Peripheral Giant Cell Granuloma: A Case Report and Review of Literature
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Abstract:
Peripheral Giant Cell Granuloma or so called “Giant cell epulis” is the most common oral giant cell lesion. It usually presents as a purplish-red soft tissue nodule consisting of multinucleated giant cells in a background of mononuclear stromal cells and extravasated red blood cells. This lesion probably does not represent a true neoplasm but it may be a reactive in nature which is believed to be stimulated by local irritation or trauma, but the cause is not known with certainty. A case of peripheral giant cell granuloma arising at the left maxillary premolar region in a 18 year old boy is being reported here. The lesion was completely excised up to the periosteum level; there was no residual or recurrence of swelling or bony defect apparent in the area of biopsy after a follow-up period of 1 year.

Key Words: Peripheral giant cell Granuloma, Epulis.

Introduction:
Peripheral giant cell granuloma (PGCG) is the most common oral giant cell lesion as a soft tissue extra-osseous purplish-red nodule. This lesion is probably not a true neoplasm but could be a reactive in nature. The initiating stimulus is believed to be due to local irritation or trauma but the cause is not known with certainty. It has also been termed as a peripheral giant cell reparative granuloma; but whether it is in fact reparative, has not been established and their osteoclastic activity appears doubtful. Their membrane receptors for calcitonin, demonstrated by immuno-histochemistry and their osteoclastic activity when cultured in vitro are evidence that they are osteoclasts (Bonetti et al, 1990; Lim & Gibbins 1995; Mighell et al, 1996), whereas other authors have suggested that the lesion is formed by cells of the mononuclear phagocyte system (Carvalho et al, 1995). The PGCG bears a close microscopic resemblance to the central giant cell granuloma, and hence some pathologists believe that it may represent a soft tissue counterpart of the central bony lesion (Katsikeris et al, 1988).

The lesion can be sessile or pedunculated, penetrating through periodontal membrane and may or may not be ulcerated. Occasionally lesions arise from the periosteum overlying edentulous area. Secondary ulceration due to trauma may give the lesions a focal yellow zone caused by the formation of fibrin clot over the ulcer.

Lesions can become large, sometimes attaining a size up to 2 cm. The clinical appearance is similar to the more common pyogenic granuloma, although the PGCG is often more bluish-purple as compared with the bright-red colour of a typical pyogenic granuloma. Recently, the PGCG associated with dental implants has been reported (Hirshberg et al, 2003). 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 tissues (Chadwick et al, 1989; Giansanti & Waldrom, 1969).

Rarely a giant cell epulis may be due to hyperparathyroidism, representing the so-called osteoclastic “brown tumours” associated with this endocrine disorder (Smith et al, 1988; Burkes & White, 1989) and is then likely to be associated with other lesions in bones and changes in the blood chemistry. The extra-osseous lesions of cherubism involving the gingiva appear very similar to giant cell epulis. However, the other distinctive clinical and radiological features of cherubism indicate the correct diagnosis (Odell & Morgan, 1998). Histologically, PGCG is composed of nodules of multinucleated giant cells in a background of plump ovoid and spindle-shaped mesenchymal cells and extravasated red blood cells. The giant cells may contain only a few nuclei or up to several dozen. Some of them are large, vesicular nuclei; others are small, pyknotic nuclei. The origin of the giant cell is unknown.

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Case Report

A 18 year old boy was referred to the Department of Oral & Maxillofacial Surgery, People’s Dental Academy, Bhopal for a non-tender exophytic lesion in the left maxillary premolar region since May, 2010 (Fig. I). Since then the lesion had gradually increased in size. It bled from time to time but the patient did not seek any treatment. The patient had no significant medical history. The clinical differential diagnoses included PGCG, pyogenic granuloma and haemangioma. The excisional biopsy was undertaken upto the periosteum level under local anaesthesia, and haemostasis was achieved by electrocautery and Surgicel. The irritational factor was seen during exploration of lesion (Fig. III). To prevent recurrence of tumour, denuded bone was treated with Carnoy’s solution. Chlorhexidine mouth rinse was prescribed post-operatively twice a day for 7 days.

On gross examination, the excised nodule was red in colour and measured 30 x 20 x 35mm in maximum dimension. There was periodontal bone loss in the maxillary left canine region (Fig. II). Due to the extensive nature of lesion, there was displacement of maxillary left canine.

Histologically, the overlying epithelium was composed of aggregates of multinucleated giant cells

Fig. I: A red exophytic, non-painful lesion arising in the maxillary left premolar area

Fig. II: Bone loss associated with the lesion, as seen on the occlusal view.

Fig. III: Irritation factor as seen during exploration of lesion.

Fig. IV. Photomicrograph showing aggregates of multinucleated giant cells in a background of mononuclear stromal cells, extravasated erythrocytes and deposits of haemosiderin (H & E Stain, 100X).
in a background of mononuclear stromal cells, extravasated red blood cells and deposits of haemosiderin (Fig. IV). After a period of 6 months, no residual or recurrence of swelling or bony defect was seen. The patient was then referred to the Department of Prosthodontics and the Department of Periodontics for a new partial denture and periodontal treatment.

Discussion:

The etiology and nature of PGCG (giant cell epulis) still remains undecided. In the past, several hypotheses had been proposed to explain the nature of multinucleated giant cells, one of them is that they are osteoclasts left from physiological resorption of teeth or reaction to injury to periosteum. Now there is a strong evidence that these cells are osteoclasts as they have been shown to possess receptors for calcitonin and were able to excavate bone in vitro (Flanagan et al 1988).

The study of Lim & Gibbins (1995) confirmed that the multinucleated giant cells reacted strongly for a monoclonal antibody (MB1) which reacts with lymphocytes and a proportion of T cells and monocytes. The MB1 antibody has previously been shown to be expressed by osteoclasts in fetal bone. Interestingly, the re-expression of the blood vessels in the lesion for the widely used endothelial cell marker factor VIII related antigen had failed to demonstrate the presence of blood vessels other than on the periphery of the lesion although these lesions appear to be extremely vascular in nature.

There is also a growing body of opinion that giant cells may simply represent a reactionary component of the lesion and are derived via blood stream from bone marrow mononuclear cells and may be present only in response to an yet unknown stimulus from the stroma. This concept is based on the results of some more recent studies using cell culture and transplantation (el Mofty & Osdoby, 1985; Cohen et al, 1988) in which the giant cells have been found to be short lived and to disappear early in culture in contrast to the active proliferation of the stromal cells.

A study by Wulling et al (2001) revealed that the stromal cells secrete a variety of cytokines and differentiation factors, including Monocyte chemo-attractant protein-1 (MCP1), Osteoclast differentiation factor (ODF), and Macrophage-colony stimulating factor (M-CSF). These molecules are monocyte chemo-attractants and are essential for osteoclast differentiation, this suggest that the stromal cell stimulates blood monocyte immigration into tumour tissue and enhances their fusion into osteoclast like multinucleated giant cells. Further more, the recently identified membrane-bound protein family a disintegrin and metalloprotease (ADAM) is considered to play a role in the multinucleation of osteoclasts and macrophage derived giant cells from mononuclear precursor cells (Abe et al, 1999).

In a recent study by Liu et al (2003), in situ hybridization was carried out to detect the mRNA expression of the receptor activator of NF-kappaB ligand (RANKL), that is shown to be essential in the osteoclastogenesis, its receptor RANKL and its decoy receptor osteoprotegrin (OPG). They concluded that RANKL and OPG expressed in these lesions may play on important role in the formation of multinucleated giant cells.

There are no pathognomonic clinical features whereby these lesions can be differentiated from other forms of gingival enlargement including pyogenic granuloma, fibrous epulis, peripheral ossifying fibroma, inflammatory fibrous hyperplasia, peripheral odontogenic fibroma, hemangiomacaverosum and papilloma. Microscopic examination is required for the definitive diagnosis(Carranza & Hogan, 2012; Chaparro-Avendano et al, 2005).

Generally, this lesion is clinically indistinguishable from a pyogenic granuloma, although a PGCG is more likely to cause bone resorption than pyogenic granuloma, the differences are otherwise minimal (Regezi et al, 2008). Microscopically, the lesion arises from, or is at least attached to the periodontal ligament or mucoperiosteum. 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. Scattered among the plump, young fibroblasts are numerous multinucleated giant cells with abundant eosinophilic cytoplasm which appear to be non-functional in the usual sense of phagocytosis and bone resorption(Regezi et al, 2008). Two types of giant cells are mainly found, one representing metabolically active cells (Type I) and the other representing dying cells (Type II). The origin of these cells has not been defined yet. However, a striking similarity between these cells and osteoclasts does exist (Katsikeris et al, 1988). Both the type of
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Recurrence rate of 5% has been reported by Giansanti & Waldron (1969). Recurrence is believed to be related to lack of inclusion of the periosteam or periodental ligament in the excised specimen (Regezi et al, 2008). A re‐excision must be performed for these cases (Neville et al, 2009). Aggressive tendencies or malignant transformation of these lesions has never been reported (Katsikeris et al, 1988). The treatment rendered in this case was surgical excision to the bone, chemical cauterization and curettage followed by oral prophylaxis. The 1 year follow‐up has shown no recurrence indicating that the given treatment along with maintenance of a good oral hygiene is sufficient to treat PGCG.

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