Original Article - Retrospective Study

An Audit of Histopathological Pattern of Peripheral Giant Cell Granuloma - A Retrospective Study

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Abstract

Introduction: Peripheral giant cell granuloma (PGCG) is a type of reactive hyperplastic lesion in the oral cavity that develops due to local irritation or chronic trauma, originating from the periosteum or periodontal membrane. It primarily affects the alveolar mucosa of the posterior mandibular region and has a peak incidence in the age range of the fourth to sixth decades of life, with a 2:1 female predilection. The aim of the study was to analyse the histopathological pattern of peripheral giant cell granuloma. **Materials and Methods:** This retrospective study was conducted at a tertiary care teaching hospital from 2018 to 2023 after obtaining the required institutional ethical board approval (SMC/UECM/2023/627/296). All the cases of maxillofacial lesions referred/reported to and which conformed to the set inclusion and exclusion criteria were included. Data were analysed by calculating the percentage of the variables. IBM SPSS version 20 software was used to analyse the descriptive data. **Results:** Out of 12 patients, four were males and eight were females. The age ranged from 20 to 60 years with an average age of 40 years. All the patients included in the study showed multinucleated giant cells and inflammatory cells, 83.3% showed fibrous stroma and 50% showed para-keratinisation and haemosiderin pigments. **Discussion:** PGCG, a reparative lesion, seems to occur mostly in the 40–60 years of life with female predilection and commonly seen histopathological features included multinuclear giant cells, inflammatory cells in all cases, 83.3% fibrous stroma and 50% both para-keratinisation and haemosiderin pigments.

Keywords: Giant cell lesion, keratinisation, multinucleated giant cells, peripheral giant cell granuloma, reparative lesion

Introduction

Peripheral Giant Cell Granuloma (PGCG) is a reactive hyperplastic lesion of the oral cavity originating from the periosteum or periodontal membrane due to local irritation. Coined by Jaffe for jaw lesions, Bernier and Cahn termed those outside the central bone as 'peripheral'. It primarily affects the posterior mandibular alveolar mucosa of women (2:1), peaking in the fourth to sixth decade.[1]

Histologically, it features multi-nucleated giant (MNG) cells amongst fibrillar connective tissue with young fibroblasts and bone spicules. Histological confirmation relies on identifying MNG cells within a connective tissue stroma, fibroblasts and osteoid spicules.[2] This study aimed to analyse the histopathological pattern of peripheral giant cell granuloma. This study quantifies PGCG histopathological patterns with some subtle variations of the cellular pattern.

Subjects and Methods

This retrospective study was conducted in the Department of Oral and Maxillofacial Surgery of a tertiary care teaching hospital from June 2018 to May 2023 after obtaining the required institutional ethical board approval (SMC/UECM/2023/627/296). All the cases of maxillofacial lesions investigated with incisional biopsy under local anaesthesia and fulfilling the following criteria were included in the study with the approval of the institutional ethical committee and all guidelines as per the Declaration of Helsinki and good clinical practice guidelines were followed. Patient consent was waived due to the retrospective nature of the study.

Inclusion criteria included histopathologically proven cases of PGCG as well as all age groups and sexes. Exclusion criteria included a follow up period of less than six months,

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incomplete records and patients not willing to participate in the study. On confirmation of PGCG, the cases were subjected to pre-anaesthetic assessment and operated under general anaesthesia for excision of the lesion. The specimens were evaluated histopathologically to ascertain the histopathological pattern. Postoperatively, the cases were followed up for at least six months to evaluate the healing and recurrence of the lesion. Data were analysed by calculating the percentage of the variables. IBM SPSS version 20 (Microsoft, USA) software was used to analyse the descriptive data.

Results

Twelve patients fulfilling the set criteria were included in the study, consisting of four males and eight females with an average age of 40 years. In eight patients, the lesion was seen in the maxillary arch and four patients in the mandibular arch. The dominating variety of inflammatory and MNG cells [Figures 1-4] was observed in 12 cases. Histopathologically, other varieties observed are summarised in Table 1.

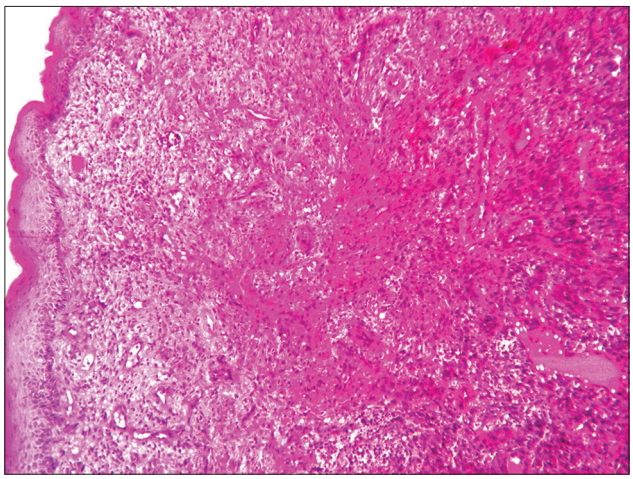

Figure 1: Haematoxylin & Eosin stained parakeratinisation (10x)

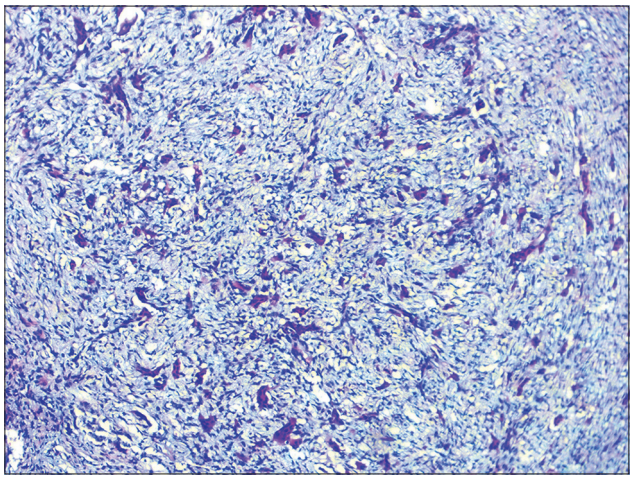

Figure 3: Haematoxylin & Eosin stained multi-nucleated giant cells and fibrous stroma (10x)

Discussion

PGCG is a lesion with a multifactorial aetiology, and several authors have proposed numerous reasons. The term 'peripheral giant-cell granuloma' is favoured due to the absence of a reparative response in these lesions. This lesion commonly appears on the gingiva or alveolar mucosa and typically presents as a painless, clearly outlined, reddish-purple growth that can either be sessile or pedunculated and originates from the gingival mucosa. The primary sources of PGCG include the lamina propria of the gingival tissue, the periodontal ligament membrane and the periosteum of the alveolar bony ridge.[1]

In some cases, it may become secondarily infected and breached epithelium/ulcerated. PGCGs are generally smaller than 2 cm in diameter, and factors such as impaction of food, tooth extractions, defective dental restorations, ill-fitting dentures and calculus contribute locally to their formation.[2] These lesions may manifest due to chronic local irritation of the gingival tissue. The hypothesis suggests that PGCG is a more robust periosteal response to irritation factors than those linked with the development of the more prevalent lesion,

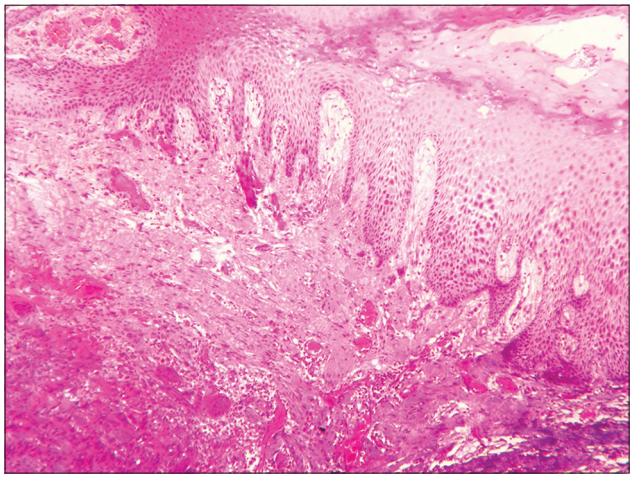

Figure 2: Haematoxylin & Eosin stained inflammatory cells (10x)

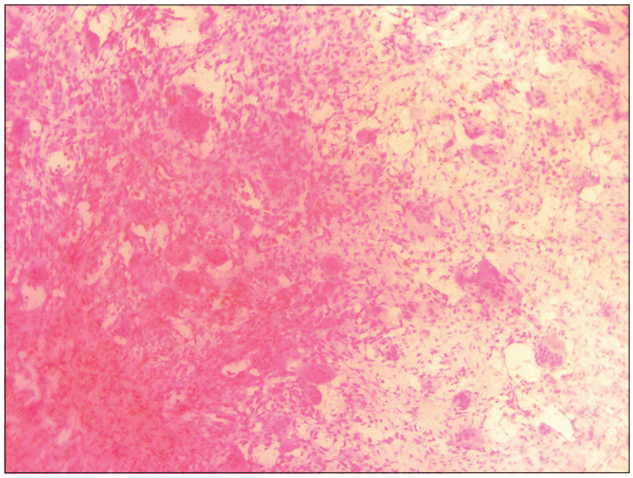

Figure 4: Haematoxylin & Eosin stained hemosiderin pigmentation (10x)

Table 1: Histological pattern

Type of cells	Number of patients (%)
Inflammatory cells	12 (100)
Multinucleated giant cells	12 (100)
Fibrous stroma	10 (83.3)
Haemosiderin pigmentation	6 (50)
Parakeratinisation	6 (50)

pyogenic granuloma, as the periodontium reacts differently to similar irritants.[3] Differential diagnoses based on a clinical presentation can be pyogenic granuloma, peripheral ossifying fibroma and pregnancy tumour.

The PGCG develops over the course of life, reaching its highest occurrence during the mixed dentition years and between the ages of 30 and 40 years. In the current study, 66.6% (8) were females and 33.34% (4) were males affected with PGCG.

Gunhan M *et al*.,[4] studied 26 cases of PGCG, and found that sex hormones may influence these lesions. Their research indicated that giant cells might be a possible target of oestrogen, with 60% more women than men supporting this hypothesis, but not progesterone action. Ojanotko-Harri *et al*.,[5] suggest that the co-occurrence of inhibited inflammatory cell function and active progesterone levels during pregnancy alters the plaque-induced inflammatory response, leading to excessive gingivitis.

The lower jaw is somewhat more commonly affected by this condition than the upper jaw.[3,6] According to the present study's findings, the lesion is associated with both the maxilla and mandible in the ratio of 1:1. Lesions can grow large, with some reaching a diameter of 2 cm. Even though PGCG often presents with a more bluish-purple hue due to haemorrhagic patches rather than the bright red hue of a normal pyogenic granuloma, the clinical representation is comparable to that of the more prevalent pyogenic granuloma. Despite the inflammatory and MNG cells seen in all the cases, none of the cases presented with recurrence or any complication postoperatively.

Even though PGCG grows within soft tissue, there may be occasionally 'cupping' or surface erosion of the alveolar bone crest beneath, which may make it difficult at times to discern whether the protrusion is a peripheral lesion. The gingiva-related extraosseous lesions of cherubism resemble giant cell epulides in appearance. The additional distinguishing clinical and radiological cherubism traits, however, will help to make the correct diagnosis. The preferred treatment modality involves complete surgical excision after eliminating local irritants to decrease the recurrence rate (10%–15%).[2]

Histologically, PGCG consists of clusters of large, multinucleated cells set against a background of hefty mesenchymal cells in the ovoid and spindle shapes as well as extravasated red blood cells (haemosiderin pigmentation). The larger cells within PGCG may exhibit a variable number of nuclei, ranging from a few to several hundred. Some feature prominent, vesicular nuclei, while others display smaller, pyknotic nuclei. The origin of these large cells remains unknown.[6]

In the current study, all cases presented with the presence of MNGs, and inflammatory cells with moderate lymphocytes in most cases. In a few cases of the present study, scattered and diffused patterns of lymphocytes were seen. This correlates with the features of the reactive inflammatory type of giant cell lesion. Furthermore, the majority of cases presented with the fibrocellular connective tissue matrix contain fibroblasts and blood vessels. In addition, half of the cases showed both para-keratinisation and haemosiderin pigmentation together. No significant correlation between the presence of fibrocellular stroma was seen with the chronicity of lesion presentation.

Previous explanations regarding the nature of MNGs have proposed two main ideas. One is that they are residual osteoclasts resulting from normal tooth resorption or a response to periosteum injury. The second idea is that these cells could be osteoclasts, as they exhibit the ability to excavate bone *in vitro* and express calcitonin receptors.[6] However, an emerging body of research suggests an alternative perspective. These large cells may be a reactive component of the lesion, originating from bone marrow mononuclear cells through the bloodstream. They might only appear in response to some unidentified stimulus from the stroma. Recent research, including studies involving cell culture and transplantation, has provided support for this theory. Notably, these studies revealed that unlike stromal cells, large cells have a short lifespan and disappear in a culture.[7,8]

As per Scotto di Carlo *et al*.,[9] stromal cells secrete various cytokines and differentiation factors, such as monocyte chemoattractant protein-1, osteoclast differentiation factor and macrophage-colony stimulating factor. This suggests that stromal cells promote the influx of blood monocytes into tumour tissue, facilitating their fusion into osteoclast-like MNG cells. These chemicals play a vital role in monocyte chemoattraction and are essential for osteoclast differentiation. A disintegrin and metalloprotease, a family of membrane-bound proteins recently discovered, is also thought to be involved in the multinucleation of osteoclasts and large cells produced by macrophages.

In a study by Brooks *et al*.,[10] Liu Bo described *in situ* hybridisation to identify messenger ribonucleic acid expression of the recently discovered receptor activator of nuclear factor-kappa B ligand (RANKL), its receptor, receptor activator of NF-kappa B (RANK) and its decoy receptor, osteoprotegerin (OPG). RANKL plays a vital role in osteoclastogenesis. The researchers concluded that the presence of RANKL, OPG and RANK in these lesions could be pivotal in the formation of MNG cells.

Conclusion

PGCG, a reparative lesion, seems to occur mostly in the 40–60 years of life with female predilection. Multinuclear giant cells and inflammatory cells, predominantly lymphocytes are frequently observed in all cases. In addition, approximately 83.3% of cases exhibit a fibrous stroma rich in fibroblasts and blood vessels, while 50% of cases display both para-keratinisation and the presence of haemosiderin pigments. Regardless of the histological pattern, there was no recurrence in the reported case series.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Jindal DG, Kushwaha SS, Joshi S, Sepolia N, Jindal V, Jain K. Peripheral giant cell granuloma: A case report with review on its histogenesis and recurrence. Dent J Adv Stud 2019;7:95-8.
2. Shafer WG, Hine MK, Levy BM, editors. Benign and malignant tumors of the oral cavity. In: A Textbook of Oral Pathology, 8th ed. Philadelphia: W.B Saunders Co ,1983:189.
3. Patil KP, Kalele KP, Kanakdand VD. Peripheral giant cell granuloma: A comprehensive review of an ambiguous lesion. J Int Clin Dent Res Organ 2014;6:118-25.
4. Günhan M, Günhan O, Celasun B, Mutlu M, Bostanci H. Estrogen and progesterone receptors in the peripheral giant cell granulomas of the oral cavity. J Oral Sci 1998;40:57-60.
5. Ojanotko-Harri AO, Harri MP, Hurttia HM, Sewón LA. Altered tissue metabolism of progesterone in pregnancy gingivitis and granuloma. J Clin Periodontol 1991;18:262-6.
6. Tandon PN, Gupta SK, Gupta DS, Jurel SK, Saraswat A. Peripheral giant cell granuloma. Contemp Clin Dent 2012;3:S118-21.
7. Gomes CC, Diniz MG, Bastos VC, Bernardes VF, Gomez RS. Making sense of giant cell lesions of the jaws (GCLJ): Lessons learned from next-generation sequencing. J Pathol 2020;250:126-33.
8. Ohri T, Singh B, Nand T, Singh N. Peripheral giant cell granuloma – A case report. J Adv Med Dent Sci Res 2020;8:19-22.
9. Scotto di Carlo F, Whyte MP, Gianfrancesco F. The two faces of giant cell tumor of bone. Cancer Lett 2020;489:1-8.
10. Brooks PJ, Glogauer M, McCulloch CA. An overview of the derivation and function of multinucleated giant cells and their role in pathologic processes. Am J Pathol 2019;189:1145-58.