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# Giant cell Granuloma: Histological comparison and a review

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***Abstract***---Central giant cell granulomas (CGCG) constitute about 10% of benign jawbone lesions. Approximately one-third of CGCG exhibit local aggressive behavior with bone destruction and a tendency to recur.[1] Jaffe (1953) was the first to distinguish central giant cell granulomas (CGCG) of the jawbones from other giant cell lesions of bones and originally called them"central giant cell reparative granulomas" since they were believed to be a reactive-reparative process that might heal spontaneously.[1] Recently the World Health Organization has defined it as localized benign but sometimes aggressive osteolytic proliferation consisting of fibrous tissue with hemorrhage and haemosiderin deposits, presence of osteoclast-like giant cells and reactive bone formation. Many authors have established the differences with other lesions of giant cells. The clinical behavior of CGCG varies from a slowly asymptomatic swelling to an aggressive lesion that manifests with pain, cortical perforation, and root resorption.[2] On the other hand the peripheral giant cell granuloma is a reactive exophytic lesion of the gingiva and alveolar ridge that usually occurs as a result of local irritating factors such as plaque, calculus, chronic infection, chronic irritation, tooth extraction, inproperly finished filling, unstable dental prosthesis, and impacted food which originates from the periosteium or periodontal ligament. It is also known as Giant cell epulis, Giant cell reparative granuloma,


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osteoclastoma, and giant cell hyperplasia. It can be developed at any age, though it is more common between the 5th and 6th decade of life, and shows a slight female predilection. [7]

***Keywords***---central giant cell granuloma, peripheral giant cell granuloma.

**Introduction**

This article presents few cases of peripheral giant cell granuloma and central giant cell granuloma both with review of literature. Central giant cell granuloma (CGCG) is widely considered to be a non-neoplastic lesion. CGCG is a localized osteolitic lesion with varied biologic behavior of aggression which affects the jaw bones. The etiology of CGCG is unknown, but some indications implicate genetic abnormalities. The mandible is twice as likely to be involved as the maxillary. Over 60% of the cases described in the literature occur in patients under 30 years of age, although CGCG may also develop in children and the elderly. Females are more frequently affected than males.[3] Based on clinical and radiographic features, several groups of clinicians have proposed that CGCG of the jaw may be divided into non-aggressive and aggressive lesions. Most cases are non-aggressive, exhibit few or no symptoms, and are detected coincidentally at the time of the radiologic dental exam. The aggressive pattern is characterized by large lesions with swelling of the jaw, rapid growth, pain, paresthesia, cortical bone perforation or thinning, root resorption, and recurrence.[3]

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 tumour, aneurysmal bone cyst, traumatic bone cyst and jaw tumour of hyperparathyroidism. Their relationship to each other, however, is ill defined. The histological similarities cease with the finding of multinucleated giant cells of osteoclastic origin and the lesions themselves greatly differ in their genetic origin, etiopathogenesis and clinical behaviour.[4] The Peripheral giant cell granuloma (PGCG) is a relatively common tumor-like growth of the oral cavity. It is also known as giant cell epulis or peripheral giant cell reparative granuloma. It accounts for 7% of all benign tumors of the jaw. Although PGCG is the least commonly diagnosed among the various hyperplastic gingival lesions (pyogenic granuloma, fibrous hyperplasia, peripheral ossifying fibroma) it is a common giant cell lesion found in the oral cavity. It is probably a reactive lesion caused by local irritation or trauma1 which resulted in gingival or mucosal hemorrhage. The aggressive factors include trauma, tooth extraction, badly finished restorations, plaque, calculus, chronic infections and impacted food.

The origin of the multinucleated giant cells is unknown; some believe them to show immunohistochemical features of osteoclasts, while others suggest them to arise from mononuclear phagocyte system. Other possible sources include osteoblasts, endothelial cells and spindle cells. PGCG seems to be influenced by hormonal stimulus, especially estrogen. PGCG occurs exclusively on gingiva or edentulous alveolar ridge as variable sized, sessile or Pedunculated lesion which is usually deep red to bluish red and bleed easily. The final diagnosis however

relies on the histological diagnosis. Histologically, fibroblasts are the basic elements. Scattered among the fibroblasts are abundant multinucleated giant cells. Islands of metaplastic bone occasionally may be seen. Numerous capillaries may be seen along with areas of hemorrhage, hemosiderin and inflammatory cells throughout the cellular connective tissue. The treatment is usually local surgical excision down to underlying bone along with scaling of adjacent teeth to remove any source of irritation and to minimize risk of recurrence.[6]

**Discussion**

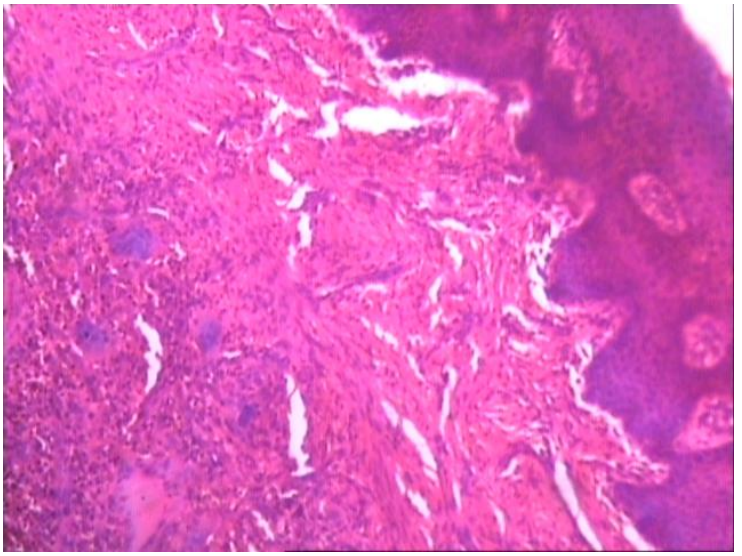
Central Giant Cell Granuloma is a rare disease. It can occur at any age but presents most frequently in the 2nd and 3rd decades and involves the maxilla more than the mandible. It is twice as frequent in females. World Health Organization defines it as an intra-osseous lesion consisting of cellular fibrous tissue and contains many foci of haemorrhage, aggregations of multinucleated giant cells and occasionally trabeculae of woven bone. Frequently it is only a painless swelling, but growth in some casesis so rapid and the mass can also rarely erode through bone particularly of the alveolar ridge to produce asoft tissue swelling. Although lesion is expansive and invasive, it does not usually involve perinueral sheets, for this reason parasthesia is usually not observed in these patients. Despite the fact that the course of the disease is considered benign, there still exist some reports in literature where metastasis has been observed. Furthermore malignant transformations to osteosarcoma or fibrosarcoma have been reported.[5]

**Histologically**

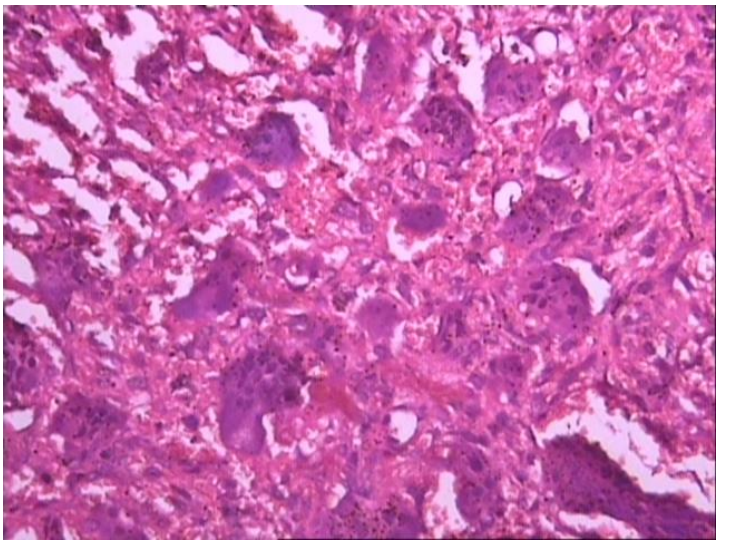
It is indistinguishable from other giant cell lesions of the bone like cherubism and aneurysmal bone cyst. Giant cell granuloma forms a lobulated mass of proliferative vascular connective tissue packed with giant cells. These giant cells are seen lying in vascular stroma. These giant cells have a patchy distribution and signs of bleeding into the mass and deposits of hemosidrin are frequently seen.[3] Ultra structurally the proliferating cells include spindle-shaped fibroblasts, myofibroblasts and inflammatory mononuclear cells. Sparse strands of collagen fibers partly subdivide the lesion which may contain a few trabeculae of osteoid or bone. [5]

Histologically PGCG consist of a nonencapsulated mass of the tissue composed of a delicate reticular and fibrillar connective tissue stroma containing large number of ovoid and spindle shaped young connective tissue cells and multinucleated giant cells. The giant cell in some instances resembles osteoclast and in other cases are considerably larger than the typical osteoclast. Capillaries are numerous particularly around the periphery of the lesions and giant cell may be found at the lumina of these vessels. Foci of hemorrhage with libretion of hemosiderin pigment and its subsequent ingestion by mononuclear phagocytes as well as inflammatory cell infiltration are also characteristic feature. Spicules of newly formed osteoid or bone are often found scattered throughout the vascular and cellular fibrous lesion. A histochemical study of this lesion has been reported by shklar and Catado with distinct difference observed in different multinucleated giant cells with respect to the distribution of tyrosine and sulfhydryl groups.

Some authors suggest that giant cells may be derived from proliferating giant cells associated with the resorption of deciduous tooth roots. Some believe that they arise through fusion of endothelial cells. A recent study of giant cells in the PGCG by electron microscopy has been reported by sapp. And he found that these giant cells ultrastructurally contained sufficient number of features in common with the osteoclast.[8] On the other hand CGCG is made up of loose fibrillar connective tissue stroma with many interspersed proliferating fibroblast and small capillaries. The collagen fibers are not usually collected into bundles.however group of fibers will often present a whorled appearance. Multinucleated giant cells are prominent throughout the connective tissue but not necessary abundant. These giant cells vary in size and contain few to several dozen nuclei. There are also presence of foci of extravasated blood and hemosiderin pigment some of it phagocytized by macrophages. Foci of new trabeculae of bone are also seen. there is a debate whether the giant cells are of fibroblast in origin or from monocytes/macrophages. In the recent study by itonga et al indicate that the giant cells in the CGCG of the jaw are osteoclast like and formed from the monocytes/macrophages precursors which differentiate into osteoclast.[8]



Peripheral giant cell Granuloma



Central Giant Cell Granuloma

**Treatment**

CGCG. Treatment in most cases involves surgical removal of the lesion by curettage in the case of low-aggressive types of granuloma, and wide excision in more advanced cases. However, sparing surgical treatment (currettage) is related to a greater risk of relapse than radical management. En bloc resection of large CGCG of the aggressive type is often associated with the necessity to restore bone defect, most often with a free flap with, microanastomosis. An alternative to surgical treatment is local injectable steroid therapy, calcitonin, interferon alfa 2A, bisphosphonates or denosumab therapy. . It is advisable to determine the level of calcium, phosphorus and parathyroid hormone in the blood serum in order to avoid an incorrect diagnosis.[9] PGCG. Treatment consists of local surgical excision down to the underlying bone, for extensive clearing of the local factors or irritants is also required. If resection is only superficial, the growth may recur. Exposure of all bony walls following thorough surgicalresection responds satisfactorily most of the times. Recurrence rate of 5.0-70.6% (average 9.9%) has been reported in various epidemiologic studies.[10]

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