

CASE REPORT

Plasma cell granuloma in the oral cavityP.C. Anila Namboodiripad¹, Malathi Jaganath², B. Sunitha³ & A. Sumathi⁴¹Department of Oral and Maxillofacial Pathology, KLE Society's Institute Of Dental Sciences, Bangalore, Karnataka, India²Department of Clinical Microbiology, KLE Society's Institute Of Dental Sciences, Bangalore, Karnataka, India³Department of Oral and Maxillofacial Pathology, KLE Society's Institute Of Dental Sciences, Bangalore, Karnataka, India⁴Department of Oral Medicine and Radiology, KLE Society's Institute Of Dental Sciences, Bangalore, Karnataka, India**Key words:**

mandibular bone, plasma cells, plasma cell granuloma

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Abstract

Plasma cells are terminally differentiated B lymphocytes which are typically found in the red pulp of the spleen, medulla of the lymph nodes, tonsils, lamina propria of the entire gastrointestinal tract, mucosa of the nose and upper airway, and sites of inflammation. They are characterised by basophilic cytoplasm with an eccentrically placed nucleus. They range in size from 14 to 20 µm. A plasma cell's main function is to produce immunoglobulins or antibodies. Plasma cell granuloma is a plasma cell lesion which merits discussion because it is typically found in the oral cavity. This lesion is not a neoplastic process, nor is it associated with a monoclonal expansion of a single plasma cell; instead, this is a reactive, inflammatory lesion which usually involves the gingival tissue.

Introduction

Plasma cell granuloma is a rare non-neoplastic lesion that was first described in 1973 by Bahadori and Liebow¹. Its exact incidence is unclear. This lesion's aetiology, biologic behaviour and most appropriate treatments are unclear, and little is known about the prognosis. It consists of a proliferation of inflammatory cells, with a predominance of plasma cells, in a fibrovascular background.

Plasma cell granuloma has been classified as an inflammatory pseudotumour which may occur in any organ or soft tissue, including the lung^{2,3}, vagina, bladder and larynx^{1,4,5}.

The causes of an inflammatory pseudotumour are unknown. Some authors believe this tumour is a low-grade fibrosarcoma with inflammatory (lymphomatous) cells. The propensity of inflammatory pseudotumours to be locally aggressive, to frequently be multifocal and to progress occasionally to a true malignant tumour supports this idea.

In some cases, inflammatory pseudotumour is thought to result from inflammation following minor trauma or surgery, or to be associated with other malignancy⁶⁻⁸.

An autoimmune mechanism has also been implicated. In one case, inflammatory pseudotumour was associated with vasculitis and inferior vena caval thrombosis, with anti-C3 and antifibrinogen deposits found in the vessel wall⁹.

There appears to be a subset of inflammatory pseudotumours that occurs secondary to infection. Organisms found in association with inflammatory pseudotumour include mycobacteria associated with spindle cell tumour, Epstein-Barr virus found in splenic and nodal pseudotumours, actinomycetes and nocardiae found in hepatic and pulmonary pseudotumours, respectively, and mycoplasma in pulmonary pseudotumours⁶.

There have been case reports of inflammatory pseudotumour associated with infections caused by other organisms, including *Mycobacterium avium-intracellulare* complex, *Corynebacterium equi*, *Escherichia*

coli, *Klebsiella*, *Bacillus sphaericus*, *Pseudomonas*, *Helicobacter pylori* and *Coxiella burnetii*¹⁰.

Plasma cell granuloma occurs most often in the lung and conducting airways, but has also been found in other organs such as the spleen, stomach, pancreas, liver, thyroid, larynx, orbit, heart, kidney and retroperitoneum. Intracranial³¹ and spinal cord plasma cell granulomas have also been described infrequently (a total of 38 cases)^{11,12}. In exceptional cases, plasma cell granulomas have involved different organs in the same patient¹.

Plasma cell granuloma has been called by different terms, for example, inflammatory myofibroblastic tumour, inflammatory pseudotumour, inflammatory myofibroblastic tumour, inflammatory myofibrohistiocytic proliferation and xanthomatous pseudotumour¹. Microscopic examination of inflammatory myofibroblastic tumour revealed plump spindle cells set in a myxoid vascular stroma admixed with inflammatory cells. Tumour cells were immunoreactive for vimentin, smooth muscle actin and KP1 (CD68), and negative for desmin, S-100 and Epstein–Barr virus-latent membrane protein. The recorded positivity for ALK³⁵, p53, MDM2, CDK4, pRb and Ki-67, despite the absence of bcl-2 reactivity, strongly favours the neoplastic origin of the studied tumour¹³. Presence of clonal cytogenetic abnormalities supported the neoplastic origin of this process¹⁴.

The most considered common treatment for plasma cell granuloma is a complete resection; however, in some cases, total surgical excision is not possible. Radiotherapy³⁶ and/or steroid therapy³³ have sometimes been successfully used to treat patients with non-resectable lesions¹ but discordant results have also been reported¹. Clinicians should however be aware that an inflammatory myofibroblastic tumour may mimic a reactive process¹⁴.

Batasakis, in 1983, described the interrelationships between the different neoplastic plasma cell disorders presenting in the head and neck¹⁵. Plasma cell granulomas are seen in the salivary glands¹⁴, and progenitor cells located in the bone marrow differentiate into bone marrow plasma cells, which are the cells of origin for multiple myeloma and solitary plasmacytoma of bone⁵.

Plasma cell granulomas of the oral cavity are seen primarily on the periodontal tissue. These lesions are often single. Maxillary and mandibular gingiva are equally involved. Bone loss may occur. These lesions have no sex predilection and may occur at any age. On histological evaluation, plasma cells are prominent but are intermixed with abundant other cellular elements, namely lymphocytes, neutrophils, eosinophils and

histiocytes, and usually surrounded by connective-tissue septae⁵. They are microscopically characterised by a vascular stroma with reactive inflammatory cells, including but not limited to plasma cells. No cytologic abnormalities are usually present. Russell bodies, which are intracytoplasmic eosinophilic hyaline droplets, may also be seen. Treatment of this condition is frequently unsuccessful and may include excision, cryotherapy or radiation¹⁶.

With respect to prognosis, plasma cell granuloma seems to be a generally benign, non-recurring condition; nevertheless, local aggressiveness and recurrences may complicate the outcome of the disease⁵.

Case report

A healthy male patient, 35 years of age, visited the Department of Oral Medicine and Radiology, KLE Society's Institute of Dental Sciences, Bangalore, India, with a complaint of a mass in relation to lower left back teeth for the past month. No relevant past history or medical history was present but he gave a history of tobacco chewing for the past 15–16 years. Vital signs were normal. On examination, no extraoral swelling was noticed. On intraoral examination, a nodular swelling in relation to lower left first molar (36) and lower left second molar (37) (Figs. 1–5) was seen and 36,37 showed no caries. The teeth were not in alignment in relation to the lower left quadrant. The teeth were stained (+++) and there was calculus (+++) and gingival recession in relation to the involved teeth. Bleeding on probing was seen. No other significant findings were noted. The patient was advised a radiographic examination. The Orthopantomogram revealed a widening of periodontal ligament space



Figure 1 Showing the facial view of the patient.



Figure 2 Shows the lingual positioning of the 37 and 38.



Figure 4 Shows the swelling in relation to 36,37. The colour of the swelling is similar to that of the surrounding normal mucosa.



Figure 3 The intraoral view of the swelling in relation to the teeth.



Figure 5 Another view of the innocuous swelling.

around 36,37. (Fig. 6) Incisional biopsy was performed and was sent for histopathological examination. The section revealed a large number of chronic inflammatory cells, predominantly plasma cells together with neutrophils, and lymphocytes in the connective tissue stroma. The plasma cells showed no dysplastic features. A probable histological diagnosis of a solitary plasmacytoma was made (Figs. 7–9). Immunostaining for κ (kappa) and λ (lambda) light chains confirmed a polyclonal plasma cell population after which a confirmatory diagnosis of plasma cell granuloma was made. The lesion was completely excised, and extraction of 36,37 was also done under local anaesthesia. The patient failed to turn up for a follow-up but reported that the lesion had completely healed.

Discussion

The phenomenon of plasma cell infiltrate was first described by Zoon^{17,30} in 1952 when he described balanitis plasmacellularis. Since then, plasma cell infiltrates have been found on the vulva, buccal mucosa, palate, nasal aperture, gingiva, lips, tongue, epiglottis, larynx and other orificial surfaces.

During the late 1960s and early 1970s, cases of plasma cell infiltrates of the lips, gums and tongue were described primarily in the dental literature under the names atypical gingivostomatitis^{18,19}, idiopathic gingivostomatitis¹⁹ and allergic gingivostomatitis¹. The lesions were thought to be a result of a reaction to chewing gum, dentifrices and other foreign substances^{11,16,20,21}, although extensive allergy testing had

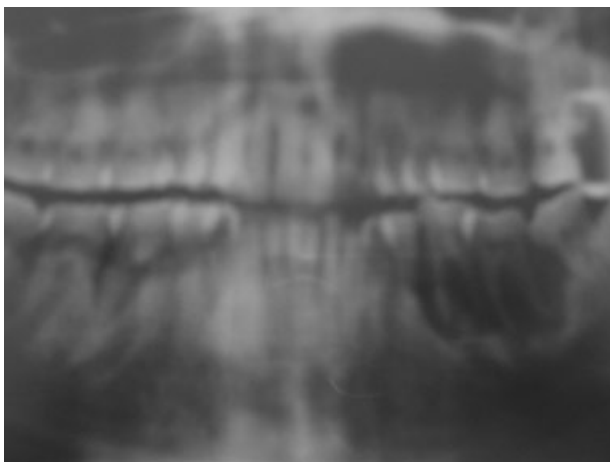


Figure 6 OPG radiograph showing a radiolucency around the roots of 36,37 region.

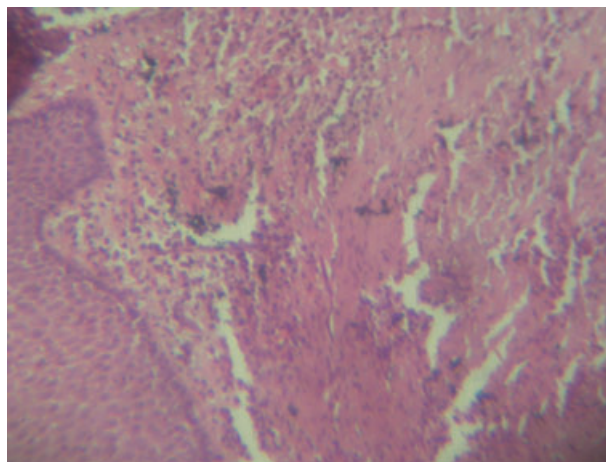


Figure 8 10x view of the plasma cell granuloma showing numerous plasma cells in the sub-epithelium.

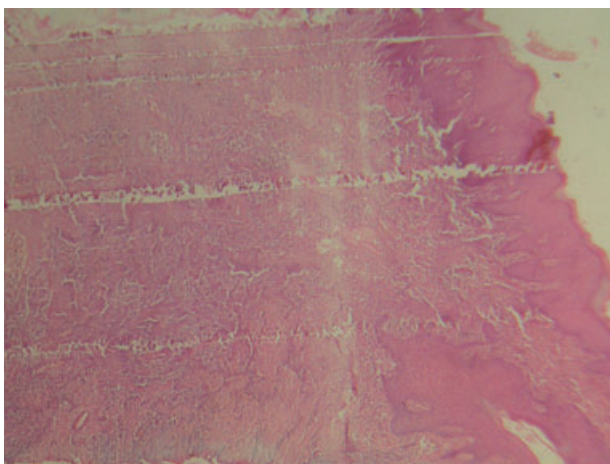


Figure 7 Scanner view of the entire section of the lesion.

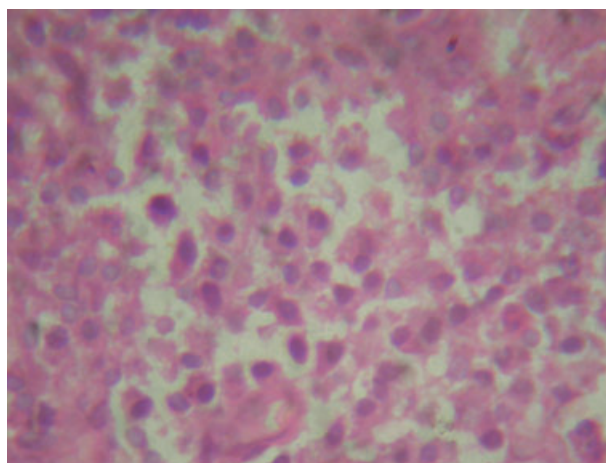


Figure 9 100x view of the plasma cells showing the eccentrically placed nucleus.

been inconclusive¹. Sherman and Luders simplified the nomenclature in 1960 and 1973, respectively, by grouping the infiltrates by anatomy under the titles plasmacytosis circumorificialis and plasmacytosis mucosae. However, additional terms have been used in the literature to describe plasma cell infiltrates of the aerodigestive tract such as plasma cell gingivitis^{16,21,22}, plasmacytosis of the gingiva^{12,32} and plasma cell cheilitis²³. In 1986, White *et al.*¹⁹ grouped all plasma cell infiltrates of the aerodigestive tract under the name 'plasma cell orificial mucositis'^{34,37} because of the fact that all the cases reported had clinical and histological findings that were indistinguishable from one another, eliminating the need for separate names for each anatomic area. Since that time, plasma cell orificial mucositis, or variants of the name, such as mucous

membrane plasmacytosis and plasma cell mucositis, have been used to describe benign plasmacytic lesions of the aerodigestive tract in the majority of cases reported^{16,22,23}.

Other disorders may present with lesions that appear similar clinically or histologically including fungal infection, carcinoma, syphilis, lichen planus, cicatricial pemphigoid, allergic or contact mucositis, sarcoidosis, cheilitis granulomatosa, plasma cell granuloma, plasmacanthoma, rhinoscleroma, Rosai-Dorfman disease, Melkerson-Rosenthal syndrome, multiple myeloma, solitary plasmacytoma, lymphoma and extramedullary plasmacytoma. Several of these diagnoses can be ruled out by histology or further testing for an infectious process¹⁶.

Fungal infection can mimic mucous membrane plasmacytosis but is usually distinguished by absence of fungal hyphae upon microscopic examination, negative result on maceration with potassium hydroxide, no growth on culture on Sabourauds Dextrose Agar, or a lack of response to treatment with nystatin.

Histological examination of the tissue can exclude carcinoma from the differential diagnosis¹⁶.

Mucous membrane lesions are present in one-third of patients with secondary syphilis²⁴, and histology can show superficial and deep perivascular infiltrate of plasma cells, lymphocytes and macrophages distributed in a band-like pattern in the dermis, accompanied by psoriasiform epidermal hyperplasia and hyperkeratosis^{20,29}. However, negative serologic tests for syphilis and the absence of spirochetes on a silver stain of tissue sections can rule out secondary syphilis as the cause for the mucous membrane lesions.

Only two cases of inflammatory myoblastic tumour (plasma cell granuloma) of the bone have been reported in the literature, both by Sciot *et al.*, which exhibited an aggressive expanding growth into the surrounding soft tissue³.

Plasma cell granulomas tend to locate in the oral cavity, primarily on the periodontal tissue^{22,24,25} and exact incidence of these cases have not been reported in literature. This lesion probably represents the oral counterpart of the cutaneous angioplasmocellular hyperplasia²⁴.

These lesions are often single, whereas the lesions of mucous membrane plasmacytosis tend to be multiple. On histological evaluation, plasma cells are prominent but are intermixed with abundant other cellular elements and usually surrounded by connective-tissue septae, distinguishing it from mucous membrane plasmacytosis⁵.

On the basis of histology, extramedullary²⁶ or primary cutaneous plasmacytoma needs to be considered. This tumour is found in the upper respiratory tract in approximately 80% of cases, especially in the nasal cavity and sinuses, nasopharynx and larynx, and can be sessile, polypoid or pedunculated⁵. Histologically, plasmacytomas are composed of a diffuse infiltrate of plasma cells in the dermis and subcutaneous tissue. There is minimal to prominent nuclear atypical of the plasma cells and on immunohistochemistry they are monoclonal, distinguishing plasmacytoma²⁶ from plasmacytosis. Gene-rearrangement studies can be done if immunohistochemistry is inconclusive.

The aetiology of this condition is unclear but is believed to be a non-specific inflammatory response, in the form of a plasma cell infiltrate, to an unknown

exogenous agent. Attempts to induce plasma cell infiltrations on mucosal and non-mucosal surfaces by allergic and irritant stimuli were not successful²⁷.

Roman²³ hypothesised that plasma cell gingivitis^{18,28} may be associated with low levels of serum IgA and secretory IgA, which allows localised, repetitive, sub-clinical infections that could lead to the plasma cell infiltrate.

Aiba¹⁹ points out that a plasma cell infiltrate is a rare histological feature in ordinary inflammatory dermatoses but is often found around such epidermal neoplasms as actinic keratosis, Bowen disease, squamous cell carcinoma and syringocystadenoma papilliferum. The authors hypothesise that, although the inciting factor of the plasma cell infiltrate is unknown, it is plausible that similar mechanisms are involved in both the mucosal and skin plasma cell infiltrate conditions.

Dalrymple and Henry Bence-Jones, a surgeon and physician respectively, first described the neoplastic proliferation of plasma cells characterised by marked proteinuria and bone pain in 1846. In 1873, Rustizky in Kiev coined the term Multiple Myeloma after describing the case of a 47-year-old farm servant who developed a tumour under the skin of his temple that displaced his eye. Autopsy revealed eight additional lesions, which originated in the bone marrow. Schridde in 1905 was the first person to describe an extramedullary plasmacytoma, and Ewing and Foote in 1952 were the first to present a large series of cases.

With regard to the case that visited our institution, the histological features were in contrast to the above-mentioned cases. A probable diagnosis of solitary plasmacytoma was made and the polyclonality of plasma cells with the kappa and lambda chain immunostaining pointed to the conclusive diagnosis of plasma cell granuloma.

Conclusion

Plasma cell granuloma is a diagnosis of exclusion, distinguished primarily on the histological finding of a marked submucosal plasma-cell infiltrate, after conditions such as infection and plasmacytoma have been eliminated. The aetiology of this condition is unclear but is believed to be a non-specific inflammatory response, in the form of a plasma cell infiltrate, to an unknown exogenous agent. This report reinforces the existence of inflammatory pseudotumours in the oral region as well as the need for clarification of the unknown nature of inflammatory pseudotumours.

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