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PLAZMA ĆELIJSKI GINGIVITIS – NEUOBIČAJEN SLUČAJ ISTOVREMENE POJAVE OBOLJENJA KOD BRATA I SESTRE

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Plasma cell gingivitis – an unusual case of simultaneous disease occurrence in two siblings

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Short Title: Plasma cell gingivitis-a case report

Abstract

Introduction: Plasma cell gingivitis (PCG) is a relatively rare disease that usually occurs on the anterior maxillary and mandibular gingiva. It manifests as extreme redness, swelling and gum tissue enlargement with propensity for bleeding, accompanied by extensive infiltration of plasma cells in the lamina propria. While the disease etiology remains unclear, its presentation is mostly attributed to non-specific inflammatory reaction to certain foodstuffs or ingredients in oral hygiene products. Case description: A 9-year-old boy and 11-year-old girl were brought for exam by their mother because of fiery red lesions on the gingiviva. The lesions had the same clinical features and identical localization, and were concomitantly present in both siblings. After excluding other oral or systemic diseases with similar clinical manifestations, a diagnosis of PCG was established (most likely due to chewing gum). Conclusion: While being a purely benign, PCG clinical appearance may mask much more detrimental conditions. Consequently, each such lesion
requires due attention. To date, familial tendency for the development of such a condition has not been reported.

Key words: plasma cell gingivitis, idiopathic gingivostomatitis, plasma cell mucositis

Introduction

Plasma cell gingivitis (PCG) is a relatively rare disease that can affect the gingiva only, or involve other parts of the mouth, usually lips and tongue. It typically manifests as pronounced redness of the anterior maxillary and mandibular gingiva, clearly demarcated towards the mucogingival junction and the surroundings, whereby the gingiva is edematous and enlarged, with a pronounced tendency toward bleeding. The disease severity ranges from clearly delimited to diffuse lesions affecting the lateral gingiva as well. If lips and tongue are also affected, the disease is characterized by filiform and fungiform papillae atrophy and deepening grooves on the dorsal surface of the tongue, along with swollen and fisurated lips, mainly the lower one. The lesions are usually asymptomatic, although some patients may complain of pricking, burning sensation and even pain. Changes may occur in
other parts of the oral cavity, and can extend to the entire upper aerodigestive tract. Similar cases involving other periorificial mucous membranes have been reported as well\(^1,2\). PCG is also often referred to as gingival plasmacytosis, idiopathic gingivostomatitis, or plasma cell mucositis. Irrespective of the nomenclature, characteristic histological findings are the same, with marked plasmacellular infiltration in the lamina propria. While the disease etiology is presently unclear, available evidence is indicative of a nonspecific inflammatory reaction to some exogenous antigen. Various food additives and preservatives, along with artificial sweeteners found in candy, chewing gum and oral hygiene products are commonly cited as the likely causative factors\(^3\). PCG is a benign condition and there is no evidence of association with the development of plasma cell neoplasm. But the clinical appearance of the disease may resembles leukemia infiltration, lichen planus, discoid lupus, pemphigoid and myeloma. Therefore, along with allergy testing, diagnostic procedure requires hematological screening and histopathological examination\(^4\). The therapies offered vary and often fail to yield the desired therapeutic results. Even extensive allergen tests may not reveal the responsible allergen. Similarly, drug treatment, in particular use of steroids, may prove ineffective\(^5\). Hence, for more severe cases surgical excision of the affected tissue is recommended. Existing literature reports on PCG cases with various potential etiologies and diverse clinical presentation. Familial propensity, to the best of our knowledge, had not been reported thus far. Searching the Medline database, we found 46 journal articles on PCG published between 1965 and 2015. Not one of the cases described pertained to PCG diagnosed in family members. In this article, we present a case of PCG characterized by nearly identical localization and clinical appearance, simultaneously present in two members of the same family—a brother and a sister.

Case description

Nine-year-old boy was brought to the clinic by his mother due to the gingival redness observed by her son’s dentist during a routine checkup. As she was unaware of this condition, and the boy had no complaints, she could not indicate when the redness occurred. The mother was alarmed by the fact that she subsequently noted almost the same lesion at virtually the same spot in her 11-year-old daughter’s mouth, whom she also brought in for an exam. According to her, both children were healthy, they had no allergies and did not take any prescription medications. The children reported that they were
unaware of the disease onset; they also confirmed lack of any subjective complaints and could not indicate any potential cause of redness.

Extraoral examination did not reveal any specificities in either sibling. Intraorally, on the gingiva surrounding the upper right central incisor, fiery-red lesion with brighter red pinpoints, clearly demarcated from the surrounding tissue, was noted in both children. In the boy’s case, the lesion was about 1 cm in diameter, flat and almost macular, affecting the attached gingiva only, while the one observed in his sister was larger, slightly elevated, and affected both attached and marginal gingiva (Figure 1). Based on the clinical appearance, age and general good health of both siblings, a preliminary diagnosis of plasma cell gingivitis was established. It was explained to the mother that, in order to reach a final diagnosis, further tests would be needed. Also, it was stressed that it would be advisable to attempt to relate the gum redness with potential modifications in dietary or oral hygiene patterns because the condition like this could be a reaction to some food, especially candy, chewing gum or a toothpaste ingredient. Mother pointed out that the entire family had been using the herbal toothpaste for some time, while children regularly chew gum (“the stronger the better”, in the words of her son). Based on these assertions, the patients were advised to discontinue the use of the herbal toothpaste as well as chewing gum consumption and were invited for a checkup in one week’s time, at which time blood work results and microbiology findings would be reviewed. At the subsequent visit, clinical picture remained unchanged. The swabs were negative for bacteria and fungi in both children while complete blood count and differential were normal. The children were scheduled for the next control visit after completing allergy and immunology testing. After three weeks, at the next appointment, although the mother confirmed that the entire family no longer used herbal toothpaste and the children were adamant that they stopped chewing gum, clinical presentation was virtually unchanged, without visible signs of lesion regression. The allergy testing for the most common inhaled allergens (house dust, animal hair, feathers, tobacco, mould, bacteria, grass pollen, weed pollen and tree pollen) and the most frequent food allergens (chicken eggs, wheat flour, soya bean, peanut, fish-based products, carrot, cow’s milk) were negative, with the normal total serum immunoglobulin E (IgE) levels. Other immunoglobins (IgG, IgM, IgA), complement (C3, C4), C-reactive protein (CRP), rheumatoid factor (RF), transferrin, ferritin, haptoglobin and serum protein electrophoresis were also within the normal range. Similarly, auto-antibodies (ANA, AMA, APCA, ANCA, ASMA, and ANA on Hep2 cells) were negative for both siblings.
After a two-week treatment with topical 0.1% triamcinolone in orabase, which failed to yield any improvements, the excision biopsy was performed. The lesions were excised completely and specimens were sent for pathohistiological analysis. Pathohistological findings revealed that excised portions of the mucous lining had the same morphological characteristics in both children and were comprised of mucous membrane fragments covered with stratified squamous epithelium with mild parakeratosis, with moderately elongated epithelial ridges. In both cases keratinocyte distribution and maturation was normal. The entire lamina propria was edematous and occupied with diffuse, heavy infiltrate of mature, well-formed plasma cells, with eccentric nuclei and homogeneous eosinophilic cytoplasm. In addition, moderate dilation of capillary blood vessels was noted (Figures 2 and 3). These pathohistiological results supported the plasma cell gingivitis diagnosis.

At the assessments following surgery, both siblings were asymptomatic and free of lesions, including their last appointment six months after surgery. Unfortunately, they failed to attend subsequent follow ups.

Discussion

Plasma cell gingivitis has been reported in literature since the 1960s. However, disease etiology remains unclear. Early publications suggested allergic nature of this condition. Owings in 1969 speculated that the lesions were caused by an autoimmune response to certain anaerobic bacteria from gingival crevice. Other causes like fungal infection, undetectable hormonal imbalance or decreased vitamin intake have also been postulated. In 1971, Kerr and co-workers described eight PCG cases concomitant with cheilitis and glossitis, ascribing these to hypersensitive reaction to certain chewing gum ingredients. These authors noted that all patients were habitual gum chewers and all experienced marked improvements in the symptoms two weeks after abstaining from gum use, with complete lesion absence within one month from gum chewing cessation. In addition, Kerr and colleagues reported that, in some patients, lesions reappeared after chewing gum for 15 minutes. Since then, other authors also reported similar cases, leading to the conclusion that PCG is likely an allergic reaction to various artificial sweeteners and preservatives, typically found in candy or chewing gum, but also present in toothpaste and mouthwash. Even though the allergen typically remains unidentified, many researchers cite cinnamon,
clove, chili peppers and essential oils such as peppermint, spearmint and wintergreen, as likely allergens\textsuperscript{8}.

The case described here is noteworthy due to the fact that PCG in this case had familial occurrence, which is, to the best of our knowledge, the first case of its kind described in literature. Moreover it is unique due to the fact that the disease had almost the same appearance and affected the same gingival region simultaneously in two siblings.

According to Sollecito and Greenberg, three types of plasma cell gingivitis are presently recognized; PCG caused by known allergens, neoplastic PCG, and PCG of unknown etiology\textsuperscript{9}. We postulate that, in our case, PCG is an allergic reaction to some chewing gum ingredient, even though we failed to establish that with certainty. Our hypothesis is based on the children self-reported penchant for chewing gum. Also, according to their mother, both siblings not only chew gum at home, but are often reprimanded by their teachers for chewing gum during class. It is thus likely, even though refuted by the children, that they deposit the gum during the class in the fornix, rather than throwing it away, and resume chewing in the intermission. While these are merely suppositions, they fit the clinical picture, given that the lesions had particular localization, were well demarcated and indicative of contact-induced allergy. In addition, the habit of keeping chewing matter between the cheek or lip and gum is not unknown. It is particularly familiar with tobacco chewers who usually place tobacco in the sulcus where it is retained for several hours. In the existing literature, a PCG case was reported in an individual with propensity for chewing khat leaves, which were frequently deposited in the sulcus resulting in mandibular gingiva and buccal mucosa reddening and swelling\textsuperscript{10}. Our supposition is, however, countered by the fact that, in contact-induced allergy, similar changes would be expected in the alveolar and upper lip mucosa as well. These regions were clinically healthy in both children examined in this work. Similarly, we would expect the lesions to disappear or at least regress once the children stopped chewing gum, which did not occur. While it had been noted that PCG may persist despite the elimination of the suspected allergens, it is also reasonable to question whether the siblings did indeed stop chewing gum as they so adamantly claim.

Burkhart emphasize that the term PCG is currently utilized when the histological picture is dominated by a mass of plasma cells, suggesting that this is indicative of a Type IV hypersensitive reaction that is not life threatening, but rather a delayed, cell mediated response\textsuperscript{8}. As PCG is a benign lesion, it is essential to exclude in the differential diagnosis
other oral or systemic diseases with similar clinical manifestations and localisation. Comprehensive medical history, hematological analyses and immunological assays should be performed in order to exclude acute leukemia, multiple myeloma and lupus. Further diagnostic assessments should include diet history and allergen testing, as their findings can be indicative of causative factors. Elimination of other inflammatory conditions like desquamative gingivitis, lichen or other dermatological disorders with oral presentation is often impossible without examining the tissue under the microscope\textsuperscript{2,10}.

Disease treatment varies and there is presently no standardized protocol that clinicians should follow. Although allergen remains elusive in most cases, the first line therapy should commence with exclusion of all known potential allergens, as this may result in improvements in some cases. However, as with other recommended therapy modes, such measures often fail to yield satisfactory results. Also, oral hygiene improvements and professional periodontal care usually result in the reduction of the marginal gingivitis, without any beneficial effects on the attached gingiva. Moreover, anti-fungal therapy even with the positive Candida albicans diagnosis, as well as corticosteroid application, whether topical, intralesional or systemic, does not always produce improvements\textsuperscript{5,11}. Consequently, excision biopsy of the lesion, wherever applicable, including the case presented here, followed by histological analysis might be not only the best diagnostic approach, but also most beneficial therapeutic option.

Conclusion
Plasma cell gingivitis is a rare condition, most likely allergic in nature. While being a purely benign, clinical appearance and localization may mask much more detrimental conditions. Consequently, each such lesion requires due attention.

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Figure legends

Fig. 1. A flaming-red sharply demarcated lesion on the anterior gingiva in two siblings: a 9-year-old boy (1a) and 11-year-old girl (1b)

Fig. 2. Histological findings in the boy: Stratified epithelium with dense inflammatory infiltrate in the lamina propria (2a) HE x50. Inflammatory infiltrate is composed mainly of mature plasma cells (2b) HE x400

Fig. 3. The same histological findings in the girl: Stratified epithelium with dense inflammatory infiltrate in the lamina propria (3a) HE x100. Inflammatory infiltrate is composed mainly of mature plasma cells (3b) HE x630

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