Gingival Plasma Cell Granuloma: A case Report of Multiple Lesions

Gingival Plasma Cell Granuloma: A case Report of Multiple Lesions

Wei Lu* / Gang-gang Qi** / Xiao-jun Li*** / Fu-ming He**** / Bo Hong*****

Background: *Plasma cell granuloma (PCG) is a rare benign pseudotumorous proliferation of unclear etiology that is mainly situated in the lungs. Gingival PCG is an even more peculiar lesion that usually occurs in middle-aged or elderly individuals and clinically manifests as a solitary entity.* ***Case report:*** *A 15-year-old male with no underlying medical conditions presented with multiple gingival masses in the right maxilla, which were initially thought to be epulis. The lesions were resected completely and the excisional biopsies sent for histological examination. Immunohistochemical (IHC) stain revealed dense polyclonal plasma cell infiltration with positive expression of both kappa and lambda light chains, confirming a diagnosis of gingival PCG. Subsequently, the affected gingiva healed uneventfully, with no sign of recurrence over 2 years of follow-up.* ***Conclusions:*** *The present report depicts an extremely unusual case of gingival PCG occurring in a juvenile with multiple lesions, which is worth attention in clinical pediatric dentistry. Excisional-biopsy and histological investigations are imperative for a confirmative diagnosis and to exclude potential aggressive conditions. Complete resection of lesions seems to be a valid treatment, while long-term clinical follow-up is still needed.*

Keywords: *plasma cell granuloma, excisional biopsy, histological analysis, immunohistochemical staining*

INTRODUCTION

Plasma cell granuloma (PCG) is a rare, usually benign pseudotumorous proliferation in response to an idiopathic antigenic cue. It typically manifests as a pseudotumorous entity caused by dense infiltration of plasma cells in the subepithelium.[1, 2] Various terms have been applied to PCG, including inflammatory pseudotumor, inflammatory myofibroblastic tumor, inflammatory myofibrohistiocytic proliferation and xanthomatous pseudotumor.[3] The term "inflammatory pseudotumor" is interchangeable with the term "PCG" in numerous publications due to the overlap of their morphological appearances.[4, 5] The definite incidence and biological nature of gingival PCG as neoplastic or reactive are ambiguous, owing to the inconsistent nomenclature. Although it has usually been deemed a non-neoplastic reactive lesion,[6] Zoon[7] has indicated dense infiltration of plasma cells is often seen around epidermal neoplasms that is a rare histological feature in ordinary inflammatory dermatoses.

PCG is most frequently located in the lung and conducting airways;[8] however, diverse extrapulmonary sites such as the oral cavity,[9, 10] skin[11] and central nervous system[12] have also been reported to demonstrate occurrences of PCG. Synchronous and metachronous factors may be involved in exceptional cases.[9] Gingival PCG seems to be an extremely rare disease, with few documented cases.[13-23] It was first described in 1968 as a highly uncommon and inflammatory lesion in the gingiva.[13] Gingival PCG has also been considered a subtype of plasma cell gingivitis due to the identical histological feature of polyclonal plasmacytic proliferation.[24]

From a histological perspective, PCG is considered non-neoplastic and reactive. It consists of reactive inflammatory cells in the subepithelium of the vascular stroma, and its cellular constituents

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are predominantly plasma cells as well as some lymphocytes, eosinophils, mast cells and histiocytes.[21] Immunohistochemically, the lesion exhibits immunoreactivity to CD138 and to kappa (κ) and lambda (λ) light chains, which indicates polyclonality and helps distinguish PCG from other monoclonal disorders.[25]

Plasma cells differentiate from B lymphocytes in that their major function is producing immunoglobulins or antibodies.[26] Dense infiltration of plasma cells may cause congestive vasodilation and alteration of local blood flow.[9] Previously reported cases of gingival PCG indicate that it is usually associated with chronic antigen exposure,[6, 13] although the exact etiology remains obscure. Dental plaque,[27] plasma cells induced antigen–antibody host reaction,[13] Epstein-Barr virus antigens,[28] congestive vasodilation,[9] amlodipine,[20] cyclosporine[15] and a parasitic etiology[29] have also been suggested as etiologic factors.

Gingival PCG merits discussion because it may occur across a wide age range; has potential malignancy; and is easily confused with epulis, pyogenic granuloma, fibroma, peripheral giant-cell granuloma and other neoplastic diseases. Histological examination is the only currently accepted method for reaching a final diagnosis.[30] Therefore, excisional biopsy and histological examination are mandatory for diagnosing PCG and for differentiating it from other aggressive diseases, regardless of clinical impression.[23]

Up to now, no case report of gingival PCG in juveniles has been published in any general or pediatric dentistry literature. This report describes an unusual case of gingival PCG manifesting as multiple lesions. We have restricted the term "plasma cell granuloma" to describe lesions other than "plasma cell gingivitis" or "inflammatory pseudotumors" due to the focal mass effect[24] and to the absence of spindle-cell proliferation, which is a typical histological feature of inflammatory pseudotumors.[5] In addition, we have thoroughly reviewed the pertinent English-language literature.

Case report

A 15-year-old male was referred to the Department of Periodontics of Zhejiang University Affiliated Stomatology Hospital, Hangzhou, Zhejiang, China, for evaluation of bright-red, elevated, slightly painful masses in the right maxillary anterior region for the previous 6 months. The patient complained that the lesions bled easily when he ate hard foods and that they interfered with daily oral-hygiene practices. Moreover, the lesions were aesthetically unappealing because they were located in the anterior region. The patient's medical history was non-contributory. Intra-oral clinical examination revealed the patient had markedly poor oral-hygiene status with abundant plaque and detectable subgingival calculus; the calculus index was 2.[31] All marginal and papillary gingiva of the entire dentition exhibited redness, frangibility and conspicuous edema, particularly in the anterior region. Notably, a bright-red, exophytic, pedunculated, well-circumscribed and tumor-like soft tissue mass (8×6 mm^2) was present in the labial interproximal gingiva between the middle and lateral incisors of the right maxilla (Fig. 1A). The lesion had a broad stalk attached to the gingiva, and the surface was lobulated with dense dots. Similarly, relatively small masses were present in the interproximal gingiva between the maxillary right lateral incisor and canine, as well as between the canine and first premolar (Fig. 1B). These soft-tissue masses demonstrated a strong tendency to bleed, even with gentle provocation, and induced slight pain when subjected to palpation.

Fig 1. Presurgical clinical appearance. (A) A bright-red, exophytic, pedunculated, well-circumscribed and tumor-like soft tissue mass (8×6 mm^2) in the labial interproximal gingiva between the middle and lateral incisors of the right maxilla. (B) Two relatively small masses (yellow arrows) in the interproximal gingiva between the maxillary right lateral incisor and canine, as well as between the canine and first premolar.

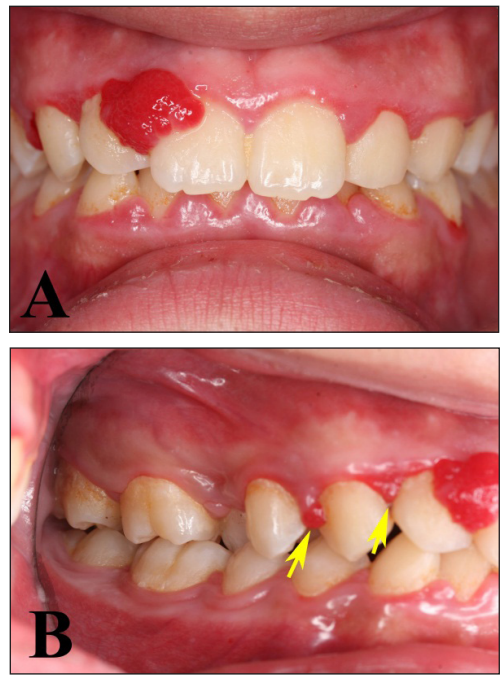


Figure 2. Surgical resection of the lesion. (A) Excision of the tumor-like tissue and debridement and elimination of underlying inflammatory agents. (B) The excised tissues were approximately 8×6 mm^2 and 5×2 mm^2. (C) Suturing the flap. (D) The wound healed uneventfully during the 2-week post-operative period.

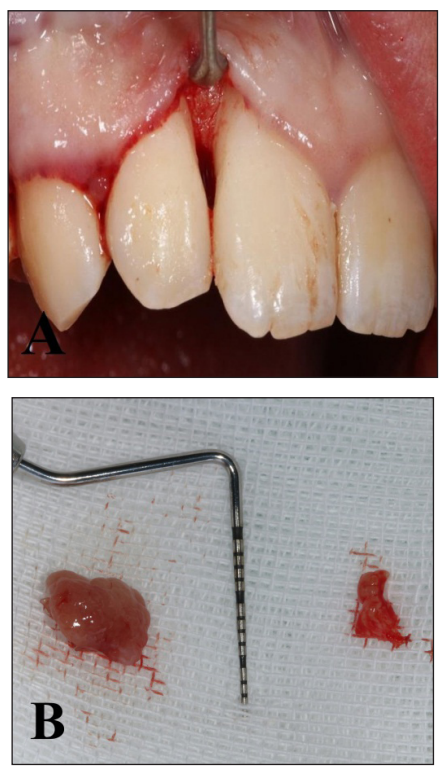
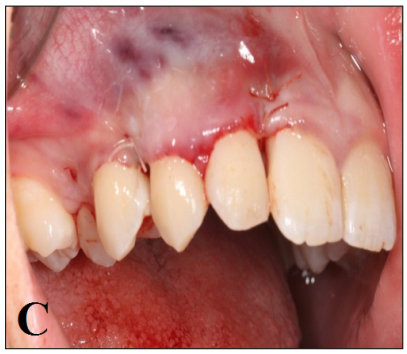
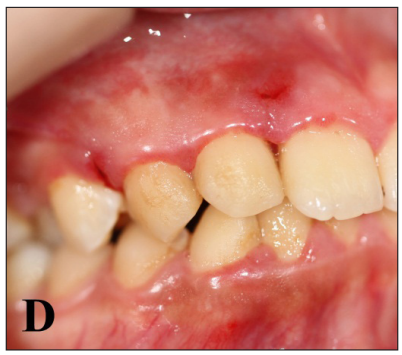


Figure 2. (Continued) Surgical resection of the lesion. (A) Excision of the tumor-like tissue and debridement and elimination of underlying inflammatory agents. (B) The excised tissues were approximately 8×6 mm² and 5×2 mm². (C) Suturing the flap. (D) The wound healed uneventfully during the 2-week post-operative period.





A panoramic radiograph revealed no osseous involvement. The routine hematological-investigation results were within normal limits. Gingivoplasty with complete resection was performed under local anesthesia (Fig. 2 A-C), and histological examinations were conducted based on excisional biopsies. Two weeks after surgery, the affected gingiva healed uneventfully (Fig 2D), and inflammatory symptoms diminished.

Histological investigations included hematoxylin and eosin (H&E) and immunohistochemical (IHC) staining with κ and λ light-chain antibodies. Microscopic images after H&E staining revealed hyperplastic epithelium with elongated rete ridges (Fig. 3A) and predominantly dense infiltration of plasma cells and other chronic inflammatory cells in the subepithelium (Fig. 3B). Eosinophilic globular bodies, known as Russell bodies, were observed in the cytoplasm of plasma cells. Proliferation of capillary and vascular endothelial cells was also noted in the connective tissue. IHC staining revealed a polyclonal pattern and mixed populations of both κ (Fig. 4A) and λ light chains (Fig. 4B). Consequently, clinicopathological characteristics were in agreement with those of PCG, which helped establish the final diagnosis.

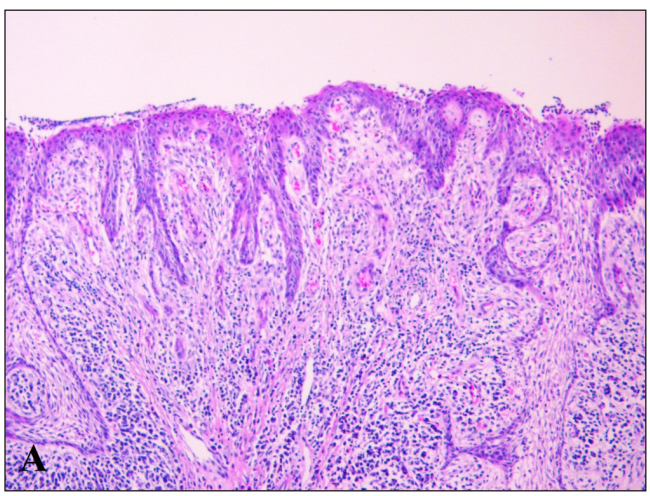
2-year postoperatively, no sign of recurrence was reported by phone contact and the patient's guardian refused to attend for follow-up evaluation due to some personal reasons. All investigations in the present case followed the guidelines of the Helsinki Declaration.

DISCUSSION

The present report seems to be the first case of gingival plasma cell granuloma (PCG) in a juvenile with multiple clinical lesions. The abundant dental plaque caused by markedly poor oral hygiene and generalized chronic periodontitis have been speculated to be the genesis of these lesions.

The clinical presentations, age and gender distributions of pertinent publications of gingival PCG were summarized in Table 1. Gender does not appear to be a risk factor, but this type of disease is more frequently found in middle-aged and elderly individuals (35-79 years). In the present case, the patient was surprisingly a juvenile.

Figure 3. Histopathological micrograph. (A) Low-magnification image (original magnification ×4) displays hyperplastic epithelium with widened rete pegs. (B) High-magnification image (original magnification ×100) displays dense plasma cell infiltration. Yellow arrows indicate plasma cells.



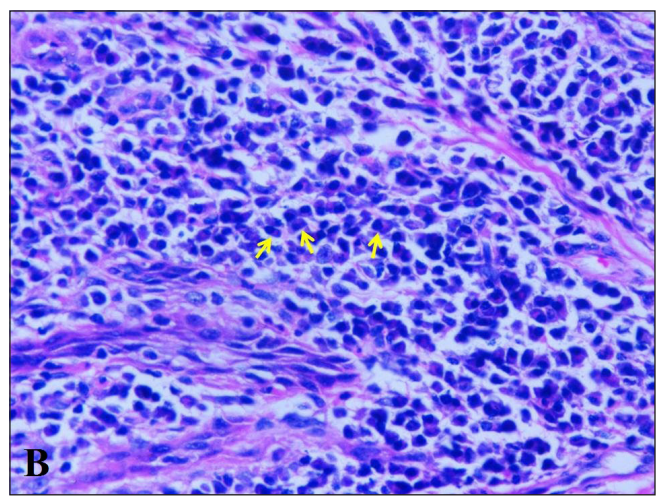
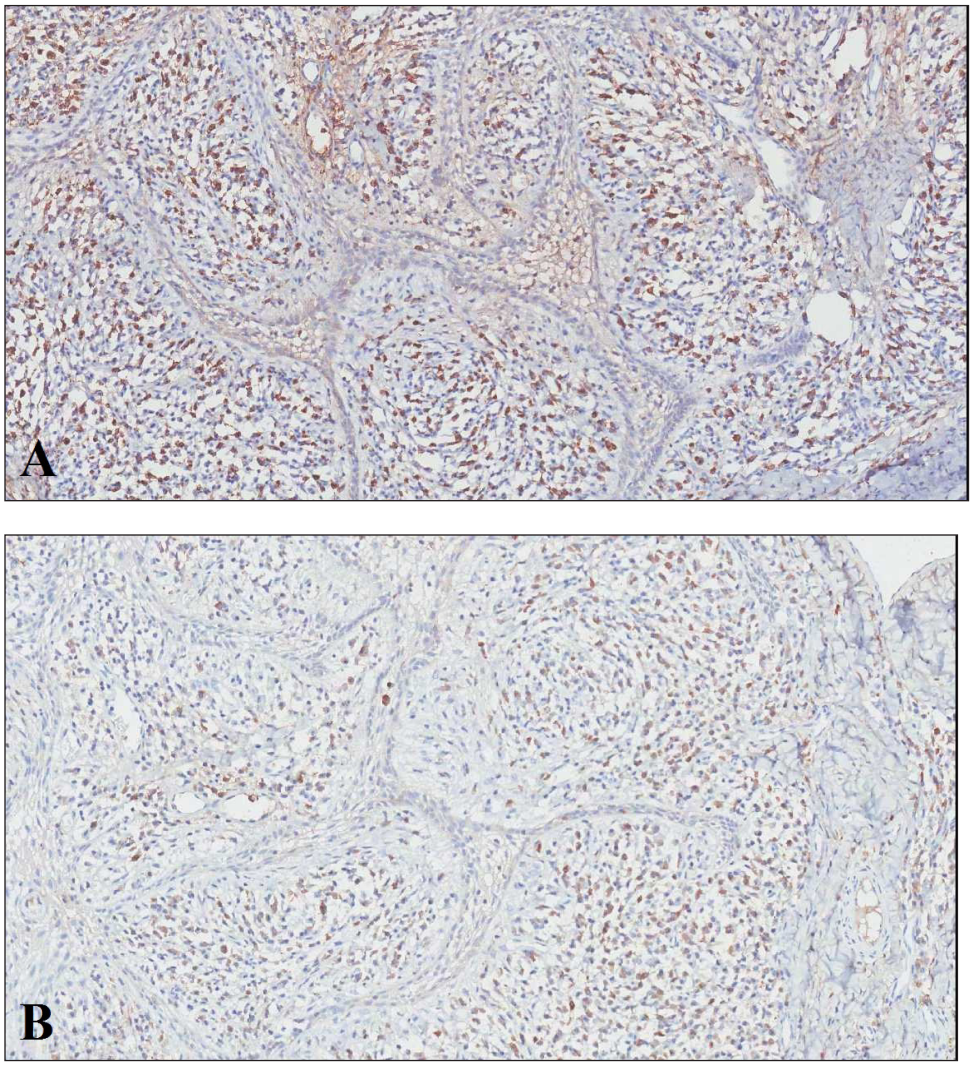


Figure 4. IHC staining showing (A) intense cytoplasmic expression for κ light chains (original magnification ×10) and (B) mild cytoplasmic expression for λ light chains (original magnification ×10).



The labial interproximal gingiva of maxilla was superiorly involved, and symptoms were consistent with those of previously reported publications (Table 1). As a matter of fact, in the oral cavity, PCG is primarily found in the periodontal tissue, of which the gingiva is the most frequently affected region.[4, 6, 13, 16, 32] The maxillary and mandibular gingiva have equal incidences of gingival PCG accompanied by possible bone loss.[26] The disease usually manifests as a solitary, well-circumscribed and exophytic lesion. The lesion can either be asymptomatic[6] or bleed easily due to its friable nature.[25]

The histological findings of our case conform to the principal appearance of gingival PCG, which consists of prominent plasma cells intermixed with other substantial cellular constituents, including lymphocytes, neutrophils, eosinophils and histiocytes, in a fibrovascular background. Aggregates of plasma cells are separated by interwoven collagen and fibroblasts.[2, 14] Cytological abnormalities do not commonly occur. Occasionally, Russell bodies, existing as intracytoplasmic eosinophilic hyaline droplets, may be observed. Obliterative phlebitis has been discovered in 2 cases.[21] IHC analysis is mandatory to determine exact clonality and diagnosis. IHC staining of gingival PCG uniformly shows positivity for both κ and λ light chains. The ratio of κ to λ light chains in PCG is 2:1, while in malignant lesions the ratio is likely greater than 10:1.[33] Furthermore, PCG also shows immunoreactivity to CD138, which is a typical marker used to identify plasma cell differentiation.[25] Staining of immunoglobin G (IgG), A (IgA) and M (IgM) types of heavy chains reveals polyclonality, and the ratio of IgG-producing to IgA-producing cells is 5:1.[9] In the present case, we stained κ and λ light chains using cytoplasmic-staining method. Results revealed a polyclonal staining pattern, which is in accordance with the typical IHC staining features of PCG.

Plasma cell infiltrates in connective tissue can be observed in malignant, autoimmune, reactive, infectious and idiopathic conditions.[34] Gingival PCG must be distinguished from plasma cell–rich lesions such as plasma cell mucositis, plasma cell gingivitis, extramedullary plasmacytoma and multiple myeloma, as well as other oral-cavity lesions such as epulis, pyogenic granuloma, fibroma and

peripheral giant-cell granuloma.[6, 10] Clinical appearance, histological features and clinicopathological correlation are crucial factors for differential diagnosis. As in the present case, excisional biopsies, histological examinations and IHC staining are required for diagnosing PCG and for differentiating it from other aggressive diseases.

Differential diagnosis from plasma cell neoplasms such as multiple myeloma and plasmacytoma is essentially important. Statistically, 14% of multiple myelomas are present orally, whereas 24% manifest as solitary plasmacytoma that gradually progresses to multiple myeloma. Meanwhile, soft-tissue plasmacytoma tends to affect the head and neck.[18, 35] Histological examination facilitates exclusion of carcinoma from differential diagnosis. Moreover, T-cell marker analysis by direct immunofluorescence can establish the lesion's origin as neoplastic or reactive.[36] Regarding IHC features, both multiple myeloma and plasmacytoma are monoclonal plasma cell neoplasms, whereas PCG represents a polyclonal plasma cell infiltration.[10, 21, 37] Both types of neoplastic lesions have a considerable proportion of atypical plasma cells that display various cellular sizes, multinucleated forms and diverse numbers of mitoses. Multiple myeloma, a malignant neoplasm of the bone marrow, may be a progression of a solitary myeloma; this is considered an early expression of myelomatosis rather than an independent entity. The median age of patients is approximately 60 years, and people of African descent are most susceptible.[38] The histological appearance consists of a diffuse infiltration of neoplastic and variably differentiated plasmacytoid cells, which are aggressive in nature and completely replace normal tissue.[39] By contrast, extramedullary plasmacytoma is a plasma cell mass located outside the bone marrow and is often discovered in the mucoperiosteum of the nasal cavity, the maxilla and the mucosa of the soft palate. Histologically, it is composed of a diffuse infiltration of plasma cells with rare inflammatory cells and the absence of Russell bodies. Although gingival PCG may be far less fatal than those two neoplastic diseases, there is abundant evidence indicating its potential malignancy.[1, 40, 41]

The most common practical solution for gingival PCG is complete resection (Table 1). Surgical excision not only determines diagnosis but also contributes to prognosis.[23] It is also suggested that involved adjacent teeth should be extracted.[13, 20] In addition, steroid therapy[42] has been recommended as a successful treatment for non-resectable lesions.[3] In terms of prognosis, the incidence of recurrence is low (Table 1), although local aggressiveness and possible recurrence may complicate the prognosis of gingival PCG.[2]

CONCLUSIONS

The present report depicts an unusual case of a 15-year-old male who displayed multiple gingival masses in the right maxilla that were histologically verified as PCG. This was in contradiction to previous publications reporting that gingival PCG is frequently found in only middle-aged or elderly individuals and clinically manifests as a solitary entity. Excisional biopsy and histological investigation help doctors exclude potentially aggressive conditions and establish a confirmative diagnosis. Although gingival PCG is usually benign and treated conservatively, its unclear biological nature means that it still requires long-term clinical follow-up.

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