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Peripheral giant cell granuloma of anterior maxilla in a 50-year-old female: A case report

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Abstract
The peripheral giant cell granuloma (PGCG) is a non-neoplastic reactive exophytic polyploidy arising 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 behaviour, 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.

Keywords: reactive hyperplasia, localized growth, peripheral giant cell granuloma, trauma, surgical excision, maxilla, multinucleated giant cells

Introduction

As a response to chronic irritation excessive proliferation of connective tissue occurs leading to various reactive lesions in the oral cavity. These lesions include peripheral giant-cell granuloma (PGCG), pyogenic granuloma, peripheral fibroma, fibro-epithelial hyperplasia and peripheral ossifying fibroma [1]. These lesions can be called as either a peripheral or central giant cell reparative granuloma as suggested by Bernier Cahn [2]. Waldron and Shafer found these lesions did not contain any reparative characteristics and did not differ from any other benign giant cell tumor of bone histologically [3]. Bhaskar *et al.* in 1959 subdivided giant cell granuloma into central and peripheral types [4]. Central giant cell granuloma (CGCG) occurs within the bone and those occurring on edentulous alveolar processes or gingiva are called PGCG. Prevalence of PGCG is higher than CGCG. Although the CGCG exists as a rare entity accounts only 7% of total benign lesions of the jaws leading to debilitating condition especially in young patients. The incidence rate has been reported of PGCG varies from 5.1% to 43.6% The aim of this case report is to illustrate an example of an aggressive peripheral giant cell granuloma (PGCG) and to discuss a reasonable differential diagnosis, based on the age of the patient, history and clinical features [5]. Its etiology is dubious and many authors have put forth different causes. One of theory suggests that PGCG originates from the periodontal membrane surrounding the tooth or from the periosteum of the bone. Sood *et al*. stated that PGCG is presumably a reactive lesion caused in response to local irritation or trauma. The predisposing factors include trauma, overhanging and poorly contoured restorations, plaque, calculus, ill-fitting dentures, chronic infections and impacted food [6]. Bodner *et al*. suggested that these lesions comprise of an abnormal proliferative response to aggregation [7]. Some studies have shown that extraction might lead to the development of PGCG. Mighell *et al*. reported a case, where there was an occurrence of PGCG 2 months post the orthodontic 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 [8].Vittek *et al*. in 1982 found progesterone and oestrogen receptors on human gingiva [9]. A study conducted by Matter *et al*. suggested that PGCG was propagated by pregnancy rather than being "pregnancy dependent" [10]. Previous literature reported rare occurrence of PGCG as an oral manifestation of hyperparathyroidism without any significant bone involvement [11, 12]. PGCG was reported by Buchner *et al.* [13] as the least encountered lesion among all the reactive lesions, comprising of about (18.7%), and was (1.25%) of all the biopsies included in his study. As PGCG is a soft tissue lesion that presents on gingiva and alveolar mucosa; features are thereby nonspecific and in some cases bone involvement occurs. Clinical features may include mobility of associated teeth.

Radiographic presentation may be superficial bone resorption and widening of periodontal ligament space, resorption of teeth and bony spicules at base of lesion. When the lesion involves edentulous areas, the cortical bone exhibits a concave resorption beneath the lesion, this typical feature is known as "levelling" effect [14].

Case Report

A 50-year-old female patient was reported by her mother to the Department of Oral Medicine, Radiology & Diagnosis with a chief complaint of swelling in the upper right front jaw region since one month. Patient gave no history of trauma or any other associated significant history. Extra oral examination revealed facial asymmetry due to extra oral diffuse swelling of right middle one third of face. Intraoral soft tissue examination on inspection revealed the solitary dome shaped swelling of size 3x4cm extending from permanent right maxillary lateral incisor to permanent right first premolar region on palatal as well as labial aspect (Figure 1). The lesion was sessile, irregular with overlying surface with pinkish red hue. On palpation the lesion was soft and tender with tendency to bleed. Radiologic examination (Panoramic radiograph) revealed no specific features extending from right maxillary lateral incisor to first premolar region (Figure 2). Patient oral hygiene was poor. Hard tissue examination revealed missing 18 28 31 32 33 34 35 36 37 38 45 46 47 48 and root stump 17. Patient has generalized bone loss and generalized attrited teeth. Mobile teeth were 15 16. Deep occlusal caries was present in 44 and palatal pit caries in 27. Provisional diagnosis was given as pyogenic granuloma.Differential diagnosis of PGCG involves giant cell tumour, non-ossifying fibroma, irritational fibroma which differs from PGCG lesions in consistency and colour; pyogenic granuloma which is difficult to distinguish from PCGC lesions; Central giant cell granuloma (CGCG) which is an expansive and destructive intraosseous lesion that can perforate the cortex, mimicking PGCG. Parulis is frequently associated with a necrotic tooth or with periodontal disorder; haemangioma cavernosum, which is distinguished from PGCG lesions by their pulsatile nature. Treatment plan included surgical excision of the lesion which was performed under local anaesthesia. There were no complications in the immediate post-operative period. Histopathologic examination revealed intact stratified squamous epithelium with normal appearing lamina propria. Deeper connective tissue is fibrillar, composed of ovoid as well as spindle shaped cells along with huge number of multinucleated giant cells. Numerous blood vessels are present with few containing giant cells. Haemorrhagic foci are also present, no osteiod or bony spicules seen suggestively of PGCG. (Figure 3)

Discussion

PGCG is known to occur at any age but occurs most commonly (40%) in the fourth to sixth decade of life. Female predilection has been reported. Rarely, the lesion is painful in nature. Mandible (55%) is more affected than the maxilla; mandibular to maxillary predilection is 2.4:1 [15] with preferential location for premolar and molar region. It is manifested clinically as a painless, soft, nodular mass, usually red to reddish-blue in colour. However, PGCG has a typical bluish - red hue in contrast to pyogenic granuloma that has a characteristic bright red colour. The lesion is usually asymptomatic; however, repeated trauma due to occlusion can lead to its growth with eventual ulceration and secondary infection. A secondarily infected lesion presents a 'yellow zone' caused due to the aggregation of a fibrin clot at the ulcer site. The lesions in edentulous patients may display as either a granular mass of tissue that grows along the slopes of the edentulous ridge or as a swelling on the crest of the ridge. It can be sessile or pendunculated [16]. Histopathology of PGCG centres around 3 main features: Presence of numerous young proliferating fibroblasts, vascularized fibrocellular stroma with numerous capillaries and abundant multinucleated giant cells. Fibroblasts in the stroma form a basic element of the lesion and are plump oval to spindle-shaped. Multinucleated giant cells comprising of variable shapes and sizes are scattered all throughout the connective tissue stroma. Many giant cells are found in association with and within the lumen of the blood vessels. This has led to the name of this lesion as "giant cell sarcoma" or, in some cases, "myeloid sarcoma." Spicules of newly formed osteoid or bone are commonly present scattered throughout the lesion [17]. The presence of giant cells has been linked to various causes and many authors have put forth different schools of thoughts, as some of them believe them to be a phagocytic response to haemorrhage in a pre-existing granulation tissue, others believe that they may arise from the endothelial cells of the capillaries, periosteum, periodontal ligament, or connective tissue of the gingiva. Different theories that have been proposed to explain the origin of these cells. A traumatic mechanism on one hand and a proliferative origin on the other, in which the lesion does not arise as a consequence of prior trauma, but secondary to alterations of the vascular endothelium [18]. Ultrastructure of the cells in PGCG; according to the investigations of Sapp *et al.* [19] mononuclear cells ultrastructurally are of three types.

Type I: Cells possessing clear ovoid nuclei with a smooth outline and prominent nucleoli. Their cytoplasm contains numerous organelles, especially rough endoplasmic reticulum, mitochondria, free polyribosomes and membrane-bound vacuoles. Irregular cytoplasmic processes are present in some of these cells, often showing interdigitation with similar cells and apparent cell fusion.

Type II: These cells possess more dense elongated nuclei with deep invagination of the nuclear membrane and inconspicuous nucleoli. Dilated cisternae of rough endoplasmic reticulum, mitochondria and clear vacuoles are seen in the cytoplasm of these cells. Traces of phagocytosed collagen fibers are also evident in the cell.

Type III: In this type of cell Birbeck granules, with characteristic tennis-racket morphology and transverse striations is present. The more prominent cytoplasmic organelles found in these cells were endoplasmic reticulum, mitochondria, intermediate-sized filaments, polyribosomes and lysosomes [20]. Some molecular aspects Souza *et al.* concluded 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 the cell. Ki67 positive cells were more in PGCG. Thus, according to Souza *et al.* [21] although CGCG is more aggressive, however, PGCG is more proliferative than CGCG. Filioreanu *et al.* [22] have shown that the expression of α-SMA which is a cytoskeletal marker is highly correlated with

myofibroblasts in the granulation tissue of PGCG. This denotes increased fibroblastic activity of the lesion. The study conducted by Amaral *et al*. have found that giant cell lesions that include PGCG, CGCG, and cherubism presents increased levels of NFATc1, overexpression of which increases osteoclasts fusion as well their differentiation. The study concluded that the development and progression of giant cell lesions of the jaws was possibly mediated by overexpression of NFAT in the nucleus of multinucleated giant cells. Thus, targeting this pathway can be a potential source of future molecular therapy in treating these lesions [23].

Treatment

The treatment of PGCG comprises of excision and suppression of underlying etiological factors with elimination of the entire base of the lesion. Surgical excision can be done using various methods ranging from conventional blade, an electric scalpel to cryosurgery using liquid nitrogen or cryoprobe and lasers. There is advantage of laser resection over other conventional methods as it causes less intra operative bleeding, sterilizes the wound, requires no suturing and affords improved postoperative patient comfort. Resection should not only be done superficially as the growth may recur [24]. Most lesions respond satisfactorily to thorough surgical resection, with exposure of all the bone walls. This great variation is probably attributable to the surgical technique used since recurrences re-excised up to the periosteum have not recurred thereafter. Extraction of adjacent teeth needs to be done in cases when the periodontal membrane is affected in order to ensure full resection, though this is initially contraindicated. Sliding flap operation for repair of gingival defect was described by Grupe and Warren. This technique comprises of the use of a full-thickness pedicle flap. It is moved horizontally to cover the denuded root; this may consequently lead to the exposure of the donor area's root and bone tissue. Sub marginal incision is used to preserve the marginal gingiva at the donor site. This modified technique of the sliding flap operation repairs the residual gingival defect resulting from complete surgical excision of PCGC in order to reduce the risk of gingival recession and bone dehiscence at the donor site. Original procedure can be modified in such a way that the coronal half of gingiva is undisturbed. This one stage procedure allows predictable repair of residual gingival defect in the attached gingiva and yields an excellent colour blend with the adjacent tissues.

Contraindications of this approach includes inadequate band of attached gingiva of lateral donor site, or if a shallow vestibule is present. Precautions must be taken if the facial bone at the donor site could potentially have a fenestration or dehiscence. A split-thickness flap or another surgical approach should be used in such cases. The technique, although simple, needs surgical dexterity for the operator, especially during the reflection of lateral pedicle graft as full-thickness up to mucogingival line, which is firmly attached to the underlying bone and in making partial-thickness graft apical to mucogingival line [25].

Recurrence It has recurrence rate of 5.0-70.6% (average 9.9%) has been reported in various epidemiologic studies [26]. Recurrences are believed to be related to lack of inclusion of the periosteum or periodontal ligament in the excised specimen. A re-excision must be performed for these cases. Aggressive tendencies or malignant transformation of these lesions has never been reported. PGCG lesions are self-limiting. Hence, recommended management of PGCG aims at elimination of the entire base of the growth accompanied by eliminating any local irritating factors [27].

Conclusion

A definite diagnosis of PGCG is achieved on the basis of clinical, radiographical, and histopathological examination. Conservative management should be done with minimal risk to the adjacent structures. Scrupulous knowledge of etiopathogenesis and biologic behaviour of this lesion will lead to reduction in occurrence and recurrence rates. Meticulous attention to molecular aspect of this lesion will in turn aid in designing target therapies against this pathological entity & thereby providing optimal patient care.

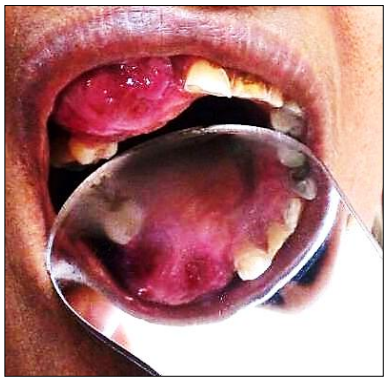

Fig 1: Exophytic mass in anterior maxilla, palatal to the dental arch with labial and interdental extension irt 12 13 14

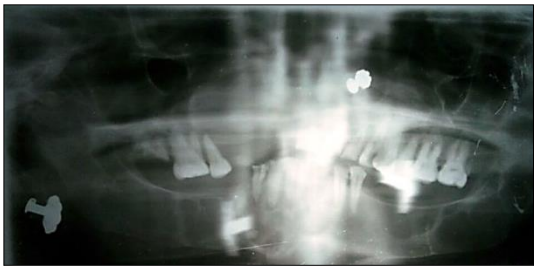

Fig 2: Panoramic radiograph

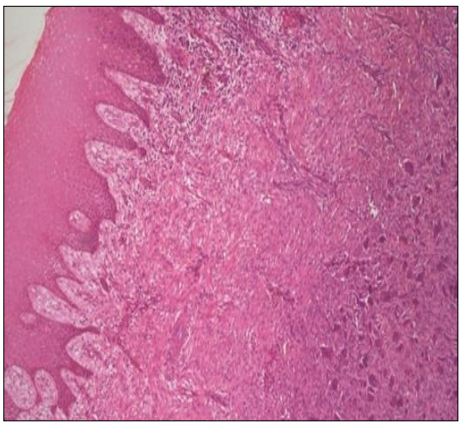

Fig 3: Photomicrograph of lesion

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