An Enigmatic Clinical Presentation of Plasma Cell Granuloma of the Oral Cavity

Abstract
Plasma cell granuloma is a rare benign lesion characterized by the infiltration of plasma cells; primarily occurring in the lungs. It is also seen to occur in the brain, kidney stomach, heart, and so on but its intraoral occurrence is a rarity. This case report one of the uncommon locations in the oral cavity affected by plasma cell granuloma, its clinical and histological features, and establishes the differential diagnosis with other malignant or benign disease entities and planning the treatment accordingly. This report discusses the diagnostic enigma and the associated terminology of plasma cell granulomas and reinforces the need for performing biopsy and a histopathological or immune histochemical study, irrespective of the clinical features and clinical diagnosis of the lesion. In this case a 52-year-old female, presented with gingival enlargement in the mandibular anterior region, treated by excisional biopsy. Histological evaluation revealed plasma cell infiltrates in the connective tissue. The immune-histochemistry revealed kappa and lambda light chains with a polyclonal staining pattern, which confirmed the diagnosis of plasma cell granuloma.

Keywords: Inflammatory pseudotumor, plasma cell granuloma, plasma cells

Introduction
Plasma cell granuloma (PCG) is a rare nonneoplastic, reactive lesion first described in 1973 by Bahadori and Liebow, consisting of the proliferation of inflammatory cells with the predominance of plasma cells. It has been classified as an inflammatory pseudotumor that can affect any organ or soft tissue, being common in lungs, vagina, and larynx.[1-3] Various synonyms used for PCG include inflammatory myofibrohistiocytic tumor, inflammatory pseudotumor, xanthomatous pseudotumor, PCG, myxoid hamartoma, lymphoid hamartoma, fibrous xanthoma, benign myofibroblastoma, pseudosarcoma, and most recently, inflammatory myofibroblastic tumor.[4] In 1968, Bhaskar et al. were the first to report such a case in the gingival tissues.[5,6] In the head-and-neck region, it has been reported in the oral mucosa,[7] temporal bone,[8] tonsil,[9] submandibular region,[10] paranasal sinuses,[11] tongue,[12] and gingival[13-18] and periodontal tissues.[19]

The exact etiology is still unknown, but hypotheses suggest that it might be seen due to a focus of irritation or, an impacted foreign body or, an idiopathic, antigenic stimulation. The common microorganisms associated with the lesion include mycobacteria, Epstein–Barr virus, actinomycetes, nocardia, and mycoplasma. Clinically, PCG presents as a nodular, polyploid mass with a relatively smooth surface. It remains asymptomatic until it reaches a sizeable dimension wherein it might get secondarily ulcerated and infected in cases of trauma.[20]

Case Report
A 52-year-old female patient reported with a chief complaint of an enlarging but painless, gingival growth in relation to the lower front region [Figure 1]. The growth was present for 2 years and was slowly increasing in size. There was no history of trauma and/or, surgery to the concerned region. The patient’s medical and social history was noncontributory and she did not take any medications. Radiographic examination was unremarkable. On examination, the growth was polypoidal, nodular, sessile, firm, nontender with regular and nonindurated borders measuring around 2 cm × 0.7 cm in dimensions, and appeared to be arising from the free

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and attached gingival region of mandibular anterior teeth with evidence of mild tooth mobility. Routine laboratory investigations were found to be normal. Based on the medical history and clinical features, a provisional diagnosis of pyogenic granuloma was made. The clinical differential diagnosis was fibroma, peripheral giant cell lesion, and peripheral ossifying fibroma. The lesion [Figure 2] was surgically excised with electrosurgical unit to minimize bleeding and postoperative discomfort [Figure 3] and subjected to histopathological examination. Vestibuloplasty was also performed to correct inadequate vestibular depth [Figure 4]. Histopathological examination revealed a dense fibrovascular connective tissue with sheets of mixed inflammatory cell infiltrates comprising predominantly of plasma cells and few lymphocytes with an overlying parakeratinized stratified squamous epithelium with anastomosing rete pegs [Figures 5 and 6]. The tissue was also subjected to immunohistochemical analysis. Immunohistochemical examination revealed kappa and lambda light chain immunoglobulin markers [Figures 7 and 8] which are used to differentiate reactive from benign and malignant lesions as was confirmed in our case, with a positive reaction revealing the lesion to be reactive rather than benign or, malignant in nature. Based on the above findings, a final diagnosis of PCG of gingiva was confirmed. The patient was re-called after every 3 months [Figure 9] for 1 year for a follow-up. Follow-up examination revealed no clinical evidence of any possible recurrence.

Discussion

Plasma cell infiltration may occur in many tissues and was first recognized by Zoon in 1952 as balanitis circumscripta plasmacellularis and plasma cell balanitis. Monoclonal plasmacytic varieties of gingival proliferations are multiple myeloma and plasmacytoma and polyclonal gingival proliferations are PCG and plasma cell gingivitis. These polyclonal reactive lesions are result of various stimuli, which often must be addressed to resolve the plasmacytic proliferation.

PCGs of the oral cavity are primarily rare solitary lesions seen on the periodontal tissue. Maxillary and mandibular gingivas are equally involved with severe bone loss. These lesions have no gender predilection and may occur at any age. Prognostically, PCG seems to be a generally benign, nonrecurring condition; nevertheless, local aggressiveness and recurrences may complicate the outcome of the disease. Clinically, PCG takes at least two morphological types in the oral mucosa: exophytic/tumor or unilateral ulcerative.

The recent WHO classification of soft-tissue tumors includes three basic variants of PCGs:

- Myofibroblast pattern loosely arranged in a myxoid edematous background, showing plasma cells, lymphocytes, eosinophils, and blood vessels
- Presence of dense aggregates of spindle cells arranged in a variable myxoid stroma and collagenized background, mixing a distinctive inflammatory infiltrate and diffuse groups of plasma cells and lymph nodes
- Predominance of collagen fibers, resembling scar tissue, with the presence of plasma cells and scattered eosinophils. This variant may have cytologic atypia with nuclear pleomorphism and increased mitotic activity; these characteristics are rare and may be associated with malignant transformation.

PCGs must be distinguished from plasma cell-rich lesions, such as plasma cell mucositis, plasma cell gingivitis, extramedullary plasmacytoma, and multiple myeloma. Histopathological examination of plasmacytoma consists of a pure infiltrate of plasma cells arranged in relatively large sheets with a fine reticular stromal, while PCG shows a capillary network as its main feature. Another feature to differentiate them is tissue replacement by the plasmacytoma, while PCG sticks to cells at the tissues.

Plasma cell mucositis is a rare plasma cell proliferative
disorder involving the mucosa of the oral cavity and upper aerodigestive tract, presenting with intensely erythematous mucosa, which shares partly similar histopathological findings with plasmacytoma and plasma cell gingivitis, thereby clinicopathological correlation is required for an exact diagnosis. Plasma cell gingivitis has been suggested to be an immunological reaction to some allergens characterized by infiltration of plasma cells into
the subepithelial gingival tissue, which appears clinically as generalized erythema and edema of the gingiva.[28]

A review of literature by Epstein et al.[29] suggested that 14% of multiple myelomas had a history of oral manifestations. Solitary plasmacytomas of bone approximately comprised of 24% of the total cases of myelomas. Soft-tissue extramedullary plasmacytomas though known to be rare tumors show a predilection for the head-and-neck region. These data justify the need to investigate oral lesions with diffuse plasma cell infiltration to rule out malignancies.

PCGs must also be differentially diagnosed from other nonneoplastic proliferative oral cavity lesions such as pyogenic granuloma, fibroma, and peripheral giant-cell granuloma.[30] Apart from all of these, metastatic tumors of the oral mucosa of which breast, lung, kidney, bone, and colon cancers are the most common primary sources.[31] Kaposi sarcoma with involvement of oral mucosa,[32] and bacillary angiomatosis, which is an acute Bartonella infection frequently observed in immunosuppressed patients with a clinically vascular appearance,[28] must be distinguished from PCGs. Furthermore, spirochetal infections arising on mucosal surfaces, such as syphilis, pinta, and yaws, show a predominance of plasma cells and should be distinguished from PCGs.[30]

If the lesion looks like an ulcer, differential diagnosis will be performed with autoimmune processes such as pemphigus vulgaris, bullous pemphigoid, mucous membrane pemphigoid and erosive lichen planus, and systemic lupus erythematosus.[33] High concentrations of IgG4 is found in PCG and other immune diseases.[34]

The most common treatment accepted for PCGs is surgical excision and/or, complete resection. Other treatment modalities include radiotherapy and steroids, which have, also, been used successfully to treat larger, nonresectable lesions in case they assume greater dimensions, are in close proximity to vital structures in the area or, are deeply seated or, infiltrating to the adjacent and subjacent tissues.[35]

**Conclusion**

PCG is a lesion that is diagnosed primarily based on histological findings. The etiology remains unclear, but it is thought to arise due to a nonspecific inflammatory response to an unknown exogenous agent. The present case report reinforces the existence of PCG on the gingiva and submitting all the excised gingival tissues for microscopic examination, irrespective of the clinical features and clinical diagnoses.

**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.

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**Conflicts of interest**

There are no conflicts of interest.

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