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Peripheral Giant Cell Granuloma- A case report and review

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Abstract:

Peripheral giant cell granuloma (PGCG) is a non-neoplastic, tumor-like reactive lesion occurring exclusively on gingiva/alveolar crest. It is thought to arise from the periodontal ligament or the periosteum. Clinically, it bears resemblance to pyogenic granuloma, peripheral ossifying fibroma and many other peripheral lesions seen in the oral cavity, thereby histopathology is mandatory for the diagnosis of this lesion. The lesion although being relatively common, but still carries a lot of ambiguity. The ambiguity is in terms of its etiology, growth potential, biological behavior (recurrence), histogenesis of its cells and its treatment. The entity further holds significance because of its notorious behavior and its high tendency to recur. The present paper describes recurrent PGCG with a comprehensive insight of the literature on its etiology, clinical, radiological, histological, ultrastructural and molecular aspects. Special attention is given on the histogenesis of cells and their types as also on the differential diagnosis and treatment of this lesion.

Key Words: *Giant cell lesion, mononuclear stromal cells, multinucleated giant cells, myeloid tumor, osteoclast, peripheral giant cell granuloma*

Introduction:

Historical background:

Peripheral giant cell granuloma (PGCG) about more than a 100 years ago.[1] Jaffe through his research affirmed that the giant cell tumors occurring at other areas of the body were poles apart from the giant cells found in the jaws and termed them (giant cells found within the jaws) as giant cell reparative granuloma.[2] Bernier Cahn suggested that these lesions should be called as either a peripheral or central giant cell reparative granuloma.[3]

Today the term PGCG is universally accepted.[4] Waldron and Shafer found that the intra-osseous lesions did not contain any reparative characteristics and histologically did not differ from any other benign giant cell tumor of bone.[5] Bhaskar et al. in 1959 subdivided giant cell granuloma into central and peripheral types.

A non-neoplastic lesion by nature, the Giant cell granuloma is distinctive in its histologic makeup. It contains multinucleated giant cells embedded in a stromal environment composed of mononuclated stromal cells along with ovoid to spindleshaped nuclei.[7]

Giant cell granulomas occurring within the bone are called central giant cell granuloma (CGCG) and those occurring on edentulous alveolar processes or gingivae are called PGCG. Although the CGCG is rare in nature, making up 7% of total benign lesions of the jaws it is at times uncompromising in nature,

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especially in young patients.[8,9] Contrary to that, PGCG is a more common giant cell lesion of the jaw and can arise either in response to local irritation or from the connective tissue of the gingiva, periodontal membrane or from the periosteum of the alveolar ridge.[10]

Conventionally, although the term "PGCG" is now a worldwide designated and acknowledged terminology, but still certain parameters regarding this lesion such as its etiology, recurrent nature, proliferative potential and derivative roots of multinucleated giant cells and mononuclear stromal cells remain obscure.[11] In 1962, Gottsegen[12] proposed that PGCG arose postperiodontal surgery while others claimed that they developed in response to local irritating factors.[2-4] One of the predisposing factors causing PGCG is poor oral hygiene, and it is most commonly found in people belonging to the lower socioeconomic strata.[13] PGCG occurs exclusively on the gingiva or edentulous alveolar ridge. The lesion mimics other reactive lesions occurring on the gingiva clinically, however, it has significantly higher rate of recurrence than other reactive lesions and thus has to be treated with caution with complete excision and clearing of the lesion.

The present paper offers a review of the literature to define the etiology, clinical, radiological, histological, ultrastructural and molecular aspects of PGCG. Special emphasis is given on the histogenesis of cells and their types as also on the differential diagnosis and treatment of this lesion.

Etiopathogenesis of peripheral giant cell granuloma:

Etiology of this lesion is not very clear, and many authors have put forth different causes. Chronic local irritation of the gingiva can lead to the manifestation of spectrum of reactive lesions, one of which is PGCG that is thought to either originate from the periodontal membrane surrounding the tooth or from the periosteum of the bone. Since it is known that periodontium responds to the similar irritants in a different way, it is postulated that PGCG is a more intense response of periosteum to the irritation factors than that associated with the formation of the more common lesion that is pyogenic granuloma.[14,15]

Chronic irritants:

Sood et al. stated that PGCG is presumably a reactive lesion caused in response to local irritation or trauma. The predisposing factors include trauma, badly finished restorations, plaque, calculus, chronic infections and impacted food.[16] Bodner et al. suggested that these lesions comprise of an abnormal proliferative response to aggregation.[17]

Tooth extractions:

Previous literature has shown some occurrence rate of PGCG postextraction, but the fact that extraction might lead to the development of PGCG is still not clear. Mighell et al. reported a case, where there was an occurrence of PGCG 2 months post theorthodontic extraction of a deciduous molar. They suggested that a healing socket rich in growth factors could possibly have stimulated the PGCG growth and eventual lesion development.[18]

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Xerostomia:

Bodner et al.[17] found in his study that there was significantly higher percentage of reports of large PGCG's (>2 cm) in people with xerostomia (oral dryness).

Hormonal influence:

Vittek et al. in 1982 found progesterone and estrogen receptors on human gingiva.[19] A study conducted by Matter et al. suggested that PGCG was propagated by pregnancy rather than being "pregnancy dependent." He stated that the lesion entirely was not hormone dependent, but was a result of various combinations of causative factors such as an immunosuppressive action of hormones along with hyper responsiveness of the gingiva to these hormones. The response of gingiva can be linked to the finding that estrogen metabolism in unhealthy gingiva is 3 times more than normal gingiva and the activity of responsible enzyme of these reactions increased gingival inflammation. Furthermore, marked female predilection of PGCG suggests a possible hormonal influence. Thus, it can be concluded that ovarian hormones influence the growth of this lesion, however the effect is secondary.[20]

Primary hyperthyroidism: Rare occurrence of PGCG as an oral manifestation of hyperparathyroidism without any significant bone involvement is reported in the literature. Although this is not a common initial presentation, hyperparathyroidism should be considered as an etiological factor when multiple lesions are present and in recurrent cases that already have

undergone various treatment modalities with no effective remission. An unwarranted production of the parathyroid hormone as seen in parathyroid tumor and chronic renal disease also initiates the formation of a giant cell lesion. Furthermore, children with X-linked hypophosphatemic rickets, a condition that is associated with subclinical hyperparathyroidism, have an increased probability for developing this entity.[21,22]

Case Report:

A 25 years old male patient, resident of Sarsaw, Saharanpur reported to Department of Oral Medicine And Radiology, with a chief complaint of irregular growth of gums and swelling in lower right back tooth region since 3 years. History dates back to 3 years when patient first noticed decayed tooth and food lodgment in lower right back tooth region. For which patient underwent extraction of the decayed tooth in lower right back tooth region. After few days of extraction, patient started experiencing small [lesser than pea size], growth in that region. With time the size of growth gradually increased and has attained this present size 2 months ago. Patient went to some private practitioner; near patient's house for some medications [nature of medication is unknown]. No changes in the growth were observed after medication. Patient was experiencing dull, continuous, non-radiating pain in lower right back tooth region since 1 day. Past Dental History revealed Patient underwent extraction of tooth in lower right back tooth

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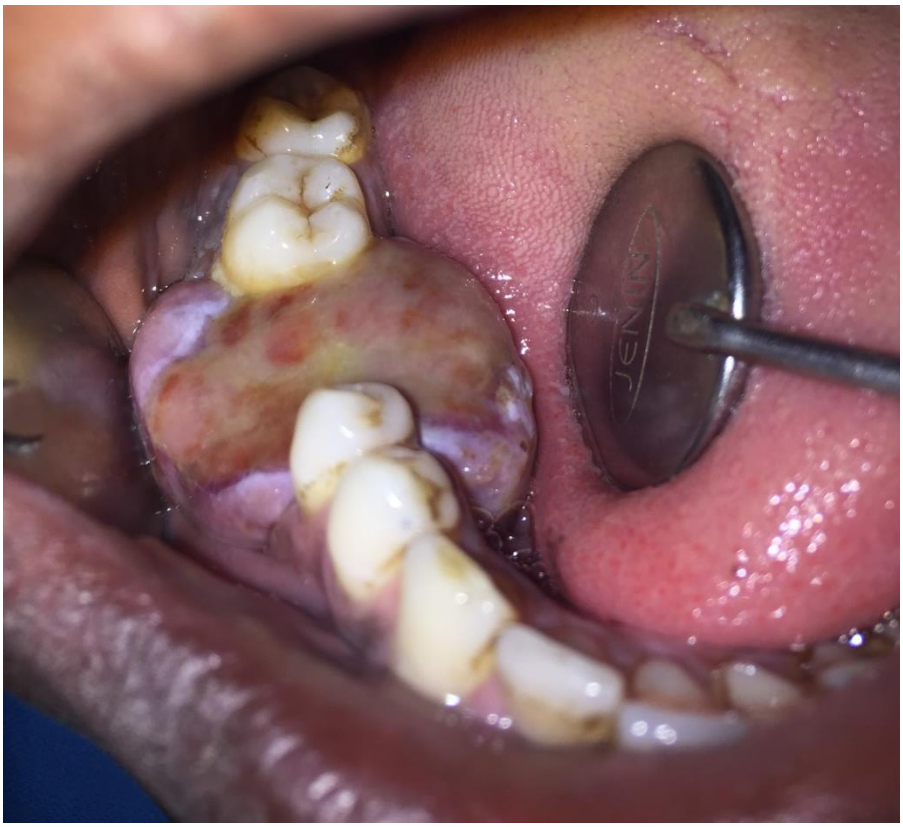
region 3 years ago. Procedure was uneventful.Patient underwent removable set of artificial teeth in upper front tooth region 2 years ago. Habit History reveals chewing tobacco 2-3 times daily since 3 years. Extra-Oral Examination revealed A bilaterally single submandibular lymph node is palpable of size 1.5cm [approximately] in diameter, firm in consistency, non- tender in nature and not fixed to the underlying surface. On Intra-oral examination: On Inspection: A solitary growth is seen on right lower back tooth region w.r.t.46 region. Growth is extending bucco-lingually from buccal vestibule of 46 region to floor of the mouth and distal of 45. Shape is roughly oval with a size of 2.5×3cm approximately. Overlying surface of growth is smooth and reddish- yellow in color. [figure 1] On Palpation: Sessile growth was present. Consistency of growth was soft to firm in nature. Growth was non-tender. No bleeding or pus-discharge was seen on manipulation.



With these provisional diagnosis was Ossifying fibroma w.r.t. 46 region. Investigations advised were IOPA w.r.t.46 region, Panoramic view, CECT face, Histopathological examination and Biopsy. OPG shows regular bone loss present on the buccal cortex extending supero-inferiorly from the alveolar cortex to 2 cm below and antero-posteriorly from mesial of 47 to apex of 45. [figure 2].

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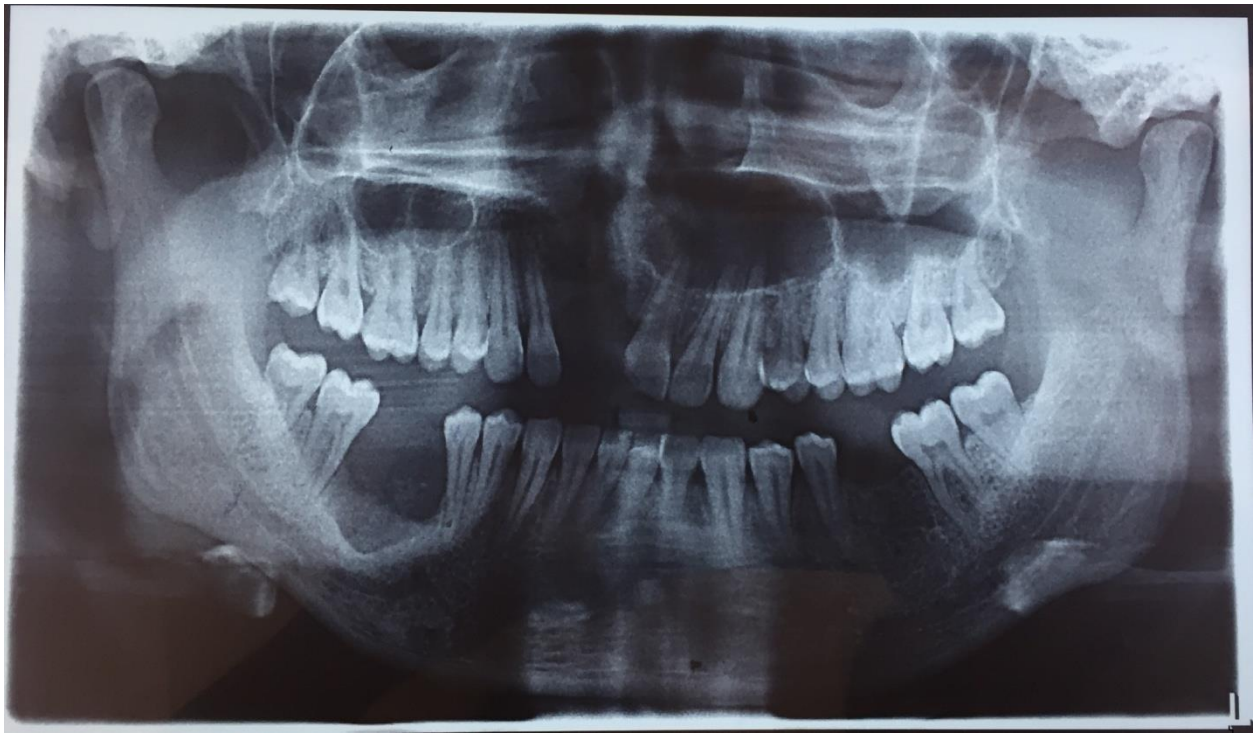

CECT face reveals irregular mottled destruction of the mandible is seen on the right side measuring 25.9mm×19mm with associated ill-defined enhancing soft-tissue mass on its inner and outer aspect with destruction of lingual as well as buccal cortex. [figure 3]

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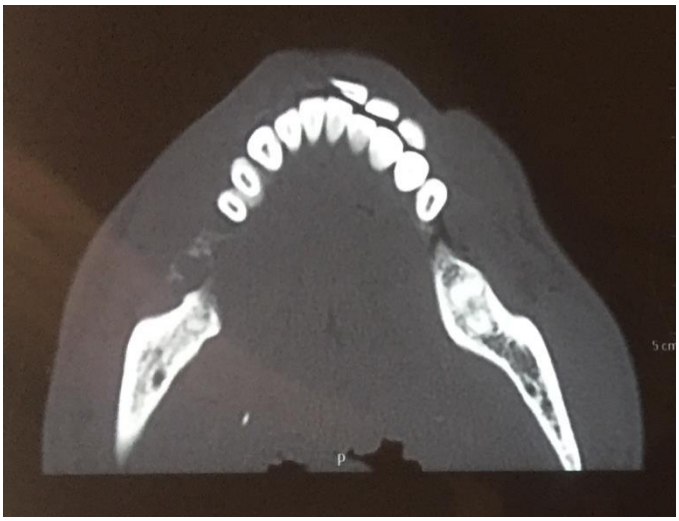

Mass is extending along the gingivo-lingual sulcus and shows ill-defined fat planes with adjacent part of the tongue. Histopathology reveals the presence of hyperplastic parakeratinized stratified squamous epithelium having long thin rete-ridges with underlying highly cellular connective tissue stroma. Connective tissue is composed of numerous multi-nucleated giant cells, endothelial lined blood vessels along with extravasated RBCs. Immature bone containing osteocytes with lacunae are evident in few areas.[figure 4]

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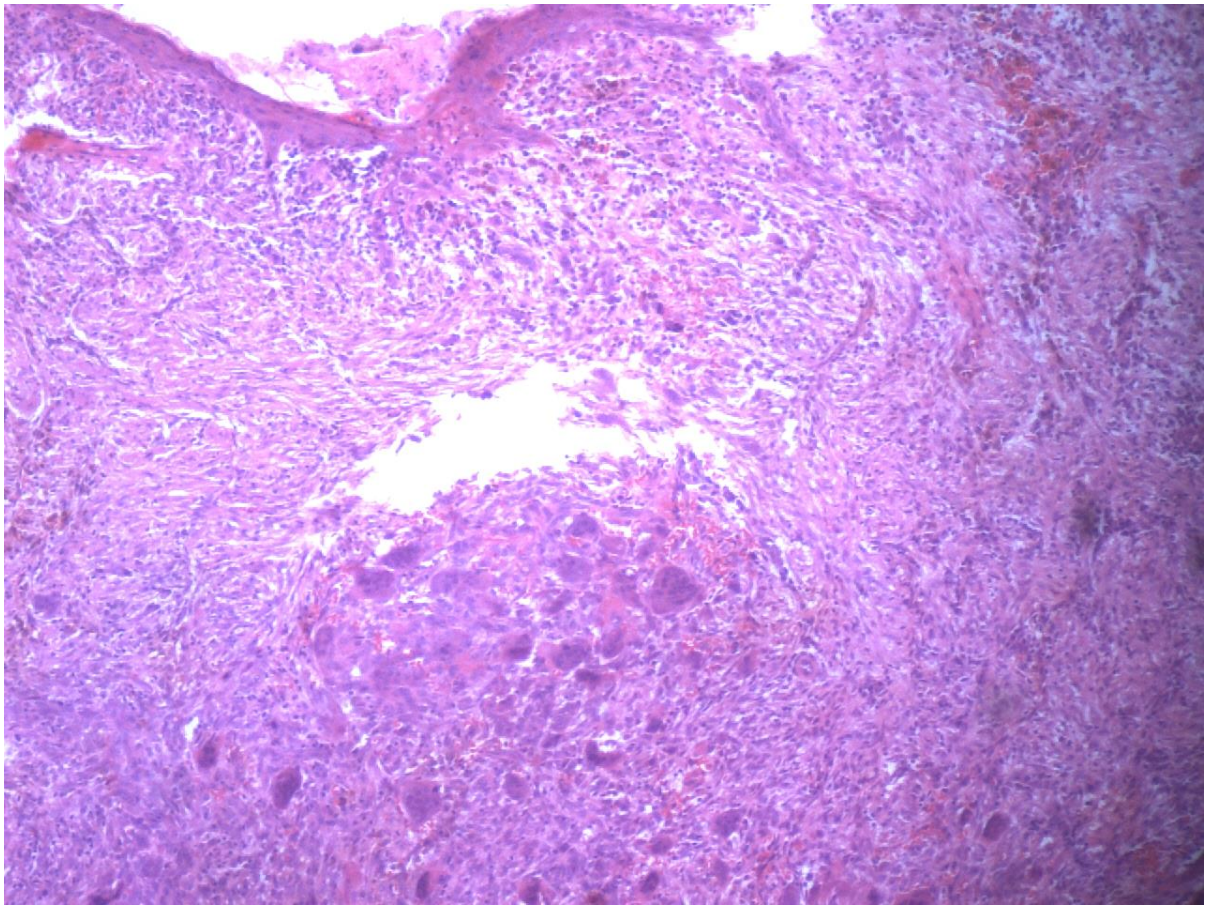

Focal areas of calcification and hemosiderin deposits are also evident. Sections show alveolar mucosal lining epithelium lined by mildly hyperplastic stratified squamous epithelium with focal pseudoepitheliomatous hyperplasia. The underlying tissue show aggregates of foreign body giant cells, fibro-angiomatous stroma along with giant cells are seen infiltrating the underlying bony tissue and destroying it. At places the giant cells are seen cuffing the bony fragments. No evidence of necrosis or increase in mitotic activity noted. With these we came to the final diagnosis of PERIPHERAL GIANT CELL GRANULOMA w.r.t. 46 region. Treatment advised was Cessation the habit., Excision of the peripheral giant cell granuloma, Maintaince of proper oral hygiene.

Discussion:

Flaitz suggested that PGCG can arise secondarily to an alteration of the endothelial cells of the capillaries.[23] Adlakha et al considered endothelial cells of the capillaries to have phagocytic response to hemorrhage in a preexisting granulation tissue, which results in the formation of PGCG.[24] Souza et al described in their study that Ki67 (proliferative marker) is expressed through G1, S, G2, and M phase of the cell cycle, and its demonstration indicates proliferative stage of these cells and Ki67-positive cells were seen largely in PGCG.[25]

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Clinically, it has been found that the incidence rate of PGCG among all oral reactive lesions varies from 5.1 to 43.6%. The age incidence of PGCG is most common in the fourth (40%) to sixth decade of life. PGCG has female predilection (65%), same as in our case. PGCG involves the mandible (55%) more than the maxilla (2.4:1), same as seen in our case. Clinical characteristic features of PGCG show an asymptomatic, soft, nodular mass with red to reddish-blue color. However, repeated trauma due to occlusion can lead to ulceration and secondary infection. Seldomly, the lesion is painful. A secondarily infected lesion presents a “yellow zone” caused by the aggregation of a fibrin clot at the ulcer site. It is usually not more than 1.5 cm in diameter. Radiographically, superficial bone resorption, widening of the periodontal ligament space, and mobility of associated teeth are usually seen. When the lesion involves edentulous areas, the cortical bone exhibits a concave resorption beneath the lesion. This typical feature is known as “leveling” effect. This feature is also referred to as “cupping” resorption by many authors.[26]

PGCG shows the same clinical features as of PG, central giant cell granuloma, peripheral ossifying fibroma, and metastatic carcinomas.[27] Microscopic examination shows the presence of hyperplastic parakeratinized stratified squamous epithelium. The connective tissue shows the presence of numerous young proliferating fibroblasts in vascularized fibrocellular stroma with numerous blood capillaries and abundant MNCs.[23]

The treatment of PGCG comprises surgical resection with elimination of the entire base of the lesion along with removal of the underlying irritant factors.[28] To avoid recurrence after treatment, extensive clearing of the lesion base and the source of irritation should be eliminated after complete excision of the lesion.[29]

Recurrence of PGCG is quite uncommon and ranges between 5 and 11%, as reported.[30] PGCGs that contain calcifications appear more likely to recur.

Conclusion:

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PGCG is a benign, reactive lesion occurring on the gingiva around teeth as well as in edentulous areas. This case report of PGCG has higher recurrence rate compared with previously published studies as the patient underwent complete excision twice within 1 month. Therefore, more cases should be reported for such kind of ambiguous reactive lesions.

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