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Gingival Plasma Cell Granuloma: An Emerging Incidence Of Rare Pathology - A Case Series And Literature Review

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ABSTRACT
Gingival Plasma Cell Granuloma (PCG) is a rare, reactive, benign lesion characterized by the predominance of polyclonal plasma cells. These lesions are often mistaken for pyogenic granuloma and plasma cell neoplasm and require ancillary studies for accurate diagnosis. The case series gives an insight on the 2 cases of PCG and the importance of clinical-histological examination for appropriate diagnosis. The first case is of a female patient who presented with buccal swelling over the right maxillary tooth region, while the second case is of a male patient who presented with bucco-palatal swelling in the left upper back tooth region. Both cases were managed by excisional biopsy and did not report any recurrences. Histological examination of both cases showed parakeratinized epithelium with plasma cell infiltrate in the connective tissue. It is thus essential to differentiate PGC from other potential malignant lesions of the oral cavity to ensure appropriate management.

INTRODUCTION
Plasma cell granulomas (PCG), also called inflammatory pseudotumor, are rare, non-neoplastic, reactive tumor-like proliferations of unknown aetiology and pathogenesis [(1)]. The term PCG is used to describe a mass effect caused by polyclonal plasmacytic infiltrates. The lesion's biologic behaviour, appropriate treatment, and prognosis are unclear. Although the most common site of occurrence is the lung, it may also be found in the brain, stomach, submandibular region, and rarely in the oral cavity [(1)]. Intraorally, it shows increased occurrence over movable tissues such as the tongue, lips, and tonsils. Incidence of the lesion on gingiva is rarely documented.The condition is shown to have no gender or age predilection [(2)]. They often occur singularly, associated with chronic antigenic exposure, and present as a nodular mass with smooth surface without significant systemic symptoms. Radiologically, they show infiltrative margins similar to a malignant tumour.PCG of the gingiva can be easily mistaken as peripheral giant cell granuloma, pyogenic granuloma, or fibrous gingival epulis, thus necessitating a histopathological examination to confirm the diagnosis. Histopathological examination shows that they are composed chiefly of polyclonal plasma cells with a background of fibrosis and spindle cell proliferation. They may also show the presence of lymphocytes, mast cells, eosinophils, or Russel bodies.
We present two such case reports, documenting the rare occurrence of the lesion and highlighting the importance of appropriate clinical-histopathological examinations to eliminate other probable diagnoses.

CASE 1
A 49-year-old female patient reported to the Department of Oral and Maxillofacial Surgery with a chief complaint of mobile front teeth for the past 1 year, and started noticing drifting of front teeth. The patient also gives a history of foul odour and bleeding gums. She was a known case of hypertension under regular medication for the past 2 years and underwent an uneventful extraction 3 years before.
Intraoral hard tissue examination revealed the presence of maxillary midline diastema, root stump related to 13, and generalized periodontitis. Swelling over the maxillary right attached gingiva was noticed during intraoral soft tissue examination. The swelling was well-defined with a smooth surface, which was erythematous in color and of size 2.5 x 1.5 cm with an anteroposterior extension from distal of 14 to the mesial aspect of 16 and supero-inferior extension from the attached gingiva to the interdental gingival crevice between 14, 15, 16 (Fig. 1). There was no evidence of discharge associated with the root stump of 13. On palpation, the swelling was afebrile and not attached to underlying hard tissue. The swelling was

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soft in consistency with well-defined margins. The skin over the swelling was compressible, non-pulsatile, and non-transilluminant. An excisional biopsy was performed, and OPG was taken (Fig. 2).

Fig 1: Gingival swelling over right maxillary region extending from distal of premolar to mesial of first molar tooth

Fig 2: Excisional biopsy of right maxillary gingival swelling

Fig 3: Hard tissue specimen with attached soft tissue

Fig 4: Soft tissue specimen

One soft tissue specimen and one hard tissue specimen with attached soft tissue were received in 10% formalin for histopathological examination (Fig. 3, Fig. 4). The histopathology of the given soft tissue specimen showed Para keratinised stratified squamous epithelium, which was hyperplastic in certain areas. The underlying connective tissue showed diffuse infiltration of chronic inflammatory cells, predominantly plasma cells, and few lymphocytes, and neutrophils. It also shows numerous blood vessels, endothelial cell proliferation, collagen fibres, and bone at the periphery. (Fig. 5, Fig. 6)
The results of clinical and histopathological findings confirmed the diagnosis of Plasma Cell Granuloma.

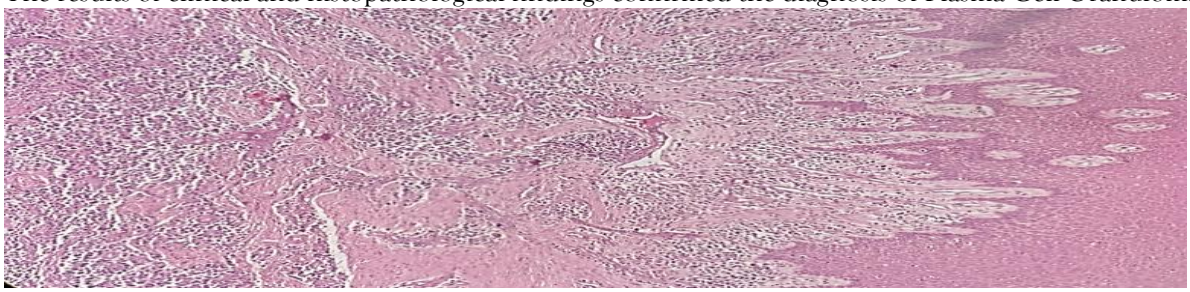

Fig 5: Histopathology of specimen showing parakeratinized stratified squamous epithelium with hyperplastic areas and blood vessels

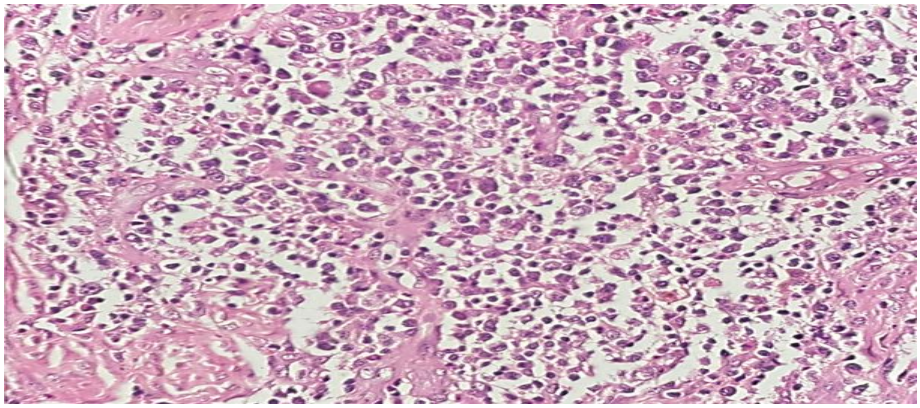

Fig 6: Histopathology of specimen showing connective tissue with infiltration of plasma cells

CASE 2

A 19-year-old male patient reported to the Department of Oral and Maxillofacial Surgery with complaints of swelling in the upper left back tooth region for the past 8 months. The patient gives a history of gradual growth of the swelling to the current size and association of pain and bleeding while brushing.

Intraoral soft tissue examination revealed smooth, regular, erythematous swelling over the left attached gingiva related to the 26 and 27 regions with bucco-palatal extension. The buccal swelling was ovoid in shape and of size 2cm X 3cm, extending superio-inferiorly from the attached gingiva to the vestibular region of 26,27. On palpation, the swelling was afebrile, non-pulsatile, non-compressible, soft in consistency, irregular with ill-defined borders, and not fixed to the underlying bone. The skin over the swelling was erythematous and showed bleeding on probing. The palatal swelling showed similar features and ranged in size 0.5 cm X 0.5 cm. On palpation, it was firm in consistency with no abnormalities of the skin over the swelling. An excisional biopsy was performed, and OPG was taken.

Two soft tissue specimens labelled A and B were received in 10% formalin solution for histopathological examination. The histopathological sections of specimens A and B showed epithelium and connective tissue. The epithelium is parakeratotic stratified squamous, and appears hyperplastic, proliferating deep into the connective tissues, exhibiting basilar hyperplasia, acanthosis, and hyperparakeratosis, and showing ulcerations in a few areas. The connective tissue shows loosely to densely arranged collagen fibres, increased vascularity, endothelial proliferation, extravasated RBC, and diffuse inflammatory cell infiltrate, predominantly plasma cells, followed by lymphocytes and few neutrophils. The section also shows microbial carriage on the surface near the ulcerated lesion.

The clinical and histopathological findings confirmed the diagnosis of Plasma Cell Granuloma.

DISCUSSION

Bhandari and Leibou, in 1973, first described a rare non-neoplastic lesion known as Plasma Cell Granuloma in the lung and vaginal tissue [(3)]. Bhaskar, Levin, and Firch first reported this pathologic entity on the gingival tissue [(4)]. Very few case reports of intraoral occurrence of the lesion have been documented since then. Kim et. al. reported gingival plasma cell granuloma in patients with cyclosporine-induced gingival overgrowth [(5)].Tumours that are mainly composed of plasma cells may be multiple myeloma, solitary myeloma, soft tissue myeloma (plasmacytoma), or plasma cell granuloma [(1)]. Multiple myeloma and solitary myeloma are tumours of the bone, whereas plasmacytoma and plasma cell granuloma are soft tissue tumours [(3)]. Differentiating the type of soft tissue tumor is mandatory, as plasma cell granuloma may be benign, but extramedullary plasmacytoma may show early stages of multiple myeloma and have a poor prognosis.WHO describes PCG as an intermediate fibroblastic/ myofibroblastic tumour composed of myofibroblastic spindle cells accompanied by an inflammatory infiltrate of plasma cells, lymphocytes, and eosinophils [(6)]. They are rare lesions related to diseases of immunoglobulin-4. Plasma cell granulomas are benign inflammatory lesions to which biopsy and histopathologic/immunologic studies must be performed to rule out potential plasma cell dyscrasias and neoplasms. Although there is no consensus regarding the exact etiopathogenesis of the tumor, it is believed to arise from foreign bodies, irritants,

drugs, and idiopathic antigenic cues or may be of immunologic origin [1, 3]. Kim et. al. suggested the presence of interleukin 6 and phospholipase, which may stimulate the aggregation of plasma cells [7]. They act by inducing plasma cell infiltrate and in cyclosporin-induced gingival overgrowth [8]. Plasma cells are terminally differentiated B-lymphocytes that secrete antibodies and provide immunity [9]. They are not commonly found in circulation and reside among other organs (spleen, bone marrow). Morphologically, a plasma cell is seen in two forms: a) exophytic firm nodular mass, b) ulcerative intra-bony lesion [2]. Histologically, they present with basophilic cytoplasm and eccentrically placed nuclei [2]. PCG commonly occurs in the oral cavity and respiratory passage, with oral lesions being described as gingivostomatitis [1]. It commonly presents as an asymptomatic, exophytic, well-demarcated lesion with a tendency to bleeding on probing. It usually disrupts the oral tissues adjacent to the lesion. It may often cause bony infiltration, leading to the misdiagnosis of malignancy [1]. The cases listed in the review of literature also show predominant occurrence over the gingiva, with most lesions being well-circumscribed and of firm consistency. The lesions presented as exophytic gingival overgrowth, which were non-pulsatile, non-compressible, and non-fluctuant (Table 1). The cases of this study also presented as solitary swellings with smooth borders and erythematous surfaces. On histopathologic examination, PCG is seen to present commonly with atrophic to hyperplastic variations of epithelium with abundant plasma cell infiltrate in the lamina propria [7]. The stroma may be collagenous or myxoid. Histological diversity of the lesion is seen due to the variable proportional arrangement of these components [10]. Immunohistochemistry plays an important role in establishing a definitive diagnosis of the lesion. Studies with immunohistochemical analysis have shown polyclonal plasma cell infiltrate with weak expression of lambda light chain- a marker of reactive lesion [9].To rule out other clinical differential diagnoses, on histopathologic examination, plasmacytoma is composed of a pure culture of plasma cells arranged in relatively broad sheets on a delicate reticular stroma, whereas the plasma cell granuloma consists primarily of a capillary network. The plasmacytomas replace the tissue, whereas in the plasma cell granulomas, plasma cell infiltrate is by its deposition through the tissues. The inflammatory cells are very scarce, with the absence of Russell bodies in the plasmacytoma, in contrast to the plasma cell granulomas.Although there is no consensus on the appropriate management of the lesion, complete resection is usually recommended. However, this may not be possible in all cases and may require medical management. Other commonly used management techniques include oral Prednisone 50 mg/day and azathioprine 150 mg/day or electrocoagulation [7]. All modes of management have provided satisfactory results with no recurrences.

CONCLUSION

Plasma Cell Granuloma (PCG) is a rare lesion of unknown aetiology and prognosis. Due to its behavior of mimicking various pathological entities, including malignant lesions, the establishment of diagnosis based solely on clinical and histopathological features is often difficult. This case report reinforces the rare occurrence of PCG in the oral cavity, especially on the gingiva. It highlights the importance of performing differential laboratory investigations for confirmatory diagnosis. This helps avoid unnecessary, extensive, and potentially destructive procedures, thus reducing the morbidity of the patients.

Table 1: Cases and literature review on plasma cell granuloma

ARTICLE	AUTHOR/ JOURNAL	YEAR OF ARTICLE	AGE / SEX	SITE	CLINICAL FINDINGS	IMMUNO HISTOCHEMISTRY	TREATMENT OPTED
Gingival Plasma Cell Granuloma : A Case Report	Somerville-Caso Santiago Walter , Ramos-Garibay José Alberto, Haces-Caso	2023	75 year Female	Alveolar crest	Well-circumscribed exophytic lesion, with a smooth surface and firm consistency in the right upper	interpapillary processes mucosal epithelium with	Surgical resection

	Alfonso Martínez-Berlanga Paulina Journal of Medical Research and Surgery				alveolar region. Pink color with whitish areas and increased vascularity		
A Rare Case of Hormone-Induced Plasma Cell Granuloma of the Gingiva	Dyna Albert, Muthusekhar M.R. , Santhosh P. Kumar , Murugesan Krishnan Cureus	2022	35 year Female	Gingiva	Multiple localized lobulated gingival growth, reddish-pink in color, non-tender, edematous, and soft in consistency with bleeding on provocation.	Mature connective tissue stroma inflammatory cell infiltrate (plasma cells) arranged as sheets; hyalinization. Para-keratinized stratified squamous epithelium of variable thickness	Surgical excision
Plasma cell granuloma in buccal mucosa: a case report and review of different case reports on plasma cell granuloma in oral cavity	Dr. Pranay Bhandari, Dr. Pratiksha Pawar, Dr. Ameya Bihani, Dr. Roopal Rathi International journal of scientific research	2021	39 year Male	Left buccal mucosa	Well circumscribed, oval in shape and on palpation it was rough with well-defined margins and firm in consistency. It was nontender, non-pulsatile, non-fluctuant and non compressible.	Parakeratinized stratified squamous epithelium, focal ulceration, dense highly inflamed connective tissue stroma consisting of chronic inflammatory infiltrate (plasma cells and few lymphocytes), endothelium lined blood vessels.	
A Case Report of a Gingival Plasma Cell Granuloma in a Patient on Antihypertensive Therapy: Diagnostic Enigma	Ruchi Gulati, Madhu Singh Ratre, Shaleen Khetarpal, Manish Varma Frontiers in Dentistry	2019	60 years Female	Gingiva	Firm in consistency and was fixed to the underlying structures. It was non-tender, non-pulsatile, non-fluctuant, and non-compressible in nature.	Stroma was fibrocellular with bundles of collagen intersecting, patchy distribution of chronic inflammatory cells (plasma cells, lymphocytes, and occasional eosinophils)	Surgical excision
Gingival plasma cell granuloma: An occult lesion of rare origin	Susmitha Hosagadde Rathnakara, Mahesh Mysore Shivalingu, Srisha	2017	55 year Female	Gingiva	Nodular sessile growths, erythematous mucosa without any secondary changes, firm in consistency,	Stratified squamous epithelium and stroma showing inflammatory infiltrate with abundant plasma cell component along	Surgical excision

	Basappa, Archana Patil Journal of Indian Academy of Oral Medicine & Radiology				nontender, non-fluctuant and non-compressible	with areas of fibrosis, plasma cells in the stroma of the lesions	
A Case of Plasma Cell Granuloma Located on the Gingiva	Neslihan Akdogan, MD, Basak Yalçın, MD, Günes ¸ Gür Aksoy, MD, Elvan Evrim Tuna, MD, and Devrim Tuba Ünal American Journal of Dermatopathology	2016	56 year Female		well-circumscribed, exophytic, nontender, firm, round, pinkish red color attached to the gingiva with a broad stalk	hyperplastic stratified squamous epithelium of the mucosa with ulceration, plasma-cell-rich inflammation and inclusions in these cells known as Russell bodies,	Surgical excision
Gingival plasma cell granuloma: An enigmatic inflammatory pseudo-tumor with literature review	Gaurav Pandav, Harjit Kaur, Sanjeev Jain, Sakshi Pandav International Journal of Contemporary Dental and Medical Reviews	2015	52 year Female	Gingiva	well defined oval shaped gingival growth bright red in color, reddish mucosa, soft in consistency, mildly tender, non-compressible, non-fluctuant, non-reducible, pedunculated	Thin parakeratinized epithelium with proliferating rete ridges, hypercellular connective tissue with inflammatory infiltrate of plasma cells and lymphocytes,	Surgical excision
Oral plasma cell granuloma: A case report of an ambiguous lesion	Manveen Kaur Jawanda, Ravi Narula, Ashutosh Nirola, Shruti Gupta, Priya Gupta Journal of ICDRO	2014	50 year Female	Gingiva	well-defined solitary growth, oval in shape with reddish smooth surface and bleed on touching.	Hyperplastic parakeratinized stratified squamous epithelium, fibrocellular connective tissue with mixed inflammatory cell infiltrate (plasma cells with typical eccentrically placed hyperchromatic, cartwheel nucleus, arranged in sheets and islands along with few lymphocytes)	Excisional Biopsy

Plasma cell granuloma of gingiva	Balaji Manohar and S Bhuvaneshwari Indian Society of Periodontology	2011	42 years Female	Gingiva	Oval in shape, firm, lobulated, and attached to the gingiva by a narrow stalk,	Stratified squamous parakeratinized hyperplastic epithelium, with underlying fibrocellular connective tissue stroma; fibroblasts, few lymphocytes, and abundant plasma cells. eccentrically placed hyperchromatic, cartwheel-shaped nucleus of the plasma cell	Excisional biopsy and gingivoplasty
Gingival plasma cell granuloma	Mangesh B Phadnaik, Nilofar Attar Indian Journal of Dental Research	2010	54 year Female	Gingiva	well-circumscribed sessile spherical mass with color same as that of surrounding oral mucosa	parakeratinized stratified squamous epithelium. Connective tissue showed inflammatory cell infiltrate (plasma cells), haphazardly arranged collagen fibers.	Excisional biopsy

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