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Gingival plasma cell granuloma- Report of 3 cases

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Conflicts of Interest: Nil

Abstract

Aim: The present article highlights 3 cases of Plasma cell granuloma (PCG) seen on the gingiva mimicking clinically as pyogenic granuloma and microscopically as plasma cell neoplasms.

Case Description: A 42-year-old woman presented with an enlarging, painless mass in the oral cavity since 6 months. Microscopically, Subepithelial connective tissue stoma showed dense mixed inflammatory cell infiltrate rich in plasma cells arranged in diffuse sheets and nodules.

A provisional diagnosis of Plasma cell granuloma was

given. The levels of IgG4 were within the normal limits. A 35-year-old female patient reported with the chief complaint of growth in upper right front region of jaw since 2 months. Histopathological sections composed of nodular infiltrates of mature plasma cells admixed with lymphocytes on the background of thick collagenized stroma with scattered fibroblasts. A 50-year-old female patient reported with the chief complaint of growth in lower front region of jaw since 2 Months. On histopathological examination, the connective tissue was fibrocellular with numerous proliferating endothelium

lined blood vessels and surrounded by plasma cells in clusters. So, a final diagnosis of PCG was made in all three cases based on clinical and histopathological findings.

Conclusion: Distinguishing the morphologic features of PCG is important to recognize this entity as a benign inflammatory reactive lesion to avoid unnecessarily extensive and potentially destructive surgery.

Clinical Significance: In all three cases, the growths were differentiated from multiple myeloma and plasmacytoma on basis of histopathological findings. It is recommended that there is a requirement for submitting all the excised gingival tissues for histopathological examination.

Keywords: Granuloma, gingiva, plasma cell, reactive, swelling.

Introduction

Plasma cell granuloma (PCG) is a rare non-neoplastic lesion first described in 1973 by Bahadori and Liebow. It mainly consist proliferation of inflammatory cells with the predominance of plasma cells.¹

PCG is also called by these names such as inflammatory pseudotumor, inflammatory myofibroblastic tumor, xantomatosis pseudotumor, fibrocystic inflammatory proliferation, benign myofibroblastoma and inflammatory fibrosarcoma.²

Plasma cell granuloma (PCG) occurs most commonly in lungs, other organs like vagina, and larynx may also be involved. In head and neck, the areas most commonly involved are the orbit and paranasal sinuses, but they have been also described in pterygomaxillary space, tonsils, ears, tongue, lip, oral mucosa, periodontal tissues and rarely gingiva.³

Bhaskar *et al.* first discovered this pathological entity on gingival tissue, since then few case reports have been documented. Clinically PCG presents as a gingival growth with well-circumscribed appearance, which is reactive and

asymptomatic. The exact incidence and etiopathogenesis is unclear and may arise due to periodontitis, periradicular inflammation due to the presence of a foreign body or may be due to an idiopathic antigen. The lesion's, biological behavior, and appropriate treatments are unclear. The most commonly considered treatment is complete resection. 3,4

PCG requires biopsy and histopathological examination to rule out possible neoplastic and plasma cell dyscrasias, and thus establish a differential diagnosis with other similar diseases such as Multiple Myeloma and Solitary Plasmacytoma.⁵

The present article highlights 3 cases of PCG seen on the gingiva mimicking clinically as pyogenic granuloma and microscopically as plasma cell neoplasms.

Case report 1

A 42-year-old woman presented with an enlarging, painless mass in the oral cavity in the month of January 2018. The mass was present since 6 months and was slowly increasing in size. On intraoral examination, the mass was polypoidal, non-tender, firm measuring 2×2 cms and was located on the labial aspect of lower gingiva extending from left central incisor to the left canine region. IOPA showed interdental bone loss with respect to 31 and 32 (Figure 1). Routine laboratory examination of blood and urine was normal. A provisional diagnosis of Pyogenic granuloma was given. The mass was excised and sent for histopathological examination.

Grossly, the lesion was solid measuring $2 \times 2 \times 1.5$ cms with smooth white surface (Figure 2). Microscopically, the mass was lined by hyperplastic stratified squamous epithelium exhibiting areas of ulceration and covered by inflammatory granulation tissue. Subepithelial connective tissue stoma showed dense mixed inflammatory cell infiltrate rich in plasma cells arranged in diffuse sheets and nodules. The plasma cells were variable in size and shape with typical eccentrically placed hyperchromatic, cartwheel nucleus. There was no evidence of immature plasma cells. In some areas eosinophillic globular Russell bodies were also seen. Thick collagenized stroma with scattered fibroblasts and proliferating blood vessels were also seen (Figure 3). A provisional diagnosis of Plasma cell granuloma was given. The patient was sent for serum valuation of IgG4 levels to rule out multiple myeloma. The levels of IgG4 were within the normal limits. So, a final diagnosis of PCG was made based on clinical and histopathological findings. A follow-up of 1 year 10 months was done and revealed no significant findings (Figure 2).

Case report 2

A 35-year-old female patient reported in the month of September 2018, with the chief complaint of growth in upper right front region of jaw since 2 months. Primarily, the growth was small in size. The lesion was painless but the patient complained of bleeding on touching and interference with oral hygiene practice. The medical history was non-significant. On intraoral examination, a single growth was present between 11, 21 on labial attached gingiva. The growth was well-circumscribed, oval in shape, and sessile. The approximating size of growth was 3 cm \times 2 cm diameter. The color of the growth was erythematous to that of surrounding mucosa.

On palpation, it was firm in consistency and fixed to underlying structures. It was non-tender and bleeding was elicited on palpation. A working diagnosis of pyogenic granuloma was made and radiographic investigations were done. Radiographic examination revealed no significant bony changes. The patient was sent for urine analysis for Bence jones proteins to rule out multiple myeloma.

The lesion was completely excised and histopathologically sections composed of nodular infiltrates of mature plasma cells admixed with lymphocytes on the background of thick collagenized stroma with scattered fibroblasts (Figure 4). Plasma cells were ovoid with eosinophilic cytoplasm, characterized by eccentrically placed cartwheel shaped nucleus. In areas, Russell bodies were also seen. Mitotic figures or nuclear atypia were not seen. Thus, the final diagnosis of plasma cell granuloma of gingiva was given. The patient was under regular follow up for one year and no recurrence was noticed.

Case report 3

A 50-year-old female patient reported in the month of March 2019, with the chief complaint of growth in lower front region of jaw since 2 Months. On intraoral examination, a nodular diffuse growth was extending from distal aspect of 43 to distal aspect of 33 on labial aspect. The growth was sessile and soft in consistency. The approximating size of growth was 4 cm x 2 cm. The colour of the growth was reddish pink to that of surrounding mucosa (Figure 3).

Radiographic examination revealed no significant bony changes. A complete blood hemogram and a routine biochemical investigations were performed which revealed no abnormality. A provisional diagnosis of pyogenic granuloma was made and the patient was sent for the excision of the mass. Histopathological examination revealed parakeratinized stratified Squamous epithelium with long and thin rete pegs and underlying connective tissue. The connective tissue was fibrocellular with numerous proliferating endothelium lined blood vessels and surrounded by plasma cells in clusters (Figure 5). The plasma cells were oval in shape with eosinophilic cytoplasm along with eccentric and hyperchromatic nuclei. So, a final diagnosis of plasma cell granuloma was made based on clinical and histopathological findings. Follow up was done for 8 months and revealed nothing significant findings.

Discussion

PCG is a highly, uncommon, reactive tumor-like lesion very rarely seen on gingival tissue whose etiology remains uncertain. Maxillary and mandibular gingiva is equally involved with severe bone loss. These lesions have no gender predilection and may occur at any age. Clinically, PCG takes at least two morphological types in the oral mucosa: exophytic/tumor or unilateral ulcerative.⁶

Almost all the cases reported in the literature showed a similar gingival exophytic growth with clinical and histological appearance of a well-circumscribed, asymptomatic reactive lesion with sheets of plasma cells treated by excisional biopsy, as in the present three cases.

Plasma cell granuloma is formed by aggregates of mature plasma cells intermixed with mesenchymal cells mostly of the fibroblast and histiocyte-type and arranged in a granulomatous pattern. Plasma cells are terminally differentiated B lymphocytes. These are characterized by basophilic cytoplasm with an eccentrically placed cartwheel shaped nucleus. They range in size from 14 μ m to 20 μ m. A plasma cell's main function is to produce immunoglobulins or antibodies.⁷

Three basic variants of plasma cell granulomas, according to WHO classification of soft tissue tumors are:

- Myofibroblast pattern loosely arranged in a myxoid edematous background, showing plasma cells, lymphocytes, eosinophils and blood vessels.
- 2. Presence of dense aggregates of spindle cells arranged in a variable myxoid stroma and collagenized background, mixing a distinctive inflammatory infiltrate, diffuse groups of plasma cells and lymph nodes.
- 3. 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.^{2, 8}

PCGs must be differentiated from plasma cell-rich lesions, such as plasma cell mucositis, plasma cell gingivitis, extramedullary plasmacytoma, and multiple myeloma. Multiple myeloma is the tumor of the bone, whereas, plasmacytoma and plasma cell granuloma are soft tissue tumors. Differentiating the type of soft tissue tumor is mandatory, as plasma cell granuloma may be benign, but plasmacytoma may show early stages of multiple myeloma. Histopathological distinction of plasmacytoma and plasma cell granuloma are given in

Sn	Plasmacytoma	Plasma Cell Granuloma
1.	Pure infiltrate of plasma cells arranged in	Aggregates of mature plasma cells intermixed with
	relatively large sheets	mesenchymal cells mostly of the fibroblast and histiocyte-
		type
2.	Monoclonal plasma cells	Polyclonal plasma cells.
3.	Fine reticular stroma	Stroma with Capillary network
4.	Mitotic activity and amyloid deposition may be	No cytologic abnormalities are usually present.
	present	
5.	Tissues are replaced by plasma cells	Plasma cells infiltrate by its deposition through the
		tissues.

Table 1. ^{2, 3, 4}

6.	Inflammatory cells are very scarce	Mixed inflammatory cell infiltrate
7.	Absence of Russell bodies	More of Russell bodies
8.	Immunohistochemistry determines the clonality	In a reactive lesion, the kappa: Lambda light chain ratio is
	of the lesion, When the kappa: Lambda light	2:1.
	chain ratio is greater than 10:1 or 1:10, reactive	
	disease is usually excluded and is suggestive of a	
	neoplastic lesion.	

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. Plasma cell gingivitis has been suggested to be an immunological reaction to some allergens characterized by infiltration of plasma cells into subepithelial gingival tissue, which appears clinically as generalized erythema and edema of the gingiva.¹

The exact etiology of PCG is not clear but many authors consider it to be a hypersensitivity reaction to allergens. Other than allergic etiology, it can also present as a reactive lesion or as lesions of unknown cause. ^{1, 4, 7, 9} The present three cases depicted here are of reactive type but there was no identifiable inciting agent.

Management of PCG involves both medical and surgical therapies. Medical therapies include topical/systemic antihistaminic, corticosteroids, and antibiotics. Surgical therapies can be laser, electro-coagulation and tissue excision. Prognostically, PCG seems to be a generally benign, nonrecurring condition; nevertheless, local aggressiveness and recurrences may complicate the outcome of the disease.⁹ However, present all three cases showed no recurrence on follow up.

Conclusion

In all three cases, the growths were differentiated from multiple myeloma and plasmacytoma on basis of histopathological findings. Distinguishing the morphologic features of PCG is important to recognize this entity as a benign inflammatory reactive lesion to avoid unnecessarily extensive and potentially destructive surgery. Thus it is suggested that there is a need for submitting all the excised gingival tissues for histopathological examination.

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Legend Figures

Figure 1a: Intraoral photograph showing localized gingival overgrowth with respect to 31, 32 and 33. 1b: IOPA showed inter-dental bone loss with respect to 31 and 32 (Case report 1).



Figure 2a: Gross photograph showing white solid mass. 2b: Follow-up photograph showing no recurrence after one year (Case report 1).



Figure 3a: Histopathological picture showing stratified Squamous epithelium with underlying connective tissue showing numerous plasma cells arranged in diffuse sheets. (H&E stain at 10x magnification). 3b: Histopathological picture showing underlying connective tissue with numerous plasma cells arranged in diffuse sheets separated by fibrous septae. (H&E stain at 20x magnification). Figure 3c: Histopathological picture showing numerous plasma cells arranged in diffuse sheets. (H&E stain at 40x magnification) (Case report 1).



Figure 4a: Intraoral photograph of the case report 2 showing well-circumscribed sessile growth present between 11 and 21 on labial attached gingiva. Figure 4b: Histopathological sections showed epithelium and connective tissue with nodular infiltrates of mature plasma cells admixed by lymphocytes on the background of thick collagenized stroma with scattered fibroblasts. (H&E stain at 10x magnification). Figure 4c: Histopathological sections showed mature plasma cells admixed with lymphocytes on the background of thick collagenized stroma with scattered Russell bodies (H&E stain at 40 x magnifications) (Case report 2).



Figure 5a: Intraoral photograph of case report 3 showed, a nodular diffuse growth extending from distal aspect of 43 to distal aspect of 33. Figure 5b: Histopathological sections revealed parakeratinized stratified squamous epithelium and underlying connective tissue was fibrocellular with numerous proliferating blood vessels surrounded by plasma cells in clusters. (H&E stain at 10x magnification). Figure 5c: Histopathological sections revealed connective tissue with numerous plasma cells in sheets. (H&E stain at 40x magnification) (Case report 2).

