



ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR2016; 2(10): 29-33
www.allresearchjournal.com
Received: 08-08-2016
Accepted: 09-09-2016

Dr. Parveen Akhter Lone
Department of Oral &
Maxillofacial Surgery Indira
Gandhi Government Dental
College Jammu, Jammu and
Kashmir, India

Dr. Tahir Ahmed
House Surgeon OMFS IGGDC
Jammu, Jammu and Kashmir,
India

Dr. Tabasum Ahmed
House surgeon OMFS IGGDC
Jammu, Jammu and Kashmir,
India

Dr. Vijay Kumar
House Surgeon OMFS IGGDC
Jammu, Jammu and Kashmir,
India

Correspondence

Dr. Parveen Akhter Lone
Department of Oral &
Maxillofacial Surgery Indira
Gandhi Government Dental
College Jammu, Jammu and
Kashmir, India

Clinico-pathologic features of central & peripheral giant cell lesions of oral cavity: Our clinical experience

Dr. Parveen Akhter Lone, Dr. Tahir Ahmed, Dr. Tabasum Ahmed and Dr. Vijay Kumar

Abstract

Giant cells are large mononucleated or multinucleated cells that are usually seen to be associated with varied physiological as well as pathological conditions. Multinucleated giant cells (MGCs) are important mediators of tissue remodeling and repair and also for removal of foreign materials and various pathogens. Depending upon the mechanism of their formation these cells assume distinctly variable phenotypes. The Giant cell Lesions of oral cavity include central giant cell granuloma (CGCG) peripheral giant cell granuloma (PGCG) aneurysmal bone cyst, cherubism, traumatic bone cyst and jaw tumor of hyperparathyroidism. This article aims to study clinico-pathological features of patients with Peripheral Giant Cell Granuloma and central giant cell granuloma and evaluating their commonest etiological features

Keywords: Multinucleated giant cells, CGCL, PGCL, hyperparathyroidism

1. Introduction

The peripheral and central giant cell lesions (PGCL and CGCL) are a group of pathological entities with similar histopathological features and whose origin has not been fully understood and still remains inconclusive from clinical as well from pathological point of view. There are a number of lesions that occur in the jaws that contain giant cells within them. They include cherubism, giant cell granuloma of the jaws, giant cell tumor, aneurysmal bone cyst, traumatic bone cyst and jaw tumor of hyperparathyroidism but PGCL and CGCL are common and more frequently encountered giant cell lesions

Central giant cell granuloma (CGCG) was classified by the World Health Organization in 2005 as a rarely aggressive idiopathic benign intraosseous lesion that occurs almost exclusively in the jaws^[1]. The central giant cell granuloma (CGCG) of the jaws accounts for approximately 7% of all benign tumors of the jaws^[2].

Peripheral giant cell granuloma (PGCG) is one of the most frequent giant cell lesion of the jaws and originates from the periosteum or periodontal membrane. It is not a true neoplasm but rather a benign hyperplastic reactive lesion occurring in response to local irritation such as tooth extraction, poor dental restorations, ill-fitting dentures, plaque, calculus, food impaction and chronic trauma^[3]

Central giant cell lesions (CGCL) are intraosseous nonproliferative lesions whose etiology is unknown. It is less common than PGCL and occurs exclusively in maxillary bones^[3, 4]. It has variable clinical manifestations and may present slow asymptomatic growth with no recurrence or rapid painful growth with recurrence^[5, 6]

The CGCG may occur at any age, but it is most commonly seen in the first 3 decades. 37.5% of CGCGs are located in the incisor, canine, and premolar regions of the mandible (Kaffe *et al*, 1996). CGCG of the jaw is usually unifocal and have traditionally been treated surgically; the common therapy being curettage or resection (Kermer *et al*, 1994; Eisenbud *et al*,^[2] Clinically, Peripheral giant cell lesions (PGCL) are reactive, extra osseous (soft gum tissue) and exophytic, located in the alveolar ridge in edentulous area or in the gum. It usually occurs as a result of local irritants such as bacterial plaque, calculus, food retention, chronic infections, chronic irritation, trauma related to exodontia, poorly finished fillings, poorly fitted dental prostheses, occlusal forces and supernumerary teeth. The lesion arises from the

periodontal ligament or mucoperiosteum and has low recurrence, mainly if the local irritant factor is eliminated [7-9].

2. Materials & Methods

The retrospective study was conducted in the department of oral and Maxillo facial surgery Government dental College and hospital. Patients with selected gingival swellings or any abnormal gingival outgrowth were included in the study. A detailed clinical examination of oral cavity involving mandible and maxilla along with detailed relevant past medical and dental history was recorded.

Radiological examination of most of patients with an orthopantomogram [as shown in (Fig. III) of one of patients] revealed a solitary well defined multilocular radiopaque lesion in the region of swelling. Incisional & excisional biopsy was done depending upon the size of lesion & diagnosis was confirmed by histopathologic examination. Intralesional injections of triamcinolone acetone were given in large aggressive central giant cell lesions in order to reduce inflammation & intra operative bleeding (in view of

its anti-inflammatory and antiangiogenic properties) followed by curettage. The combined treatment (pharmacological and surgical) is advantageous for large aggressive lesions in so far as it reduces their size, minimizing functional and physical imperfections. The post-surgical follow up has remained uneventful till date as patients have been regularly followed up for treatment.

3. Results: In this retrospective study, we examined 50 patients of all age groups to enable us to give a general perspective of prevalence of most common etiological factor involved in giant cell lesions. Out of 50 patients, 30 were selected based on signs and symptoms suggestive of giant cell lesions and remaining 20 patients were excluded on basis of histopathology suggestive of neoplastic changes. Out of selected 30 patients, 20 patients were females & 10 were males. 20 patients (80%) were between age group of 40 to 60 years with ill fitted dentures and generalized periodontitis whereas 6 patients (20%) were between 15-25 years which showed signs of poor oral hygiene, stress, pregnancy. whereas 4 patients had no relevant etiology factor.



Fig 1: Radiograph of patient with giant cell lesion



Fig 2: giant cell lesion measuring more than 2 cm



Fig 3: Peripheral giant cell lesion of patient due to ill fitted denture



Fig 4: Giant cell lesion of patient with poor periodontium

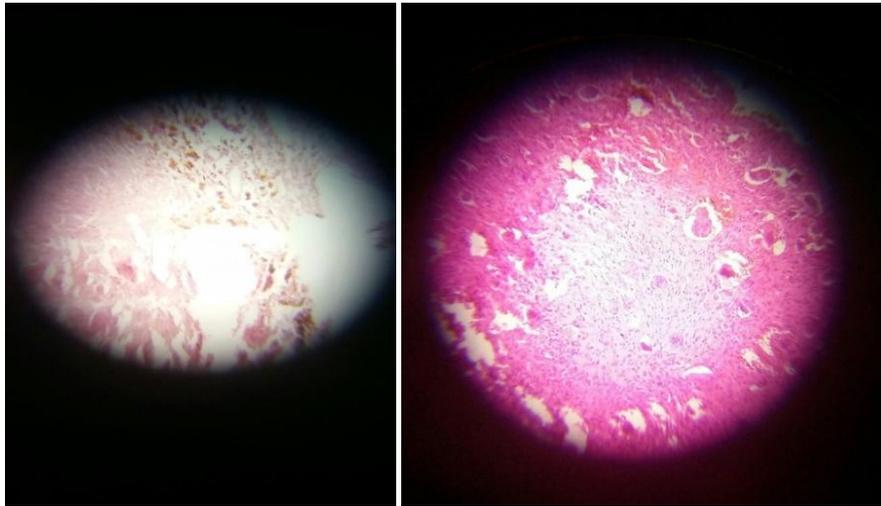


Fig 5-6: Histopathologic features of Central & peripheral giant cell lesions

4. Discussion

Peripheral and central giant cell lesion are group of pathologies that have shown great clinic-pathological variations over the years, though feature same histopathology. Peripheral giant cell granuloma (PGCG) Peripheral giant cell granuloma (PGCG), was reported as giant cell reparative granuloma by Jaffe in 1953^[10]. However, its reparative effect has not been proved yet, hence osteoclast activity seems doubtful^[11, 12].

Clinically PGCL appears as soft reddish or purplish extraosseous lesion. The lesion can be sessile or pedunculated penetrating through the periodontal membrane or it may not present any area of ulcerations. Although the PGCG develops within soft tissue, superficial resorption of the underlying alveolar bony crest is sometimes seen. On occasion, it may be difficult to determine whether the mass arose as a peripheral lesion or a central giant cell granuloma eroding through the cortical plate into the gingival soft. However ulcerations may occur subjected to trauma over the focal area of lesions. In the present study ulceration due to trauma from opposite teeth was reported in 50% of cases.

The size of lesion varies between 0.5 to 1.5cms^[10]. But lesions can become large sometimes attaining a size of up to 2cm or more. Almost all cases were reported in our study with size more than 2cms [fig 1 and fig 2].

Although PGCL arise in soft tissues, the “cup-shaped” resorption of the subjacent alveolar bone may be occasionally observed^[11, 12]. Thus, it may be difficult to determine whether the increased volume originates from a PGCL or a CGCL that ruptured the cortical bone and invaded the gingival soft tissues^[13-14]. According to Fanourakis *et al.*^[15], radiological examination is essential to determine if the lesion arises from the gingiva (peripheral) or bone (central) growing towards the surface. Dental resorption is rare^[16]

The etiology of this lesion is still not precisely defined, local irritating factors such as tooth expulsion, ill-fitting prosthesis, poor restoration, plaque, calculus, chronic infections or the effects of nutrients may play a vital role in the etiology^[15] as was seen in present study in 50% of study. The central giant cell granuloma (CGCG) of the jaws accounts for approximately 7% of all benign tumors of the jaws (Kramer *et al.*, 1991)^[2] The CGCG may occur at any age, but it is most commonly seen in the first 3 decades.

CGCL display variable clinical behavior, including slow asymptomatic growth without recurrence and fast painful growth with perforation of the cortical bone plate and ulceration of the mucosal surface.

The female gender is the most affected, possibly due to hormonal factors (pregnancy and estrogen) despite the fact that the lesions rarely express estrogen receptors^[17]. As reported in the present study also

CGCL are more common in the anterior portion of the mandible and often cross the midline^[18, 19]. 37.5% of CGCGs are located in the incisor, canine, and premolar regions of the mandible (Kaffe *et al.*, 1996)^[20] as reported in the present study

When CGCL affect multiple locations simultaneously, they are generally associated with hereditary syndromes or systemic diseases such as brown tumor of hyperparathyroidism, fibrous dysplasia, ossifying fibroma, Paget's disease or fibro-osseous lesion^[21].

Based on clinical and radiographic features, CGCL fall in two categories: non-aggressive and aggressive. The former lesions account for most cases. Furthermore, they show little or no symptoms whatsoever and slow growth without perforation of the cortical bone and root resorption of the teeth involved. The latter lesions cause pain and exhibit rapid growth, usually larger than five centimeters, producing expansion and perforation of the cortical bone, displacement of teeth and root resorption as seen in present study. Besides, there is a high recurrence rate, which generally ranges between 37.5% and 70%^[22-24]. In the present study most of the cases were non aggressive type of lesions

Regarding etiology, which is a much debated topic, there are local and systemic factors as well as possible mutations described in exons 3, 4, 9 and 11 of SH3BP2 gene. Nevertheless, the study by Teixeira *et al.*^[25] only found associations with exon 4 and the remaining ones would be more related to cherubism. Local factors comprise traumas and vascular damage, which produce intramedullary hemorrhage and intraosseous replacement fibrosis. Among the systemic causes, it is particularly worth mentioning neurofibromatosis type I, Noonan syndrome, Ramon syndrome, Jaffe – Campanacci syndrome, association with cherubism, pregnancy and hormonal disorders such as hyperparathyroidism. No consensus has been reached as to a single etiology of CGCL

For definitive diagnosis Histological investigations still remains, by far, conclusive. In PGCL the most characteristic histological features include a non-encapsulated highly cellular mass with abundant giant cells, inflammation, interstitial hemorrhage, hemosiderin deposits and mature bone or osteoid. Fibroblasts are the basic element of peripheral giant cell granulomas. (Fig 5)

CGCL, histologically, the lesion is characterized by dense proliferation of oval or spindle-shaped mesenchymal cells with multinucleated giant cells containing 4 to 20 nuclei (aggregated or not) dispersed in the fibrous stroma in a perivascular or adjacent position to areas of hemorrhage. Round macrophages, deposition of hemosiderin, extravasated erythrocytes, foci of osteoid material (bone trabeculae), dystrophic calcification and predominantly mononuclear inflammatory infiltrate, particularly surrounding the periphery of the lesion, are also found (fig 6) [26, 27] Although multinucleated giant cells are present in large quantity, they are not regarded as proliferative cells. Macrophages, mesenchymal cells and fibroblasts have been considered accountable for the lesion growth [28, 29]. These cells release cytokines that stimulate the proliferation and recruitment of blood monocytes to become osteoclast-like thus, the multinucleated giant cells are responsible for bone resorption and, consequently, the local progression of the lesion [28].

Treatment of PGCL consists of local surgical excision down to the underlying bone, for extensive clearing of the base. Removal of local factors or irritants is also required. If resection is only superficial, the growth may recur. Exposure of all bony walls following thorough surgical resection responds satisfactorily most of the times. Recurrence rate of 5.0-70.6% (average 9.9%) has been reported in various epidemiologic studies [30]

Treatment of CGCL is associated with its clinical behavior. In milder cases, a simple surgical resection followed by a thorough curettage is recommended. Nevertheless, in aggressive lesions, curettage is followed by cryosurgery, peripheral osteotomy or en bloc resection. Some treatments involve daily local application of calcitonin, corticosteroids and subcutaneous injection of interferon-2 α . Intralesional injections of triamcinolone acetonide have also been prescribed in view of its anti-inflammatory and antiangiogenic properties. The combined treatment (pharmacological and surgical) is advantageous for large aggressive lesions insofar as it reduces their size, minimizing functional and physical imperfections. The anti-angiogenic therapy in combination with curettage has proven to be a useful approach to the treatment of aggressive CGC [31-33]

5. Conclusion

The central giant cell granuloma of the jaws accounts for approximately 7% of all benign tumors of the jaws The CGCG may occur at any age, but it is most commonly seen in the first 3 decades. Although etiology is unknown Local aggravating factors comprise traumas and vascular damage, which produce intramedullary hemorrhage and intraosseous replacement fibrosis. The combined treatment (pharmacological and surgical) is advantageous for large aggressive lesions insofar as it reduces their size, minimizing functional and physical imperfections. Whereas In milder cases, a simple surgical resection followed by a thorough curettage is recommended.

6. References

- Nicolai G, Lorè B, Mariani G, Bollero P, De Marinis L, Calabrese L. Central giant cell granuloma of the jaws. *J Craniofac Surg* 2010; 21(2):383-386.
- Kermer C, Millesi W, Watzke IM. Local injection of corticosteroids for central giant cell granuloma. A case report. *International Journal Oral Maxillofacial Surgery*. 1994; 23:366-368.
- Daryani D, Gopakumar R. Central giant cell granuloma mimicking an adenomatoid odontogenic tumor. *Contemp Clin Dent* 2011; 2(3):249-52.
- DA Silva Sampieri MB *et al*. Central giant cell granuloma: treatment with calcitonin, triamcinolone acetonide, and a cystic finding 3 years and 6 months after the primary treatment. *Oral Maxillofac Surg*. 2012, 31. [Epub ahead of print],
- DE Matos FR *et al*. Immunoexpression of TNF- α and TGF- β in central and peripheral giant cell lesions of the jaws. *J Oral Pathol Med*. 2012; 41(2):194-9.
- Nogueira RL *et al*. Cyclooxygenase-2 expression in central giant cell lesion of the jaws: an immunohistochemical study. *J Mol Histol*. 2012; 43(1):59-62.
- Bansal P *et al*. Non-syndromic multiple impacted supernumerary teeth with peripheral giant cell granuloma. *Contemp Clin Dent* 2011; 2(1):41-4.
- Carvalho VM *et al*. Novel mutations in the SH3BP2 gene associated with sporadic central giant cell lesions and cherubism. *Oral Dis*, 2009; 15(1):106-10.
- DA Silva Sampieri MB *et al*. Central giant cell granuloma: treatment with calcitonin, triamcinolone acetonide, and a cystic finding 3 years and 6 months after the primary treatment. *Oral Maxillofac Surg*, 2012, 31. [Epub ahead of print],
- Jaffe HL. Giant-cell reparative granuloma, traumatic bone cyst, and fibrous (fibro-osseous) dysplasia of the jawbones. *Oral Surg Oral Med Oral Pathol*. 1953; 6:159-75.
- Papanicolaou P *et al*. Increased TNF- α , IL-6 and decreased IL-1 β immunohistochemical expression by the stromal spindle-shaped cells in the central giant cell granuloma of the jaws. *Med Oral Patol Oral Cir Bucal*, 2012; 17(1):56-62.
- Saygun I *et al*. Human cytomegalovirus in peripheral giant cell granuloma. *Oral Microbiol Immunol* 2009; 24(5):408-10.
- Amaral FR *et al*. Quantitative expression analysis of apoptotic/antiapoptotic genes and association with immunolocalization of BAX and BCL-2 in peripheral and central giant cell lesions of the jaws. *Tumour Biol*. 2011; 32(5):997-1003.
- Bansal P *et al*. Non-syndromic multiple impacted supernumerary teeth with peripheral giant cell granuloma. *Contemp Clin Dent*. 2011; 2(1):41-4.
- Fanourakis G *et al*. Expression of receptor activator of NF- κ B ligand and osteoprotegerin in peripheral giant cell granulomas of the jaws. *J Oral Pathol Med*. 2010; 39(9):687-9.
- Mannem S, Chava VK. Management of an unusual peripheral giant cell granuloma: a diagnostic dilemma. *Contemp Clin Dent*. 2012; 3(1):93-6.
- Valentine JC, Nelson BL. Central giant cell lesion. *Head Neck Pathol*. 2011; 5(4):385-8.

- 18 DA Silva NG *et al.* Treatment of central giant cell lesions using bisphosphonates with intralesional corticosteroid injections. *Head Face Med.* 2012; 8(23):1-6.
- 19 Oconnell JE, Kearns GJ. Aggressive giant cell granuloma of the jaws treated with interferon alpha: a report of two cases. *Ir J Med Sci.* [Epub ahead of print], 2012.
- 20 Kaffe I, Ardekian L, Taicher S, Littner MM, Buchne A. Radiologic features of central giant cell granuloma of the jaws. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics.* 1996; 81:720.
- 21 Orhan E *et al.* Idiopathic bilateral central giant cell reparative granuloma of jaws: a case report and literature review. *Int J Pediatr Otorhinolaryngol.* 2010; 74(5):547-52.
- 22 Florez-Moreno GA *et al.* Cytomorphometric and immunohistochemical comparison between central and peripheral giant cell lesions of the jaws. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008; 105(5):625-32.
- 23 Friedrich RE *et al.* Expression of proteases in giant cell lesions of the jaws, tendon sheath and salivary glands. *Anticancer Res.* 2010; 30(5):1645-52.
- 24 Saw S *et al.* Giant cell tumour and central giant cell reparative granuloma of the skull: do these represent ends of a spectrum? A case report and literature review. *PatholOncol Res.* 2009; 15(2):291-5.
- 25 Teixeira RC *et al.* SH3BP2-encoding exons involved in cherubism are not associated with central giant cell granuloma. *Int J Oral MaxillofacSurg.* 2011; 40(8):851-5.
- 26 LIU B, YU SF, LI TJ. Multinucleated giant cells in various forms of giant cell containing lesions of the jaws express features of osteoclasts. *J Oral PatholMed.* 2003; 32(6):367-75.
- 27 Torabinia N, Razavi SM, Shokrolahi Z. A comparative immunohistochemical evaluation of CD68 and TRAP protein expression in central and peripheral giant cell granulomas of the jaws. *J Oral PatholMed.* 2011; 40(4):334-7.
- 28 Ferretti C, Muthray E. Management of central giant cell granuloma of mandible using intralesional corticosteroids: case report and review of literature. *J Oral MaxillofacSurg.* 2011; 69(11):2824-9.
- 29 Florez-Moreno GA *et al.* Cytomorphometric and immunohistochemical comparison between central and peripheral giant cell lesions of the jaws. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod.* 2008; 105(5):625-32.
- 30 Neville BW *et al.* *Patologia oral &maxilofacial.* 2. ed. Rio de Janeiro: Guanabara Koogan, 2009, 798.
- 31 BI Y *et al.* Bisphosphonates cause osteonecrosis of the jaw-like disease in mice. *Am J Pathol.* 2010; 177(1):280-90.
- 32 Duarte AP *et al.* Increased expression of NFATc1 in giant cell lesions of the jaws, cherubism and brown tumor of hyperparathyroidism. *Oncology Letters.* 2011; 2(3):571-3.
- 33 Nogueira RL *et al.* Intralesional injection of triamcinolone hexacetonide as an alternative treatment for central giant-cell granuloma in 21 cases. *Int J Oral Maxillofac Surg.* 2010; 39(12):1204-10.