tooth displacement and mobility were not evident in the same quadrant. Orthopantogram (OPG) and intraoral periapical (IOPA) radiographs were done in all cases, with computed tomograghy (CT) scan was done in a single case, in addition. The radiological findings revealed solitary well-defined, lytic, expansile and multilocular radiolucent lesion (Fig. 2). There was root resorption of adjacent teeth. However, there was no evidence of sclerosis or internal calcification and the matrix appeared clear. CT scan of one patient revealed a fibro-osseous lesion on the labial vestibule in the region of maxillary anterior teeth. Routine laboratory investigations did not show any abnormality in any case.

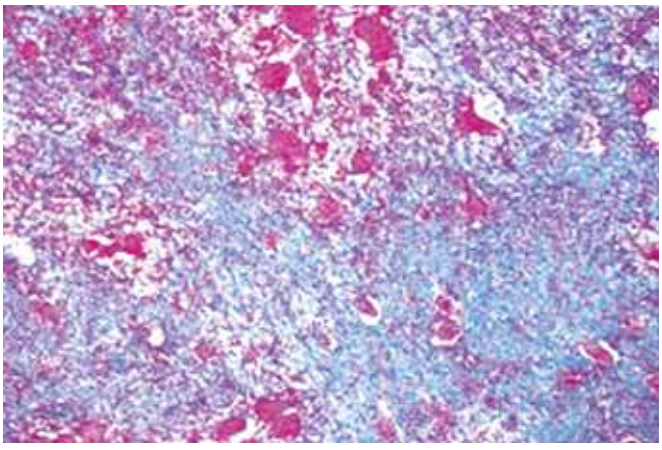


Fig. 5: Masson's trichrome stain showing blue color of collagen in the older lesion (×200)

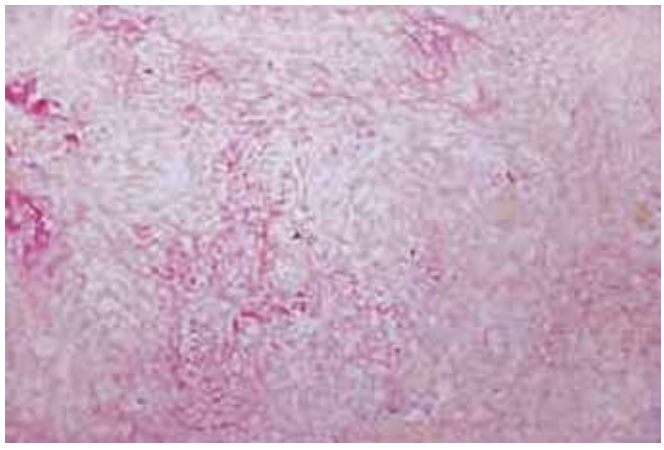


Fig. 6: Van Gieson stain imparts reddish color to collagen (×200)

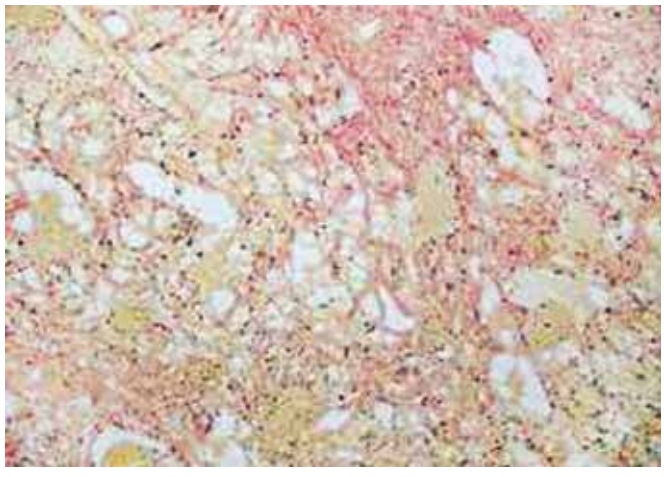
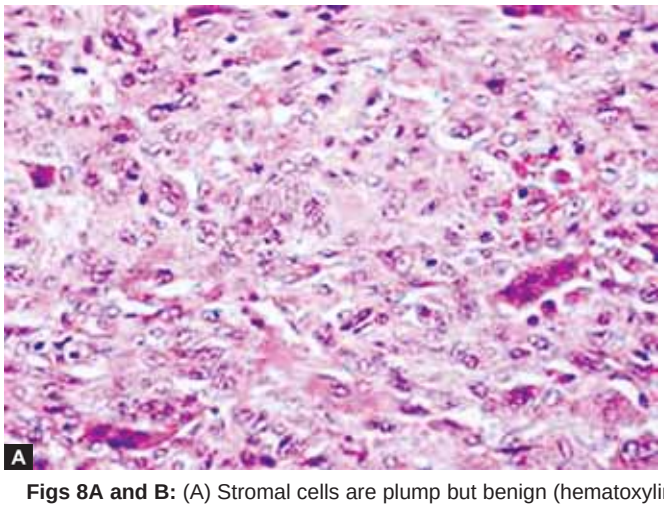
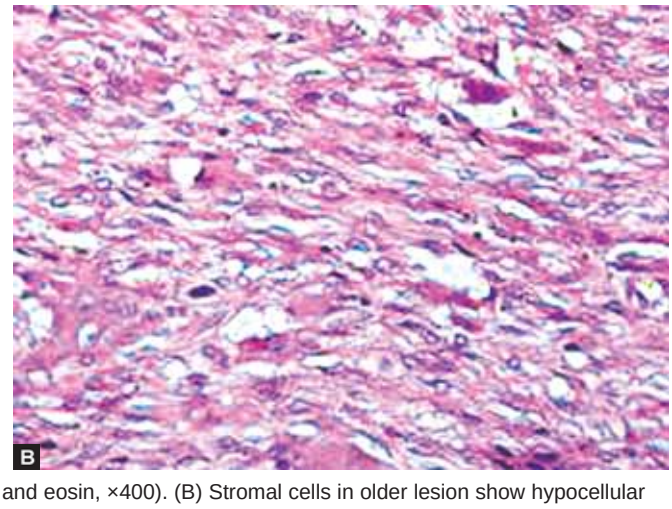


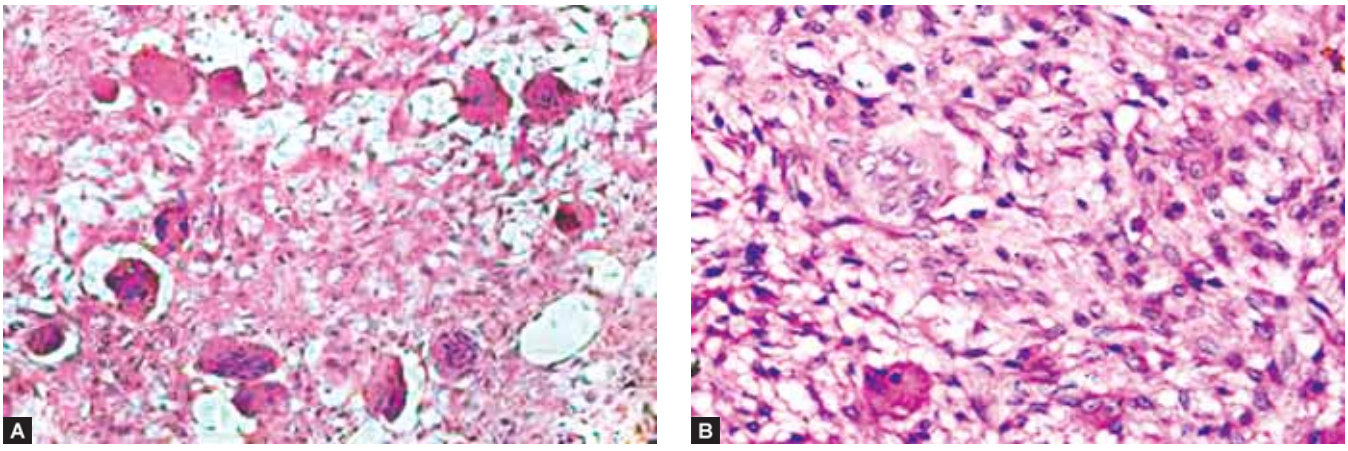
Fig. 7: Verhoeff's stain gives black color to elastic tissue (×200)



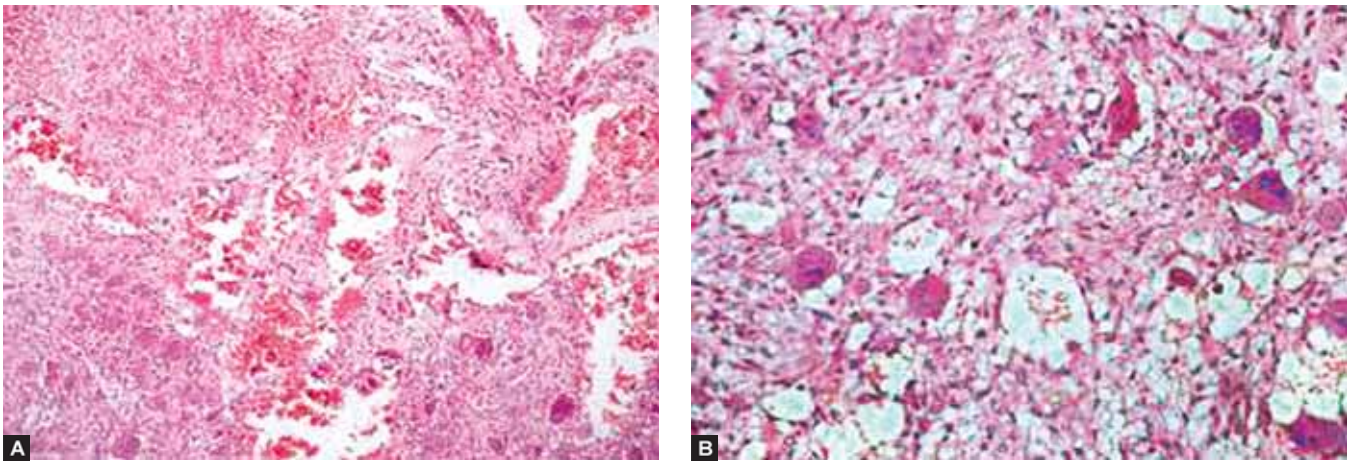


Figs 8A and B: (A) Stromal cells are plump but benign (hematoxylin and eosin, ×400). (B) Stromal cells in older lesion show hypocellular collagen (hematoxylin and eosin, ×400)

Surgical curettage was done in all the cases and submitted for histopathology (Fig. 3). Detailed histopathological features are summarized in Table 2. Special stains done in some cases included Perl's (Fig. 4), Masson's trichrome (Fig. 5), Van Gieson (Fig. 6) and Verhoeff's stain (Fig. 7). The parameters for histopathologic evaluation taken into consideration included stromal cells (bland or plump fibroblasts to hypocellular collagen) (Figs 8A and B), multinucleate giant cells (+ to +++) (Figs 9A and B), vascularity (less to rich) (Figs 10A and B), hemosiderin-laden macrophages (+ to +++) (Fig. 11) and mitoses (– or +) (Fig. 12). Based on these parameters, it was found that none of the 10 cases had abnormal mitotic activity.



Figs 9A and B: (A) Numerous multinucleate cells (4+) are seen in this photomicrograph (hematoxylin and eosin, ×200). (B) A few giant cells lying in the background of benign stroma graded as 1+ (hematoxylin and eosin, ×200)



Figs 10A and B: (A) The filed shows rich vascularity of the lesion (hematoxylin and eosin, ×200). (B) Only a few vascular channels are seen (hematoxylin and eosin, ×200)

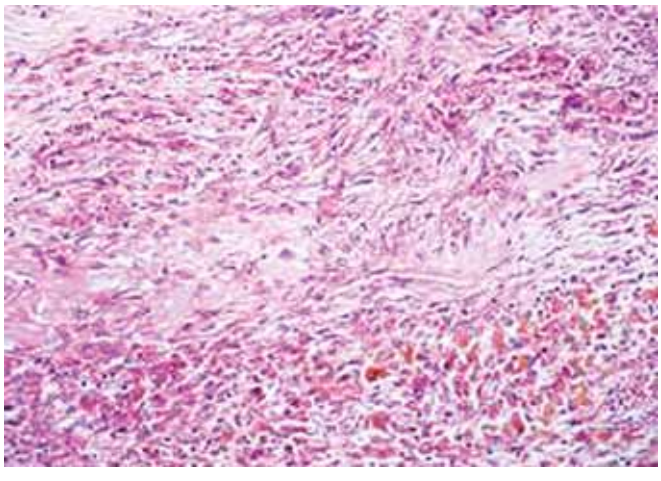


Fig. 11: Numerous hemosiderin-laden macrophages identified by golden-brown color are seen (4+) (hematoxylin and eosin, ×200)

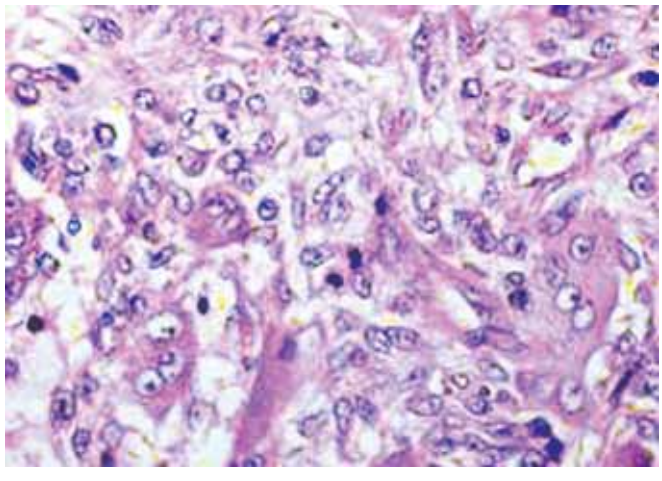


Fig. 12: A few mitotic figures are present in the stroma graded as 3+ (hematoxylin and eosin, ×400)

Hypocelluar collagen was noticeable in two cases and in both these cases the duration of symptoms was 6 months. However, no significant correlation could be drawn between other microscopic parameters and clinicoradiological findings. The final report in all cases was consistent with the diagnosis of central giant cell granuloma. Postoperative clinical follow-up for more than one year in all cases was uneventful and all teeth were vital to electric and thermal pulp testing.

DISCUSSION

CGCG is an intraosseous lesion occurring predominantly in teens and adults. Around two-third cases are diagnosed in

patients less than 30 years of age.[9] The results of present study showed 19.8 years as mean age. In conformity with other literature reports,[10] females were affected more often than males in our study too; six out of 10 cases in this study were females. A few workers have assigned female preponderance of CGCG to increased levels of estrogen in these patients.[11,12]

The mandible or lower jaw is the preferred site for CGCG, with alveolar processes of the premolar and molar regions being the most common location.[13] Of our 10 cases, six were located in the edentulous alveolar margins of the premolar region, and two each in palatal region and in attached gums between upper incisors with palatal extension. Clinically, majority of cases are asymptomatic while the aggressive ones may present with pain, swelling, root resorption, cortical perforation and/or recurrence.[14] In a study by Kruse-Losser et al,[15] 16 out of 26 patients were asymptomatic. In our study, none of the cases presented with clinical features of aggressive behavior or recurrence after one year of follow-up.

There have been several studies on radiological evaluation of CGCG and have shown unilocular areas of lucency in small early lesions while later multilocular lucency develops.[16-19] In our study, multilocularity was observed in three out of 10 cases and these were relatively larger lesions (> 1.5 cm) while others varied from 0.5 to 1.5 cm in diameter. Duration of symptoms in three cases having larger lesions ranged from 4 to 6 months.

Histologically, the World Health Organization has defined giant cell granuloma as 'a localized benign but sometimes aggressive osteolytic proliferation consisting of fibrous tissue with hemorrhage and hemosiderin deposits, presence of osteoclast-like giant cells and reactive bone formation'.[20] On histopathology, CGCG exhibits a wide spectrum of features and a highly vascular and cellular granulation tissue containing irregularly scattered multinucleate giant cells of foreign body type and mitoses in the stromal cells. Extravasation of red blood cells with hemosiderin and occasional bone formation may be seen.[6]

A number of other giant cell rich lesions in the jaw enter into the differential diagnoses. These include giant cell tumor, cherubism, aneurysmal bone cyst, traumatic bone cyst and jaw tumor of hyperparathyroidism.[21] Their relationship to each other, however, is ill-defined. In cherubism, focal arrangements of giant cells within a vascular stroma with thin-walled capillaries adjacent to the giant cells are of note. The absence of perivascular cuffing can help differentiate CGCG from cherubism. Presence of foreign body type giant cells and absence of stromal tumor cells differentiate CGCG from a GCT. Solid aneurysmal bone cyst has large blood spaces. Normal serum calcium, parathyroid hormone, alkaline phosphatase and phosphorous levels distinguish CGCG from brown tumor of hyperparathyroidism.[2] In rare cases, giant cell granulomas are an oral manifestation of hyperparathyroidism. The latter can be suspected when multiple lesions are identified and the patient suffers recurrences despite adequate treatment.

Although the etiology of CGCG is not quite clear, many authors consider the origin to comprise an abnormal proliferative response to aggression.[5] Considering that CGCG is not a true neoplasm but is rather a benign hyperplastic reactive lesion caused by local irritation or chronic trauma, different local causal factors have been implicated that include complicated dental extractions, dental restorations in poor conditions, food impaction (dental malpositioning), plaque and tartar, etc.[22,23] Despite the fact that the course of the disease is considered benign, some documented cases of metastases exist in the literature.[24] Malignant transformations to osteosarcoma or fibrosarcoma have also been reported.[25]

The conservative surgical treatment is the most accepted and traditional form of treatment of CGCG, usually involving curettage alone or along with peripheral ostectomy.[2] Radical surgical techniques of resection without continuity defect and peripheral ostectomy and *en bloc* resection have sometimes been justified for aggressive CGCG.[8] Incidence of recurrence after surgery is 4 to 20%, whereas locally aggressive giant cell lesions have a higher recurrence rate and it usually occurs due to incomplete removal of the lesion. None of our cases reported recurrence after one year of follow-up. Nonsurgical approaches like chemical cautery, electrocautery, cryotherapy have been used and newer therapies like calcitonin, interferon alpha and intra-lesional steroids are being used to avoid disfigurement.[26-30]

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