CASE PRESENTATION AND TREATMENT STRATEGY FOR PLASMA CELL GINGIVITIS

Vasu S, Thankappan P, Prabhakar GS, Angelin D. Basaloid squamous cell carcinoma in the mandibular alveolus: A rare case report with differential diagnosis. J Can Res Ther 2024;20:1092-6.
Doi: 10.4103/jcrt.jcrt_2091_22

Abstract
Plasma cell gingivitis (PCG) is an oral inflammatory condition of uncertain aitiology that affects the marginal and attached gingiva. While several clinical phenotypes have been described, gingiva in most
cases appears edematous and erythematous with a bleeding tendency. Histologically, the connective tissue is densely infiltrated by plasma cells. The non-specific clinical aspects of the disease, together with its
rarity, create a diagnostic challenge for the oral physician. Several cases have been attributed to hypersensitivity reactions, but most causative factors remain still unknown, while there is no definitive treatment strategy. We provide a PCG case of undetermined etiology treated with a galenic composition of Tacrolimus gel. While immunomodulators have been shown to be an effective therapeutic choice, we believe this is the first time a tacrolimus formulation designed specifically for oral administration has been recommended. Further studies are required to determine its effectiveness.
Keywords: plasma cell gingivitis, differential diagnosis, tacrolimus, galenic formulation.

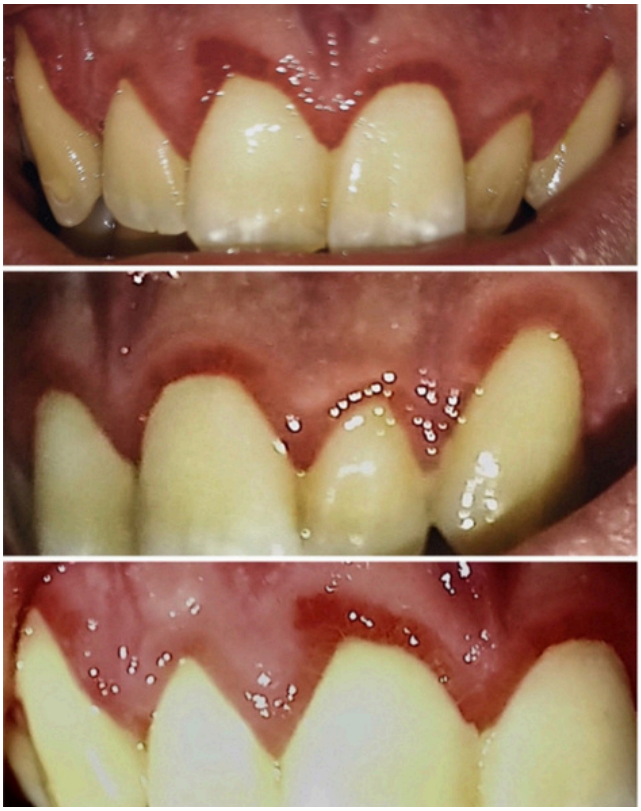

Figure 1: Clinical evaluation revealed velvety red, swollen gingiva with bleeding on probing.

Introduction
Plasma cell gingivitis (PCG) is a rare oral inflammatory condition of unknown etiology affecting the marginal and attached gingiva. Historically, PCG has been referred to with various terms such as atypical gingivostomatitis, idiopathic gingivostomatitis, allergic gingivostomatitis or other terms, highlighting its complex and poorly understood nature. I Regarding its etiology, PCG is regarded as an immune response to neoplasia, allergens (e.g., herbal dentifrices, chewing gums, mints) or an unidentified cause (1).

The clinical appearance varies and generally includes diffuse and generalized gingival erythema. Less commonly, it manifests as erythematous, keratotic verruciform, or ulcerative lesions. It frequently coexists with cheilitis and glossitis, forming plasma cell gingivostomatitis, with the maxillary gingiva being the most affected site(2).

Histologically, PCG is characterized by dense infiltration of subepithelial connective tissue with plasma cells, presenting a pseudoepithelial hyperplastic pattern with spongiotic epithelium and elongated rete pegs. The infiltrate predominantly consists of CD38+ plasma cells, occasionally accompanied by Russell bodies and eosinophils(3). While signs of neovascularization may occur, dysplasia is rare, and malignant transformation is exceedingly uncommon, with only one reported case linking plasma cell mucositis to squamous cell carcinoma(4).

The nonspecific clinical presentation of PCG can complicate diagnosis, requiring differentiation from conditions like desquamative gingivitis, mucous membrane pemphigoid, erythematous gingival hyperplasia in patients with IBD (particularly Crohn disease), granulomatosis with polyangiitis, lichen planus, discoid lupus erythematosus, leukemia, and Candida-associated lesions in HIV patients(5). The rarity of PCG and its variable clinical manifestations hinder the development of standardized therapeutic protocols, emphasizing the need for further research and clinical reporting.

Clinical case

A 22-year-old male presented with swollen, bleeding gingiva, particularly during brushing, and occasional burning. The documented medical history did not disclose any systemic problems. Initial clinical examination revealed edematous and erythematous gingiva with a smooth, friable texture affecting the free gingiva of teeth 13–23. Periapical radiographs didn't demonstrate alveolar bone loss or other abnormalities. An initial diagnosis of dental plaque-induced chronic gingivitis was made. Treatment included teeth scaling and oral hygiene instructions and a Chlorhexidine 0.12% mouthwash rinse was prescribed twice daily. Symptoms persisted after two weeks, prompting referral to an oral medicine specialist. Due to the similarity to Candida-associated linear gingival erythema, a complete blood count, vitamin C levels and viral testing were requested and a 7-day course of itraconazole (100 mg/day) was initiated. All tests, including for Vitamin C deficiency, HIV, HCV, and VDRL, were negative. A thorough clinical examination didn't reveal coexistence of any other immune-related oral mucosal conditions and there was no history for systemic autoimmune or other diseases. Histological analysis of a gingival biopsy confirmed a diagnosis of plasma cell gingivitis (PCG), showing hyperplastic stratified squamous epithelium with elongated rete ridges and dense plasma cell infiltration in the lamina propria. PAS staining ruled out Candida infection. Immunohistological staining revealed infiltration of IL-17 producing cells and positive CD138 for plasma cells.

The patient was advised to change toothpaste and we prescribed the patient a galenic formula of tacrolimus 0.03% oral gel in order to increase the stability of the medication and optimize its absorption in the oral environment. The formula contained: tacrolimus 0.03% in orabase plus by Chemco and was applied in the lesions by the patient once daily for seven days after careful drying of the lesions. The patient reported immediate symptom relief, with complete resolution of erythema within one week and no recurrence after one month.

Discussion

The diagnosis of PCG remains a matter of exclusion for the oral physician requiring differentiation from conditions such as plaque-induced gingivitis, traumatic lesions, mucous membrane pemphigoid, lichen planus, leukemia and Candida-associated linear erythema. In this case, plaque-induced gingivitis was ruled out due to the absence of improvement following scaling and Chlorhexidine use, while trauma, lichen planus, and immunobullous diseases were excluded based on clinical findings (negative Nikolsky'sign, no ulceration).

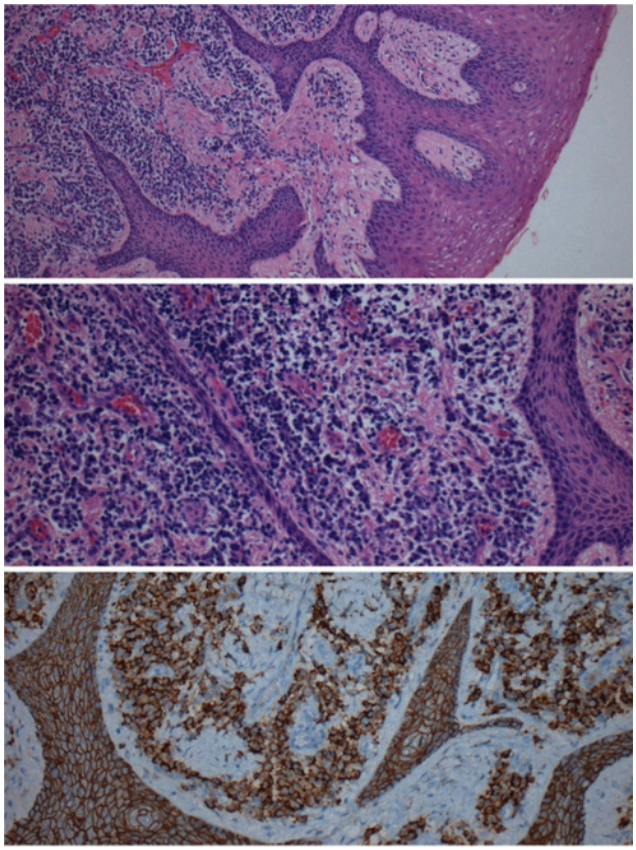

Figure 2:. Histological evaluation of the biopsy specimen A: Hyperplastic stratified squamous epithelium with elongated rete ridges and dense plasma cell infiltration in the lamina propria. (Hematoxilin-eosin, 40x),
B: Presence of mature plasma cells and Russell bodies. (Hematoxilin-eosin, 100x) , C: CD138 Immunohistochemical stain -positive for plasma cells. (10x)

Hematological and histological investigations excluded malignancies, immunodeficiencies, and Candida infection. We opted not to include a comprehensive allergy testing in our diagnostic approach as it often identifies irrelevant allergens leading to diagnostic confusion. Histological evaluation remains essential for confirming PCG, especially when blood tests are inconclusive. Histopathological analysis is crucial to distinguish PCG from conditions with plasma cell infiltration in extra-osseous sites, such as multiple myeloma and amyloidosis(6). These conditions frequently present as a localized mass rather than diffuse gingival enlargement. Immunohistochemistry can further aid in distinguishing between inflammatory and malignant conditions(7). Kappa Lambda light chain test may be necessary to rule out monoclonality of the plasma cells.

While there is no universally accepted treatment regimen, calculus removal, oral hygiene education and discontinuation of any suspected allergens are often sufficient for resolving the lesions. In cases of gingival enlargement, elimination of the allergic agent is followed by gingivectomy with beveled incisions or lasers.

Pharmacological treatments with topical and systemic immunosuppressants are frequently utilized, especially when causative agents cannot be identified or clinical signs persist (8). Corticosteroids such as Prednisone, Betamethasone, Prednisolone and Triamcinolone Acetonide are the main treatment applied, however, while effective for immediate relief, they often fail to maintain long-term remission of the lesions after their discontinuation. Moreover, their efficacy relies on the thickness of the mucosa(7). Adjunctive therapies such as antifungals, antihistamines, antivirals, and phototherapy have shown variable efficacy(2).

Topical calcineurin inhibitors, originally approved for the treatment of atopic dermatitis, have provided successful results in the management of various dermatological conditions due to their favorable efficacy and safety profile, as well as the absence of rebound effect and tachyphylaxis(9). Given the successful use of tacrolimus in treating plasma cell cheilitis and extraoral plasmacytosis(10), we decided to use it in a more stable formulation in this case of PCG. Administration of Tacrolimus results in immunomodulation through promoting the production of TGF-β and IL-10 producing cells thereby potentially suppressing proinflammatory cytokines(11). We believe that in cases when the identification of a probable causative agent is difficult, the prescription of the tacrolimus formula is an efficient method in our therapeutic armamentarium. However, due to the limited literature on its use on similar cases, more studies evaluating this treatment are required.

References

1. Gargiulo A V, Ladone JA, Ladone PA, Toto PD. Case report: plasma cell gingivitis A. CDS Rev. 1995 Apr;88(3):22–3.
2. Leuci S, Coppola N, Adamo N, Bizzoca ME, Russo D, Spagnuolo G, et al. Clinico-Pathological Profile and Outcomes of 45 Cases of Plasma Cell Gingivitis. J Clin Med. 2021 Feb 18;10(4).
3. Prasanna JS, Mutyap DA, Pantula VR, Akula S, Chinthapalli B. Plasma Cell Gingivits-A Conflict of Diagnosis. J Clin Diagn Res. 2016 Nov;10(11):ZD01–3.
4. Pepper T, Shekar K, Singh M, Brennan PA. Squamous cell carcinoma arising in mucosal plasmacytosis. Br J Oral Maxillofac Surg. 2010 Apr;48(3):208–10.
5. Joshi C, Shukla P. Plasma cell gingivitis. J Indian Soc Periodontol. 2015;19(2):221–3.
6. Kumar V, Tripathi AK, Saimbi CS, Sinha J. Plasma cell gingivitis with severe alveolar bone loss. BMJ Case Rep. 2015 Jan 16;2015.
7. Coppola N, Cantile T, Canfora F, Adamo D, Bucci P, Mignogna MD, et al. Pitfalls and Challenges in Oral Plasma Cell Mucositis: A Systematic Review. J Clin Med. 2022 Nov 4;11(21).
8. Younis RH, Georgaki M, Nikitakis NG. Plasma Cell Gingivitis and Its Mimics. Oral Maxillofac Surg Clin North Am. 2023 May;35(2):261–70.
9. Kyriakou A, Patsatsi A, Patsialas C, Sotiriadis D. Therapeutic efficacy of topical calcineurin inhibitors in plasma cell balanitis: case series and review of the literature. Dermatology. 2014;228(1):18–23.
10. Jin SP, Cho KH, Huh CH. Plasma cell cheilitis, successfully treated with topical 0.03% tacrolimus ointment. J Dermatolog Treat. 2010 May;21(3):130–2.
11. Fujimura T, Furudate S, Ishibashi M, Kambayashi Y, Tojo G ichi, Wakusawa C, et al. Successful Treatment of Plasmacytosis Circumorificialis with Topical Tacrolimus: Two Case Reports and an Immunohistochemical Study. Case Rep Dermatol. 2013 Mar 20;5(1):79–83.