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Research Article
Recurrent Peripheral Giant Cell Granuloma: A Case report

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Keywords

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Giant Cell Lesion,
Multinucleated Giant Cells,
Mononuclear Stromal Cells,
Myeloid Tumor, Osteoclasts.

Abstract

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

Introduction

The giant cell granuloma of the jaws is a non-neoplastic lesion characterized by the presence of few to many multinucleated giant cells in a cellular background composed of mononucleated stromal cells with ovoid to spindle-shaped nuclei.[1] Giant cell granuloma may occur within the bone (central giant cell granuloma [CGCG]) or on the gingiva or edentulous alveolar processes (peripheral giant cell granuloma [PGCG]). CGCG accounts for approximately 7% of benign lesions of the jaws, is locally destructive and occasionally shows an aggressive biologic behaviour, especially in younger patients.[2] In contrast, PGCG is a common peripheral soft tissue lesion and is known to arise from the connective tissue of the gingiva, periodontal membrane, periosteum of the alveolar ridge or in response to local irritation.[3] However, the reparative response is not very remarkable, therefore, the term "peripheral giant cell granuloma" is preferred and universally accepted. This entity however is under controversy regarding its etiology. In 1962, Gottsegen[4] suggested the development of peripheral giant cell granuloma often after periodontal surgeries. Other investigators considered it to arise in response to local irritating factors such as tooth extractions, ill-fitting prostheses, poor restorations, collections of food remnants and calculi.[5] Low socio-economic status of the patients and unfavourable oral hygiene also seem to be predisposing factors to peripheral giant cell granuloma.[6] Recently, Choi[7] reported the association of peripheral giant cell granuloma with hyperparathyroidism secondary to renal failure.

PGCG occurs only on the gingiva or edentulous alveolar ridge. It presents itself as a red or reddish blue nodular mass.[8] It is more common in the mandibular arch than in the maxillary arch and more often occurs anterior to permanent

first molars.[9] Malignant transformation of these lesions has never been reported. The recurrence rate after local excision is around 10%.[3] The histological features consist of a non-encapsulated highly cellular mass with abundance of multinucleated giant cells dispersed throughout. Apart from fibroblasts which are the basic element of the lesion,[10] chronic inflammatory cells are usually seen in abundance with neutrophils mainly encountered in the ulcerated base of the lesions. Hence, diagnosis of this lesion is crucial and should be included with high incidence in the list of differentials of the common peripheral soft tissue lesions of the jaws because of its high potential for recurrence and its occurrence associated with certain systemic conditions. As also, histopathology should be considered as the gold standard in its diagnosis due to its non-specific clinical and radiological features.[9]

Case Report

A 36 year old male patient visited a private dental practitioner with a chief complaint of swelling in relation to lower right back tooth region which interfered during mastication since 5 months. Patient noticed a small swelling in relation to interdental papilla in 45,46 region around 5 months back. The swelling was insidious in onset and gradually increased to present size over a period of last 5 months. The swelling was initially painless but used to show signs of inflammation and subsequent pain when was traumatized during mastication. The swelling was recurrent in nature. A similar lesion had initially appeared around 8 months back and was treated with LASER. The lesion showed recurrence after 2 weeks and was then treated using Electro-cautery. In the current situation, extra-oral examination didn't reveal any obvious abnormality. There was no associated lymphadenopathy. Intra-oral examination revealed a 1.5 x 1.5 cm, pedunculated, roughly ovoid, reddish pink, soft, nodular and non-tender gingival overgrowth on the lingual aspect of attached gingiva in relation to 44,45,46 region which extended from the distal aspect of 44 to the mesial aspect of 46. [Fig.1] Local factors were present in relation to the teeth associated with the lesion. Routine blood investigations were found normal. Serum alkaline phosphatase and serum calcium and phosphorus levels were within normal limits. Radiological examination revealed horizontal bone loss in 45,46,47 region. [Fig.2] Considering the past history and previous histopathological report that was supportive for Peripheral Giant Cell Granuloma (PGCG) and present clinical and radiographic findings, a provisional diagnosis of Peripheral Giant Cell Granuloma was given with Pyogenic Granuloma and Peripheral Ossifying Fibroma as differential diagnosis.

Knowing the previous history of recurrences, a complete treatment was planned to get the best possible results. Treatment started with non-surgical periodontal therapy including a thorough scaling and root planing and patient was put on maintenance phase. Patient was recalled after 15 days. Under local anaesthesia, localized periodontal flap surgery was performed with elevation of buccal and lingual flap after incision, thorough debridement with complete removal of sub-gingival calculus and debris was accomplished. Complete excision of the lesion was done and care was taken to remove the entire base of the lesion along with 1mm of healthy margin around the tissue. [Fig.3] The lesion was stored in 10 % formalin and sent for histopathological examination. The surgical site was sutured with simple interrupted sutures for better approximation and periodontal pack was given. After 7 days recall, periodontal pack and suture removal was carried-out and the surgical site was examined which presented with good healing. Follow up appointments were performed at 1 month, 6 months and 12 months intervals. Healing was uneventful [Fig.4] and no reoccurrence was observed even after 12 months. During this period, the patient did not report any complaints and no other treatment was needed. Histopathology showed the lesional tissue covered with a proliferating parakeratinized stratified squamous epithelium. Underlying connective tissue stroma revealed the presence of plump proliferating fibroblasts with numerous multinucleated giant cells with haphazard nuclear arrangements and few to numerous nuclei. [Fig.5a] Both types of giant cells described in literature as Type I and Type II [3,7] i.e. those that are large and with vesicular nuclei and those that are smaller in size with compact nuclei (close faced nuclei) were evident. [Fig.5b] Numerous vascular spaces with giant cells in the lumen of the blood vessels were also present throughout the sections. [Fig.5c] Certain giant cells showed pseudopodia-like extensions of their cytoplasm and appeared to engulf mesenchymal cells. Phagocytic vacuoles were evident in the giant cells. [Fig.5d] The lesion also appeared to have a pseudo-capsule like structure known otherwise as "Grenz zone". Chronic inflammatory cell infiltration chiefly consisting of lymphocytes was also present. [Fig.5e-low power, Fig.5f-high power] Connective tissue was interspersed with abundant giant cells with vesicular nuclei and prominent nucleoli signifying the high activity of cells. [Fig.5g] The presence of giant cells in the lumen of the blood vessels suggested their vascular etiologies. [Fig.5h] Numerous vascular spaces present throughout the lesion indicated the high vascularity of these lesions. [Fig.5i].

Discussion

PGCG is not a true neoplasm but rather a benign, hyperplastic, reactive lesion caused by local irritation or chronic trauma. Although the exact etiology is still not clear, many authors consider the lesion as an abnormal proliferative response.[11] Certain hormones (estrogen and progesterone) that are supposed to have an immunosuppressive action may contribute to the growth of this lesion while hyperparathyroidism has been suggested as one of the rare etiologies of the occurrence of this lesion.[12] The latter is usually suspected when multiple lesions are identified and the patient suffers recurrences despite adequate treatment.[3]

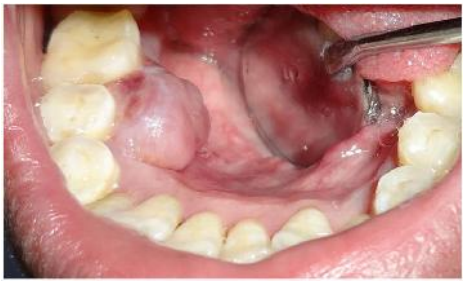

Fig.1 revealing a 1.5 x 1.5 cm, pedunculated, roughly ovoid, reddish pink, soft, nodular and non-tender gingival overgrowth on the lingual aspect of attached gingiva in relation to 44,45,46 region which extended from the distal aspect of 44 to the mesial aspect of 46.

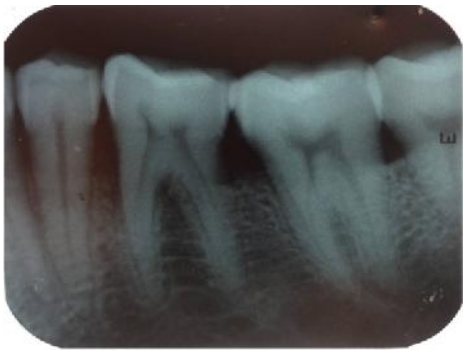

Fig.2 revealing horizontal bone loss in 45,46,47 region.

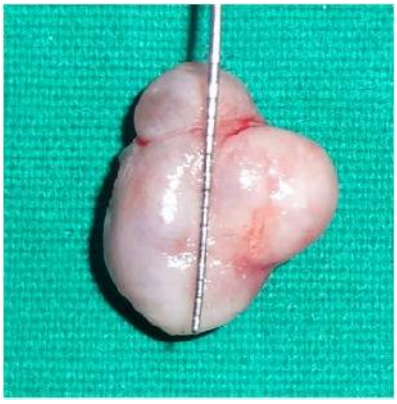

Fig.3 revealing the excised tissue with entire base of the lesion.

Fig.4 revealing uneventful healing of the tissue post-excision.

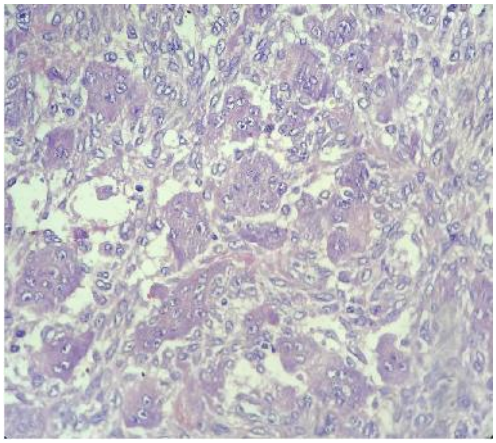

Fig.5a revealing the lesional tissue covered with proliferating parakeratinized stratified squamous epithelium and with the underlying connective tissue stroma revealing plump proliferating fibroblasts and numerous multinucleated giant cells.

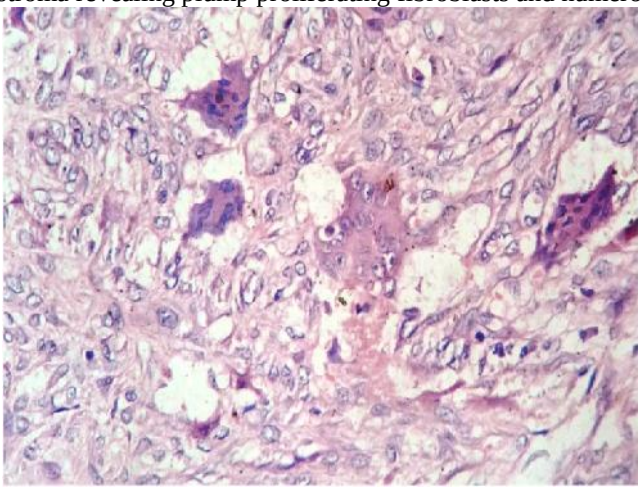

Fig.5b revealing Giant cells having different shapes and sizes with haphazard nuclear arrangements and few to numerous nuclei . Both types of giant cells as described in literature as (type I & type II) i.e. those that large and with vesicular nuclei and those that are smaller in size with compact nuclei (close faced nuclei) are evident.

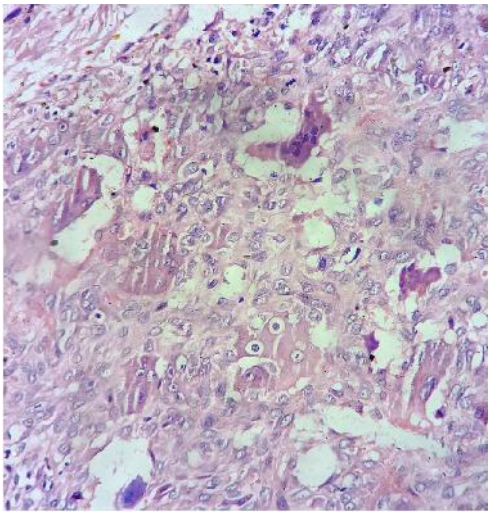

Fig.5c revealing numerous vascular spaces present throughout the section with giant cells inside the lumen of blood vessels.

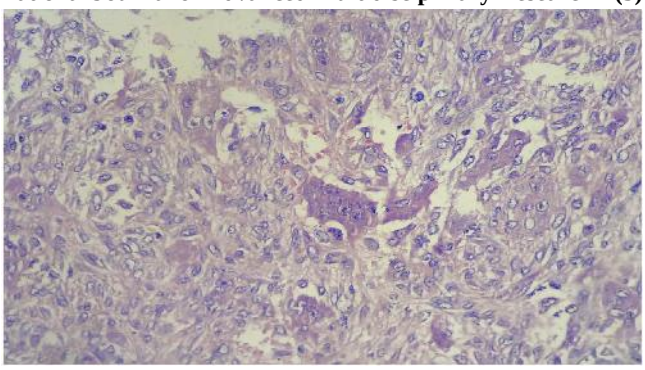

Fig.5d revealing few giant cells showing pseudopodia-like extensions of cytoplasm. Phagocytic vacuoles are evident in the giant cells.

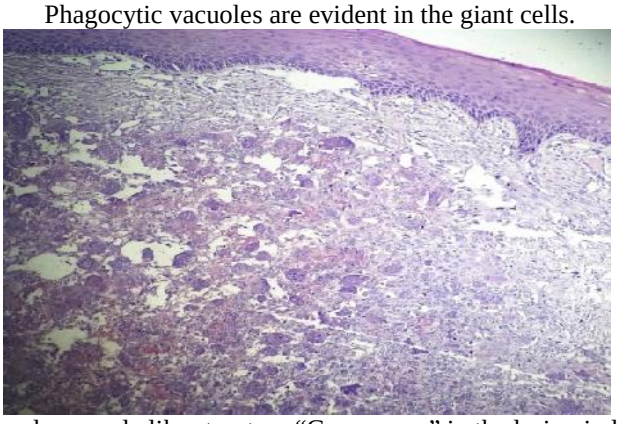

Fig.5e revealing a pseudo-capsule like structure "Grenz zone" in the lesion in low power (4x view). Chronic inflammatory cell infiltration chiefly consisting of lymphocytes is also present.

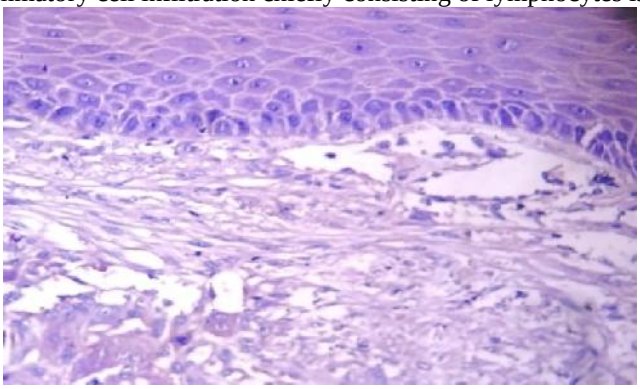

Fig.5f revealing the same in high power (10x view)

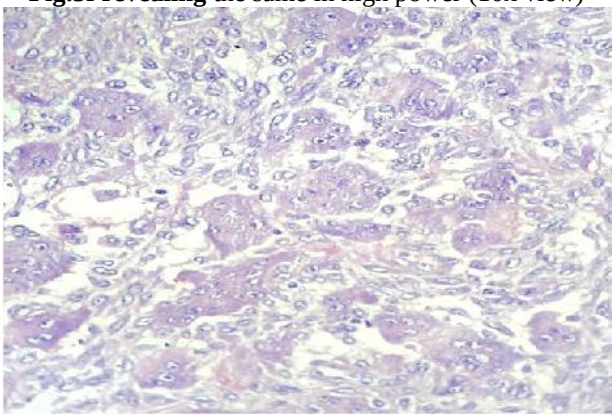

Fig.5g revealing connective tissue interspersed with abundant giant cells with vesicular nuclei with prominent nucleoli signifying high activity of cells.

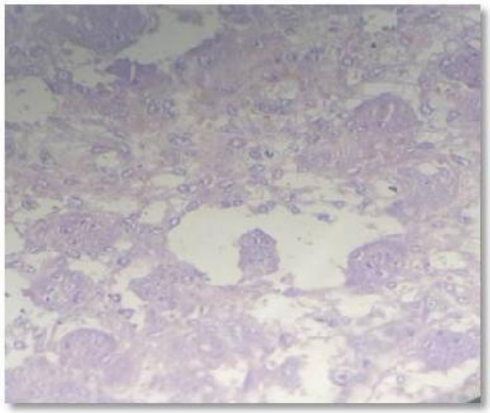

Fig.5h revealing the presence of giant cells inside the blood vessels suggesting their origin possibly from the endothelial cells.

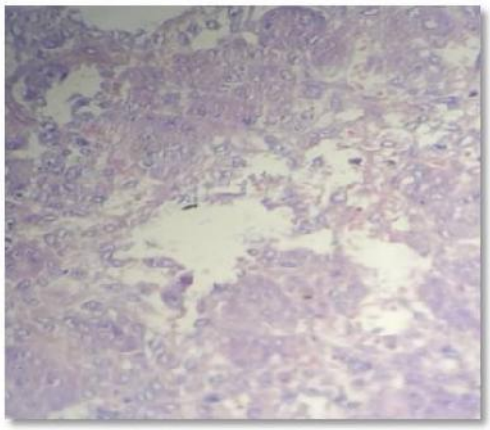

Fig.5i revealing numerous blood vessels revealing high vascularity of the lesion.

Peripheral giant cell granuloma has no specific age predilection however, highest incidence is noted in the 4th to 6th decades of life with 20–30% of the cases manifesting in the 1st and the 2nd decades of life.[13] The preferential location of the lesion according to Pindborg[14] is the premolar-molar region, though Shafer[9] and Giansanti[13] suggest that it generally occurs in the incisor and canine region. PGCG affects females more than males.[9] PGCGs are rather unique lesions of oral cavity occurring on gingival or alveolar mucosa, but never found on tissues that are not supported by periosteum, which supports evidence for its origin. The size of the lesion varies between 0.5 to 1.5 cm. Bodner et al[15] reviewed 15 cases of large (more than 2 cm) lesions suggesting its innate growth potential and showed that patients with poor oral hygiene or with xerostomia are at a higher risk to have larger lesions. The consistency of the lesion is dependent on the age of the lesion because as the time passes, maturation of the lesion (increase in collagen fibers) occurs and consistency shifts from being soft to firm.[16] Ulceration and bleeding can also be seen secondary to trauma. Radiographic features usually are not very pronounced. However, sometimes they reveal superficial destruction of the alveolar margin or crest of the inter-dental bone when the lesion is seen associated with the teeth. In cases, where the granuloma is associated with the edentulous ridge, it characteristically exhibits superficial erosion of the bone with peripheral "cuffing" of the underlying bone.[9]

The differential diagnosis of peripheral giant cell granuloma includes pyogenic granuloma,[10] fibrous epulis, peripheral ossifying fibroma, inflammatory fibrous hyperplasia, peripheral odontogenic fibroma and papilloma, all of which present with similar clinical and radiographic findings. Thus, in such cases a definitive diagnosis can only be established through histopathological examination.

The histopathology of PGCG reveals a large number of multinucleated giant cells in a well-vascularized fibro-cellular stroma. In some cases, the giant cell may be found within the lumen of the capillaries. The exact origin of giant cells is still uncertain. Many opinions have been offered in the literature as osteoblasts, phagocytes, endothelial cells and spindle cells being the progenitors for the giant cell proliferations.[17] Hemorrhage, hemosiderin pigment, inflammatory cells and newly formed bone or mature calcified material may be present throughout the cellular stroma. A zone of dense connective tissue representing a pseudo-capsule known as 'Grenz zone' usually separates the giant cell proliferations from the superficial epithelial layers.[18]

Treatment consists of local surgical excision down to the underlying bone.[8]A thorough debridement of local factors or irritants is also required.[10] If resection is only superficial, the growth may recur. Exposure of all bony walls following a thorough surgical resection responds satisfactorily most of the time. A recurrence rate of 5.0-70.6% has been reported in various epidemiologic studies.[17] Recurrences are believed to be related to lack of inclusion of the periosteum or periodontal ligament in the excised specimen.[10] A wide base re-excision of the lesion is often found to be satisfactory in treating these cases.[8] In our case, recurrence was thought to be due to an inadequate therapy and incomplete removal of the base of the lesion by laser and electro-cautery procedures. The treatment rendered in this case was surgical excision down to the level of underlying bone and curettage followed by oral prophylaxis. The 12 month follow-up of the patient showed no recurrence indicating that the given treatment along with maintenance of a good oral hygiene was sufficient for the complete cure of the lesion.

Conclusion

In conclusion, an early and precise diagnosis of PGCG is important to avoid unnecessary aggressive therapy. Complete removal of the lesion with proper periodontal therapy should be the treatment protocol to avoid recurrence. Identification of etiological factors is also important to avoid recurrence of such lesion. A definite diagnosis of PGCG on the basis of clinical, radiological and histopathological examination allows us to do conservative management with minimal risk to the adjacent hard tissues.

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