



A Case Report of a Gingival Plasma Cell Granuloma in a Patient on Antihypertensive Therapy: Diagnostic Enigma

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Article Info	ABSTRACT
<p>Article type: Case Report</p> <hr/> <p>Article History: Received: 8 March 2018 Accepted: 25 October 2018 Published: 30 April 2019</p> <hr/> <p>* Corresponding author: Department of Periodontology, Government College of Dentistry, Madhya Pradesh, India E-mail: gulati.drruchi@gmail.com</p>	<p>The aim of the present report was to discuss a unique case of gingival plasma cell granuloma (PCG) in a hypertensive patient on Amlodipine therapy. Also, we attempt to emphasize the importance of considering primary and advance investigations before making a definite diagnosis. PCG is an extremely rare, reactive, non-neoplastic lesion characterized by the predominance of polyclonal plasma cells. Drug-induced gingival overgrowth is a known side effect of Amlodipine. A hypertensive 60-year-old female patient reported with a chief complaint of swollen gums and discomfort in the upper front teeth region. A provisional diagnosis of Amlodipine-induced gingival overgrowth, combined gingival overgrowth, and fibroma was suggested. Surprisingly, histopathology revealed it to be a plasma cell lesion which was confirmed by advanced investigations, thereby establishing a confirmatory diagnosis of PCG.</p> <p>Keywords: Amlodipine; Diagnosis; Gingival Overgrowth; Plasma Cells; Plasma Cell Granuloma</p>

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INTRODUCTION

Gingival overgrowth (GO) has always been a major concern for all the clinicians in the field of dentistry in terms of diagnosis, prognosis, treatment, and prevention of its recurrence. GO, being multifactorial, can be broadly classified into inflammatory, drug-induced, conditioned, and neoplastic enlargements. Drug-induced GO (DIGO) is a well-documented, major unwanted side effect of certain drugs, mainly antiepileptics, calcium channel blockers (CCB), and immunosuppressants [1]. Amlodipine is a third-generation dihydropyridine CCB used in the management of both hypertension and angina. In 1993, Ellis et al [2] first reported Amlodipine-induced GO (AIGO). The prevalence of AIGO has been shown to be between 1.7% and 3.3% [3]. Plasma cell granuloma (PCG) is a non-neoplastic lesion characterized by the

predominance of polyclonal plasma cells. Bhaskar et al [4] were the first to report the cases of PCG in 1968. There is no sex and age predilection associated with this lesion. The precise etiopathogenesis is uncertain. However, some authors have suggested PCG as a hyper-reactive lesion to allergens/ idiopathic antigens, long-standing periodontitis, and periradicular inflammation [5]. Although PCG most commonly affects the lungs [6], other organs like the orbit and paranasal sinuses may also be involved frequently [7]. It has also been reported in the tonsils [8], tongue [9], lips, oral mucosa [10], periodontal tissues, and rarely in the gingiva [11-15]. The gingival PCG is exceedingly rare. Clinically, it presents as a nodular, polypoidal mass with a smooth surface. It has no systemic symptoms. Routine laboratory investigations are normal, and microbiological culture results



Fig. 1. Clinical presentation of gingival overgrowth (GO). (A) Left lateral view. (B) Right lateral view. (C) Occlusal view showing a pink, smooth, sessile growth extending from the distal of tooth #13 to the distal of tooth #22 (both buccal and palatal aspects) up to the incisal levels with pathologic migration of teeth

are negative. Some oral lesions have shown infiltrative margins on radiographs, giving the appearance of a malignant tumor [16]. Recently, this lesion has been reported in patients receiving Cyclosporine [17] and Amlodipine [18]. The clinical diagnosis of GO becomes cumbersome if more than one factor responsible for GO present in the same patient. Hence, careful and confirmatory diagnosis becomes utmost important for the establishment of an accurate prognosis and management of the lesion. In the present case report, we want to discuss a rare case of gingival PCG in the maxillary anterior region in a hypertensive patient on Amlodipine therapy.

CASE REPORT

A 60-year-old female patient reported to the Department of Periodontology, Govt. College of Dentistry, Indore Madhya Pradesh, India, with the chief complaint of swollen gums in upper front teeth region since one year previously. Also, she reported pain and discomfort upon mastication. The history of the present illness revealed that the growth was present since one year ago, gradually increased in size, is associated with difficulty on mastication, and interferes with maintenance of oral hygiene. On taking a proper medical history, the patient was found to be hypertensive and was on Amlodipine therapy (20 mg 1 Once a day orally) for the last 20 years. The dental history mentions extraction of some teeth due to periodontitis. On periodontal examination, GO was apparent from the distal aspect of the maxillary right canine to the distal aspect of the left lateral incisor on both buccal and palatal aspects. The overgrowth was sessile with a smooth surface and approximately $2 \times 2 \times 3 \text{ cm}^3$

in size. Bleeding on probing was positive in relation to the overall dentition including the sulcular epithelium of the region of the GO (Fig. 1). The GO was also observed in relation to the mandibular right lateral incisor. Moderately deep periodontal pockets were present in the rest of the dentition with the presence of abundant supragingival and subgingival local factors. The patient was edentulous in the mandibular arch, except for the mandibular right lateral incisor and right first premolar. No gingival enlargement was seen associated with the edentulous region. Three-degree tooth mobility (Miller's index) was present in relation to the left upper central incisor with a probing pocket depth of 8 mm. Pathological migration of teeth in the maxillary anterior region was evident, and bleeding on probing was positive. On palpation, GO was firm in consistency and was fixed to the underlying structures. It was non-tender, non-pulsatile, non-fluctuant, and non-compressible in nature. Severe horizontal bone loss in relation to the maxillary anterior teeth along with moderate generalized bone loss in the rest of the dentition was evident on the panoramic radiograph (Fig. 2).



Fig. 2. Panoramic radiograph of the patient revealed generalized horizontal moderate to severe bone loss

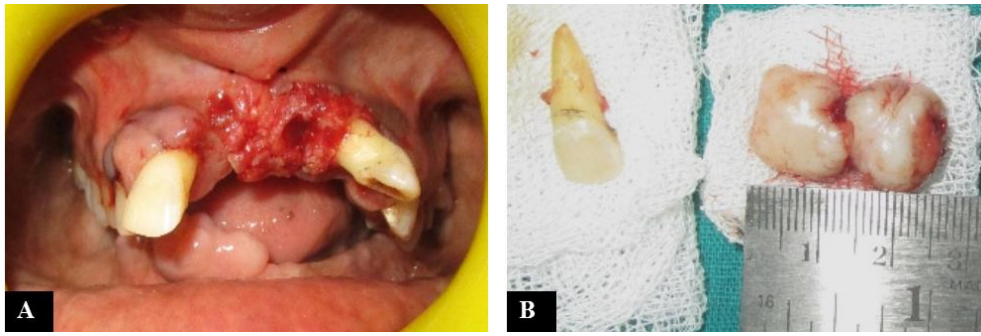


Fig. 3. Intraoperative presentation. (A) Surgical excision was performed along with the extraction of tooth #21. (B) Excised soft tissue growth with extracted tooth #21

A provisional diagnosis of AIGO, combined gingival overgrowth, and irritation fibroma was made based on the clinical findings. After the completion of phase I therapy, an excisional biopsy along with extraction of the left upper central incisor was planned, and the treatment was explained comprehensively to the patient. Amlodipine was substituted by another antihypertensive drug, angiotensin-converting-enzyme inhibitor (ACE inhibitor), after consultation with the responsible physician. With the patient's consent and after necessary hematologic investigations, surgical excision was performed under local anesthesia (Fig. 3A and 3B). The excised tissue sample was fixed in 10% formalin and was sent for histopathological examination. Antibiotics and analgesics were prescribed for the patient for five days. 0.12% Chlorhexidine mouthwash twice a day was advised. Oral hygiene instructions were reinforced. The sections stained with Hematoxylin and eosin (H&E) revealed the presence of proliferative stratified squamous epithelium at the surface with elongated rete ridges. Areas of ulceration were noted.

The underlying stroma was fibrocellular with bundles of collagen intersecting, patchy distribution of chronic inflammatory cells characterized predominantly by mature plasma cells, lymphocytes, and occasional eosinophils, suggesting a plasma cell lesion (Fig. 4A). This was further confirmed by performing immunohistochemistry (IHC) on the biopsy sample for Kappa (K) and Lambda (λ) light chains. IHC staining of the tissue section showed notable cytoplasmic positivity for both K and λ light chains (K chains more than λ chains; Fig. 4B and 4C). All these features suggest polyclonal plasma cell proliferation, confirming the histopathological features. Therefore, a confirmatory diagnosis of PCG was made based on the clinical, histopathological, and IHC analysis. Healing was uneventful after surgery. The patient was followed every week for a month and then every 3 months and thereafter for a period of 15 months. There was a significant improvement in the gingival status of the overall dentition as a result of thorough and strict plaque control measures at subsequent maintenance visits in the entire duration of the supportive periodontal therapy.

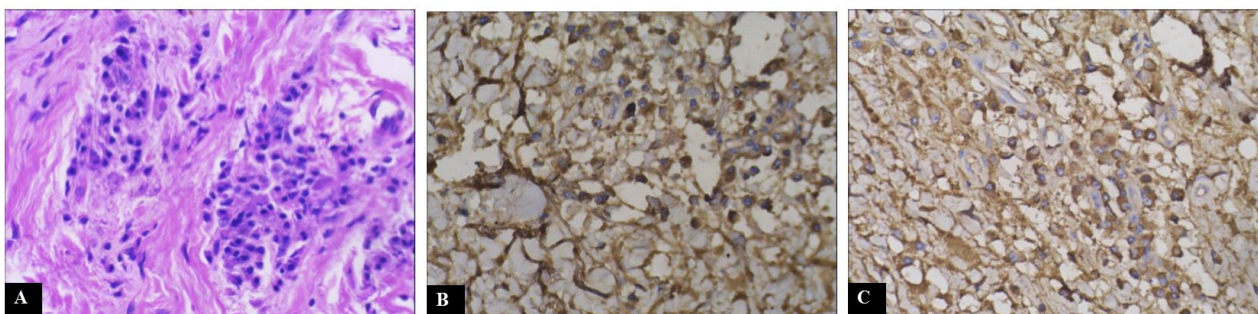


Fig. 4. Histological and Immunohistochemical (IHC) presentation of excised tissue. (A) Histopathological examination of excised tissue showing dense inflammatory infiltrates in fibrovascular connective tissue stroma consisting predominantly of plasma cells with eccentric nucleus, Hematoxylin and eosin (H&E) stain; at $\times 40$ magnification). (B) IHC staining showing strong positivity for Kappa light chains; at $\times 100$ magnification. (C) IHC staining showing strong positivity for Lambda light chains (but less than kappa light chains); at $\times 100$ magnification



Fig. 5. Postoperative follow-ups. (A) 21 days postoperatively: presenting healing of the surgical site and extraction socket with slight erythema. (B) 3 months postoperatively: showing completely healed site. (C) 15 months postoperatively: showing healthy surgical site with no signs of recurrence

No evidence of recurrence of the growth was seen during the recall visits in a period of 15 months (Fig. 5).

DISCUSSION

The present case report discusses gingival PCG and emphasizes the importance of a confirmatory diagnosis for GO. Since the patient was a known hypertensive, was on Amlodipine therapy since 20 years previously, and had generalized periodontal disease, the clinical picture of the GO has inclined us towards the provisional diagnosis of drug-induced GO, combined overgrowth, and fibroma.

The histopathological examination of the biopsy revealed profound and diffuse mature plasma cell infiltration, which was further confirmed by IHC. The presence of positivity for K and λ (2:1) light chains has led us to the confirmatory diagnosis of PCG. The histopathology of DIGO is characterized by the presence of abundant hyperplastic connective tissue and epithelium, and excess of amorphous extracellular matrix. Reactive fibroma is histologically characterized by the presence of a dense fibrous connective tissue [19].

PCG is also known as inflammatory myofibrohistiocytic proliferation, inflammatory myofibroblastic tumor, Inflammatory pseudotumor, and xanthomatous pseudotumor [19]. PCG is categorized under the intermediate category of fibromyofibroblastic tumors by the World Health Organization (WHO) [20]. Very importantly, Plasma cell lesions of the gingiva have to be distinguished from other plasma cell lesions/conditions of the body, namely multiple myeloma, osseous solitary plasmacytoma, and soft tissue myeloma (extramedullary plasmacytoma). Multiple myeloma and osseous solitary plasmacytoma are the tumors of the

bone, whereas soft tissue myeloma (extramedullary plasmacytoma) and PCG are soft tissue tumors. Differentiating PCG from soft tissue plasmacytoma is mandatory and critical as PCG is benign, while plasmacytoma is a malignant lesion exhibiting variably differentiated, monomorphic multi-nucleated plasma cells [11].

IHC determines the polyclonality of the PCG lesion; in a reactive lesion, K chains are greater than λ chains, and the K to λ light chain ratio is 2:1, whereas in case of a neoplastic lesion, the ratio may be greater than 10:1 or 1:10 [12].

Few authors have documented cases of PCG in patients on other medications. Two cases of PCG in patients on Cyclosporine drug therapy have been mentioned in the literature [17]. Both cases revealed strong immunoreactivity for interleukin-6 (IL-6) and overexpression of phospholipase-C γ 1. IL-6 is known to play an important role in the differentiation and activation of plasma cells. The authors explained this as a possible mechanism for rich plasma cell infiltration in cyclosporine-induced plasma cell GO. A similar case of PCG in a patient on Amlodipine has been reported recently; the authors have considered a multifactorial etiology for Amlodipine-induced PCG and have emphasized on the drug/cellular interaction as a possible mechanism [18].

Post-excision healing was satisfactory in the maxillary anterior region. GO in other areas of the dentition decreased significantly along with a noticeable decrease in the overgrowth in the mandibular right lateral incisor area (Fig. 5C). This can be attributed to the combination of non-surgical periodontal therapy. Although authors have suggested PCG as a hyper-reactive lesion to allergens/idiopathic antigens, long-standing periodontitis, and periradicular

inflammation [5], the accurate etiology could not be established yet. In the present case, we could not definitively identify any allergic factor, and we suggest long-standing inflammation and irritation as possible etiology since several local factors and mobile teeth were present in the area of GO.

CONCLUSION

The present case reinforces that all GOs should be comprehensively examined (histopathological and/or advanced confirmatory investigation), regardless of the clinical appearance, surgical management, and treatment success rate.

CONFLICT OF INTEREST STATEMENT

None declared.

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