Case Report

Peripheral Giant-Cell Granuloma: A Potentially Aggressive Lesion in Adults

Anupriya Sharma, Ashish Sharma[1], Suruchi Dogra[2]

Department of Dentistry, Dr. Radha Krishnan Government Medical College, Hamirpur, Departments of [1]Neurology and [2]Dentistry, Dr. Rajendra Prasad Government Medical College, Kangra, Himachal Pradesh, India

Abstract

Peripheral giant-cell granuloma (PGCG) is a nonneoplastic, reactive exophytic lesion, and is the most common oral giant-cell lesion. Clinically, it bears a 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 present paper describes a clinic case of PGCG with a comprehensive insight of the literature on its etiology, clinical, radiological, histological, and molecular aspects.

Keywords: *Giant-cell lesions, gingival lesions, peripheral giant-cell granuloma*

Introduction

Peripheral giant-cell granuloma (PGCG) is a reactive exophytic lesion[1] classified as a benign tumor of the oral mucosa. Reactive lesions are characterized by excessive proliferation of connective tissue as a response to chronic irritation. Among these types of lesions, those seen in the oral cavity include pyogenic granuloma (PG), peripheral fibroma, fibroepithelial hyperplasia, peripheral ossifying fibroma, and PGCG. PGCG is considered a reactive hyperplastic lesion; although, its etiology is not entirely known. It is believed that its pathogenesis includes an excessive activation of osteoclasts, which is associated with a proliferation of macrophages, and possibly causes major bone resorption.[2]

The lesion may appear at any age, with a maximum incidence between the fifth and sixth decades of life, and it exhibits a slight female predominance with lesions occurring more frequently in the mandible than in the maxilla.[3] Clinically, PGCG is seen exclusively on gingiva, especially in the area between the first permanent molars and incisors and presents itself as a sessile or pedunculated lesion. Ulceration may occur secondary to trauma.

Case Report

A 31-year-old male patient reported to the Department of Dentistry with a swelling in the left lower jaw for 1 year. There was a history of an exophytic mass from the past 1 year associated with the buccal marginal gingiva in the lower left quadrant. The lesion was asymptomatic, but the patient reported bleeding on brushing. History revealed that the swelling started as a small and progressively increased to the present size over a period of 1 year. There was no history of trauma, neurological deficit, fever, loss of appetite, and loss of weight. There was no similar swelling present in any other part of the body. The patient was systemically healthy.

On clinical examination, there was a slight extraoral facial swelling of the left anterior mandible, without any palpable regional lymph nodes. On intraoral examination, a single diffuse swelling was seen on the buccal surface in relation to 31, 32, and 41. The swelling measured about 16 mm × 11 mm × 10 mm. The lesion was reddish-purple and was well defined with an elastic consistency and an irregular texture. It was sessile and nonmobile. The overlying mucus membrane was intact [Figure 1]. There was a pathologic distal migration of 31, 32, and 41. Orthopantomogram and intraoral periapical radiographs showed the bone resorption and severe bone loss around 31, 32, and 41 [Figure 2].

Histopathology of the lesion confirmed that it was an ulcerated peripheral giant-cell granuloma, without

Address for correspondence: Dr. Anupriya Sharma, Department of Dentistry, Dr. Radha Krishnan Government Medical College, Hamirpur, Himachal Pradesh, India.
E-mail: anu_s_priya@yahoo.com

Access this article online

Quick Response Code:

Website: www.jiadsr.org

DOI: 10.4103/jiadsr.jiadsr_30_17

How to cite this article: Sharma A, Sharma A, Dogra S. Peripheral giant-cell granuloma: A potentially aggressive lesion in adults. J Indian Acad Dent Spec Res 2018;5:32-5.

suggestion of malignancy [Figure 3]. The lesion was covered by a parakeratinized stratified squamous epithelium, with areas of atrophy, and ulceration in its thickness. A dense proliferation of multinucleated giant cells was dispersed on a stroma of the tissue, which was highly vascularized, with areas of hemorrhage, deposits of hemosiderin, and infiltrate due to the accumulation of lymphoplasmacytic inflammatory cells. Laboratory tests showed no abnormalities with regard to calcium/phosphate metabolism or parathyroid gland function.

Treatment involved complete excision of the lesion, with elimination of entire base of the lesion, and extraction of 31 and 32. Postoperative healing was good and at 6-month follow-up. There was no evidence of recurrence [Figure 4].

Discussion

Among all reactive growths found orally, the incidence rate of PGCG varies from 5.1% to 43.6%. PGCG is known to occur at any age but occurs most commonly (40%) in the fourth to sixth decade of life. PGCG is found more commonly in females (65%) than in males (35%).[4] Although, the reason for this predilection remains obscure other lesions with a similar sex predilection have postulated the positive influence of estrogen and progesterone in leading to a higher incidence rate of the lesion, thus justifying a positive hormonal influence.[5] The postulated male-to-female ratio is about 1:1.5 or 1:2. PGCG affects mandible (55%) more than the maxilla; mandibular to maxillary predilection is 2.4:1.[6] Tyagi *et al*.[3] in their review, affirmed the maxillary to mandibular site predilection ratio of this lesion to be (1:4). Whereas Pindborg stated that the preferential location for the lesion is the premolar and molar area.[7]

The lesion is usually asymptomatic; however, repeated trauma due to occlusion can lead to its growth with eventual ulceration and secondary infection. Rarely, the lesion is painful in nature. A secondarily infected lesion presents a "yellow zone" caused due to the aggregation of a fibrin clot at the ulcer site.[8]

PGCG has shown to have an extensive array of range in sizes, that is, lesions can range anything from small papules to large masses. The lesion exhibits the unique ability of rapid growth and can reach a significant size within several months of its primary diagnosis.[3] These

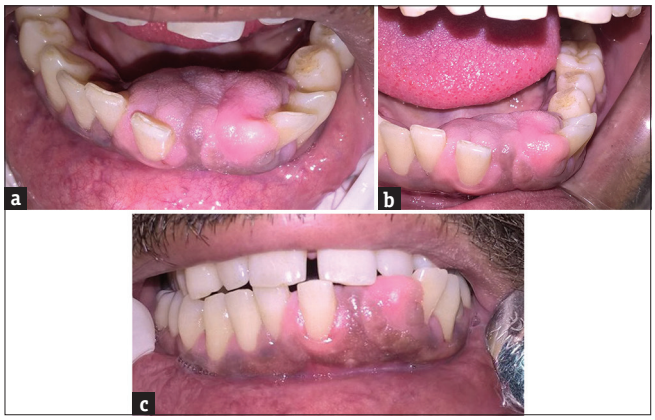

Figure 1: (a) Granulomatous lesion in relation to lower anterior teeth. (b) Granulomatous lesion showing displacement of 31, 32, 33, and 41. (c) Frontal view of granulomatous lesion

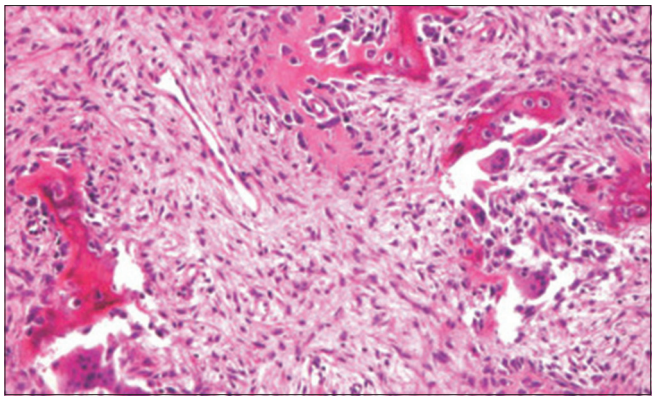

Figure 3: Histopathologic view ×10 magnification

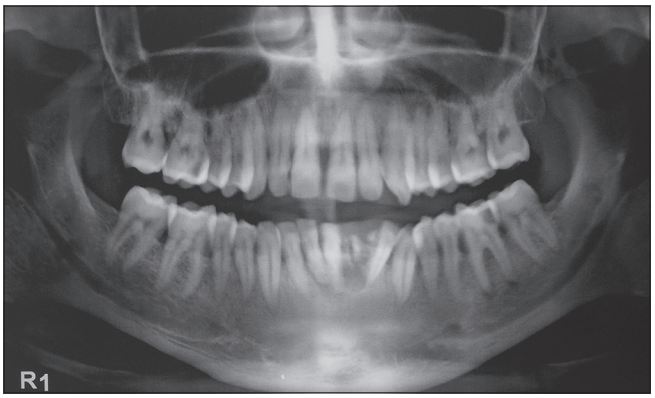

Figure 2: Orthopanoramic radiograph shows bone involvement in relation to 31, 32, and 41

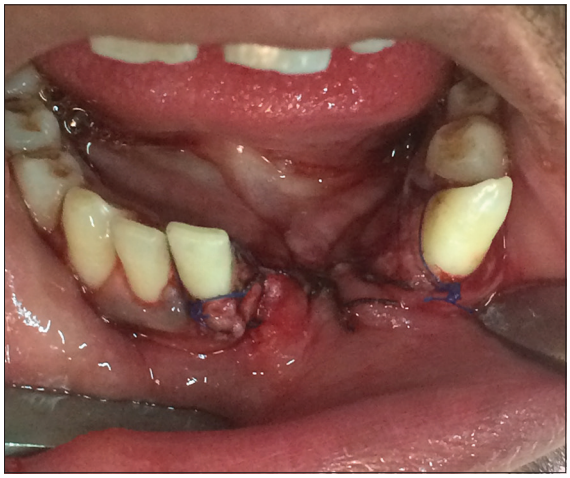

Figure 4: Postoperative view after excision of the lesion

lesions have a reported average diameter of <20 mm, but the extent of their growth capacity is not well known, but usually is approximately about 0.5–1.5 cm.[9] Rarely, the lesions attain a size of about 2 cm. However, Kaya *et al*. reported two cases of huge giant-cell granulomas of about 40 mm × 20 mm in diameter that even lead to bone resorption. PGCG's of about 5 cm are also reported in the literature.[9]

In differential diagnosis, gingival lesions that are considered to mimic the PGCG are the PG, parulis peripheral ossifying fibroma, hemangioma., central giant-cell granuloma (CGCG), and metastatic carcinoma.[9] The PG may be difficult to differentiate from the PGCG based on clinical features alone. The clinical appearance is similar to that of the more common PG; however, PGCG has a typical bluish-red hue in contrast to PG that has a characteristic bright red color. In general, the PG presents as a soft and friable nodule that bleeds freely with minimal manipulation. Unlike the PGCG, displacement of teeth and resorption of alveolar bone are not observed. Another erythematous nodule of the gingiva is the parulis, which is associated with an entrapped foreign body, a gingival pocket and/or a nonvital tooth. Pain and the expression of a purulent exudate with fluctuation in lesion size help to differentiate this inflammatory disease from the PGCG. The peripheral ossifying fibroma is a reactive gingival growth that shares similar clinical features as the PGCG.[10] Although this reactive lesion is often ulcerated and inflamed, it lacks the purple or blue discoloration that is commonly associated with the PGCG. Identification of small flecks of calcification within the tumor as seen on a radiograph aids in diagnosing the peripheral ossifying fibroma, when present. Another consideration based on the red or blue discoloration of the soft-tissue nodule is a hemangioma. Although many hemangiomas are congenital lesions, some vascular malformations increase in size during childhood. Brisk bleeding increased the warmth of the tissue and on palpation, the lesion is pulsatile. Central giant-cell granuloma is an expansile lesion which occurs within the jaws (central lesion). X-ray shows radiolucency within the jaws often crossing the midline. It is commonly associated with hyperparathyroidism. Metastatic carcinomas, when localized in the gums provoke irregular bone destruction below the exophytic lesion. Consistency is hard and margins are indurated. The patient gives a history of previous malignancy.[4]

According to a study conducted by Bodner *et al*.,[11] following are the factors that contribute to the growth of PGCG:

a. Compromised systemic health
b. Poor oral hygiene
c. Oral dryness
d. Ill-fitting dentures.

As the PGCG is a soft-tissue lesion that presents on gingival and alveolar mucosa; X-ray features are thereby nonspecific. Occasionally, bone involvement beneath the lesion has been seen that presents as superficial bone resorption, and thus, it can be discerned easily on periapical radiographs. Widening of the periodontal ligament space is also seen which is often accompanied by the mobility of associated teeth. Alveolar crest region or margin at interdental bone level of the lesion and associated teeth also exhibits resorption.[6]

In some cases, a detailed examination of this lesion reveals vertically oriented bony spicules at the base of the lesion; this can be attributed to the foci of the bone metaplasia in some cases.[9] PGCG being a type of reactive lesion, radiographs occasionally reveal irritating factors such as subgingival calculus.[11] When the lesion involves edentulous areas the cortical bone exhibits a concave resorption beneath the lesion, this typical feature is known as "leveling" effect.[6] This feature is also referred to as "cupping" resorption by many authors. Apart from the factors mentioned above, X-rays are also important for distinguishing whether the lesion is of gingival (i.e., peripheral) origin or of bone (central) origin that spread toward the surface.[12]

Histopathology of PGCG centers around three main features as follows:[13]

a. Presence of numerous young proliferating fibroblasts
b. Vascularized fibrocellular stroma with numerous capillaries
c. Abundant multinucleated giant cells.

In addition, hemosidrin pigments are seen in the stroma of the majority of the sections of PGCG.[4]

Fibroblasts in the stroma form a basic element of the lesion and are plump oval to spindle-shaped. Multinucleated giant cells comprising 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.[12]

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 hemorrhage in a preexisting granulation tissue,[13] others believe that they may arise from the endothelial cells of the capillaries, periosteum, periodontal ligament, or connective tissue of the gingiva.[14]

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 the proliferative stage of the cell. Ki67-positive cells were more in PGCG. Thus, according to Souza *et al*. although CGCG is more aggressive, however, PGCG is more proliferative than CGCG.[15] Filioreanu *et al*. have shown that the expression of alpha-smooth muscle actin which is a cytoskeletal marker is highly correlated with myofibroblasts in the granulation tissue of PGCG. This denotes the increased fibroblastic activity of the lesion.[16] The present study conducted by Amaral *et al*. have found that giant-cell lesions that include PGCG, CGCG, and cherubism present increased levels of NFATc1, overexpression of which increases osteoclasts fusion as well their differentiation. The present study concluded that the development and progression of giant-cell lesions of the jaws were possibly mediated by overexpression of nuclear factor of activated T-cells in the nucleus of multinucleated giant cells. Thus, targeting this pathway can be a potential source of the future molecular therapy in treating these lesions.[17]

The recurrence rate of 5.0%–70.6% (average 9.9%) has been reported in various epidemiologic studies. A recurrence rate of 5% has been reported by Giansanti and Waldron,[18] whereas a study by Eversole and Rovin showed a recurrence of 11%.[19] Recurrences are believed to be related to lack of inclusion of the periosteum or periodontal ligament in the excised specimen. A re-excision should be performed for these cases.[20] Aggressive tendencies or malignant transformation of these lesions have never been reported. PGCG lesions are self-limiting. Hence, recommended management of PGCG aims at the elimination of the entire base of the growth accompanied by eliminating any local irritating factors.[21]

Conclusion

The primary approach to managing the soft-tissue conditions should be an excisional biopsy and subsequent histopathology. The oral hygiene instruction should be one of the first steps in management as good plaque control could help reduce the number of recurrences.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Verma PK, Srivastava R, Baranwal HC, Chaturvedi TP, Gautam A, Singh A, *et al*. Pyogenic granuloma – Hyperplastic lesion of the gingiva: Case reports. Open Dent J 2012;6:153-6.
2. Jaffe HL. Giant-cell reparative granuloma, traumatic bone cyst, and fibrous (fibro-oseous) dysplasia of the jawbones. Oral Surg Oral Med Oral Pathol 1953;6:159-75.
3. Tyagi P, Jain A, Tyagi S. Peripheral giant cell granuloma – A case report. Ann Essences Dent 2011;1:109-12.
4. Shafer WG, Hine MK, Levy BM. A Textbook of Oral Pathology. 4th ed. Philadelphia: W B Saunders Company; 1983. p. 185-6.
5. Shirani G, Arshad M. Relationship between circulating levels of sex hormones and peripheral giant cell granuloma. Acta Med Iran 2008;46:429-33.
6. Chaparro-Avendaño AV, Berini-Aytés L, Gay-Escoda C. Peripheral giant cell granuloma. A report of five cases and review of the literature. Med Oral Patol Oral Cir Bucal 2005;10:53-7.
7. Pindborg JJ, editor. Atlas de Enfermedades de la Mucosa Oral. 5th ed. Barcelona: Ediciones Científicasy Técnicas; 1994. p. 186.
8. Goyal R, Kalra D, Aggarwal S. Peripheral giant cell granuloma: A case report. Guident 2011;5:76-7.
9. Kaya GS, Yalcýn E, Tozoðlu U, Şipal S, Demirci E. Huge peripheral giant cell granuloma leading to bone resorption: A report of two cases. Cumhuriyet Dent J 2011;14:219-24.
10. Mishra MB, Bhishen KA, Mishra S. Peripheral ossifying fibroma. J Oral Maxillofac Pathol 2011;15:65-8.
11. Bodner L, Peist M, Gatot A, Fliss DM. Growth potential of peripheral giant cell granuloma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;83:548-51.
12. Sood S, Gulati A, Yadav R, Gupta S. Peripheral giant cell cell granuloma – A review. Indian J Multidiscip Dent 2012;2:435-40.
13. Adlakha VK, Chandna P, Rehani U, Rana V, Malik P. Peripheral giant cell granuloma. J Indian Soc Pedod Prev Dent 2010;28:293-6.
14. Flaitz CM. Peripheral giant cell granuloma: A potentially aggressive lesion in children. Pediatr Dent 2000;22:232-3.
15. Souza PE, Mesquita RA, Gomez RS. Evaluation of p53, PCNA, ki-67, MDM2 and agNOR in oral peripheral and central giant cell lesions. Oral Dis 2000;6:35-9.
16. Filioreanu AM, Popescu E, Cotrutz C, Cotrutz CE. Immunohistochemical and transmission electron microscopy study regarding myofibroblasts in fibroinflammatory epulis and giant cell peripheral granuloma. Rom J Morphol Embryol 2009;50:363-8.
17. Amaral FR, Brito JA, Perdigão PF, Carvalho VM, de Souza PE, Gomez MV, *et al*. NFATc1 and TNFalpha expression in giant cell lesions of the jaws. J Oral Pathol Med 2010;39:269-74.
18. Giansanti JS, Waldron CA. Peripheral giant cell granuloma: Review of 720 cases. J Oral Surg 1969;27:787-91.
19. Eversole LR, Rovin S. Reactive lesions of the gingiva. J Oral Pathol 1972;1:30-8.
20. Neville BW, Damm DD, Allen CM, Bouquot JE, editors. Soft tissue tumors. In: Oral and Maxillofacial Pathology. 3rd ed. St. Louis: Saunders; 2009. p. 507-63.
21. Shadman N, Ebrahimi SF, Jafari S, Eslami M. Peripheral giant cell granuloma: A review of 123 cases. Dent Res J (Isfahan) 2009;6:47-50.