Case Report

Oral Plasma Cell Granuloma: An Enigmatic Lesion
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Abstract
We present a case of oral plasma cell granuloma in a 44 year old man with misleading clinical features of a red and white lesion on the gingiva in relation to the tooth #44 - #46 which was associated with advanced crestal bone loss and ill-defined radiolucency. Histopathology and immunohistochemistry demonstrated the polyclonal nature of the cells and yielded a diagnosis of plasma cell granuloma. This lesion merits discussion because it is typically found in the oral cavity and it reinforces the existence of inflammatory pseudotumors in the oral cavity. This report also discusses the diagnostic enigma and the associated terminology of plasma cell granulomas in the light of WHO description of the lesion.

Keywords: Granuloma; Plasma Cells; Pseudotumor; Gingiva; Oral Cavity; Xanthoma.

Introduction
Plasma cell granuloma was first described by Bahadori and Liebow in 1973 as a rare non-neoplastic lesion which may occur in any organ or soft tissue, including the lung, vagina, bladder and larynx. Since then it has been described by many authors using different terms for example; inflammatory myofibroblastic tumour, inflammatory pseudotumor, inflammatory myofibrohistiocytic proliferation and xanthomatous pseudotumor. Plasma cell granulomas of the oral cavity are primarily rare solitary lesions seen on the periodontal tissue. Maxillary and mandibular gingiva is equally involved with severe bone loss. These lesions have no sex predilection and may occur at any age. Histopathologically, plasma cells are prominent but are intermixed with abundant other cellular elements, namely lymphocytes, neutrophils, eosinophils and histiocytes, and usually surrounded by connective tissue septae. They are microscopically characterised by a vascular stroma with reactive inflammatory cells, including plasma cells but not limited to them. No cytologic abnormalities are usually present. Russell bodies, which are intracytoplasmic eosinophilic hyaline droplets, may also be seen. Treatment of this condition may include excision, cryotherapy or radiation. Prognostically, plasma cell granuloma seems to be a generally benign, non-recurring condition; nevertheless, local aggressiveness and recurrences may complicate the outcome of the disease. This paper presents a peculiar case of oral plasma cell granuloma that clinically mimicked an epithelial malignancy and aims at discussing the diagnosis and classification of the lesion in the light of the present recommendation of the WHO.

Case Report
A 44 year old Indian male security guard came to the Oral Medicine clinic of Penang International Dental College with a complaint of missing upper and lower teeth and a need for dentures. History revealed a recent extraction of a mobile tooth, without any complications. He was a known diabetic under medication and gave a history of tobacco and processed betel nut (paan parag) chewing habit since the last six years. Patient used to chew the quid at least five to six times a day and hold the quid for as long as possible in the right buccal vestibule. He also gave a history of smoking cigarettes for the past ten years. No known drug or food allergies were reported. On examination the gingiva and alveolar mucosa in relation to tooth #44, #45 and #46 region were erythematous; with a white diffuse non-scrapable patch measuring about 2 x 3cm (Fig 1a). There was no bleeding noticed.

Radiographic examination showed advanced crestal bone loss with ill-defined radiolucency surrounding the apices of the teeth. Loss of trabecular pattern was noticed with teeth #44 - #45 region. (Fig 1b) Based
on the history and presentation a clinical diagnosis of early squamous cell carcinoma was suspected and the lesion was subjected to a biopsy along with extraction of the teeth. Histopathology showed soft tissue composed of parakeratinised epithelium which appeared thinned out, ulcerated, spongiotic with no evidence of dysplasia (Fig 1c). Underlying connective tissue was moderately dense, fibro-collagenous and densely infiltrated by inflammatory cells mainly plasma cells, few lymphocytes and few areas of acute inflammatory cells. Sheets of plasma cells with binucleate forms were noted in a highly vascular stroma with edematous areas, extravasated RBC’s and hemosiderin pigmentation was also noted. These features ruled out an epithelial malignancy but raised suspicion of a plasma cell neoplasm (Fig 1d).

A diagnostic workup for suspected plasmacytoma comprising of serum electrophoresis, urine analysis and lateral cephalogram showed no abnormal findings. The tissue sections were subjected to Immunohistochemistry studies for kappa and Lambda light chains which showed strong intracellular positivity. This suggested a polyclonal proliferation of plasma cells (Fig 1e and f). The histopathology and immunohistochemistry results lead to the microscopic diagnosis of plasma cell granuloma. The post operative healing was uneventful and thereafter the patient was followed up for period of one year with no evidence of recurrence.

**Discussion**

Plasma cells are terminally differentiated B lymphocytes that provide protective immunity through the continuous secretion of antibodies. They are commonly seen in chronic inflammatory infiltrates and were first
described by Zoon in balanitis plasma cellularis in the year 1952. Since then, plasma cell granulomas have been documented in the vulva, buccal mucosa, palate, nasal aperture, gingiva, lips, tongue, epiglottis, larynx and other orificial surfaces.\(^7\) Plasma cell granulomas were considered to be highly uncommon, non-neoplastic, reactive lesions, which were first brought to the attention of health care practitioners during the late 1960s and early 1970s. They have now been described as Inflammatory myofibroblastic tumor and classified by the WHO in the year 2002 under intermediate (rarely metastasizing) fibroblastic / myofibroblastic tumours with ICD-O code - 8825/1.\(^2\) The WHO describes the lesion as a distinctive lesion composed of myofibroblastic spindle cells accompanied by an inflammatory infiltrate of plasma cells, lymphocytes, and eosinophils.\(^9\)

It occurs primarily in soft tissue and viscera of children and young adults. Microscopically, inflammatory myofibroblastic tumour show plump spindle cells set in a myxoid vascular stroma admixed with inflammatory cells. Tumour cells are 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 tumour.\(^10\) Presence of clonal cytogenic abnormalities also supports the neoplastic origin of this process.\(^11\)

Some authors believe this tumour to be a low-grade fibrosarcoma with inflammatory (lymphomatous) cells. The propensity of plasma cell granulomas to be locally aggressive, to frequently be multifocal and to progress occasionally to a true malignant tumour favours this concept. In some cases, it is thought to result from inflammation following minor trauma or surgery, or to be associated with other malignancies.\(^5,12\) Other mechanisms suggested include auto immune\(^13\), mixed bacterial infections\(^6\) and Epstein – Barr Virus.\(^12\) But the exact aetiology, behaviour and prognosis of plasma cell granuloma is still enigmatic.

A review of literature by Epstein et al\(^14\) suggested that 14% of multiple myelomas had history of oral manifestations. Solitary plasmacytomas of bone approximately comprised of 24% of the total cases of myelomas. Soft tissue extramedullary plasmacytomas though known to be rare tumors show a predilection for the head and neck region. This data justifies the need to investigate oral lesions with diffuse plasma cell infiltration to rule out malignancies. Oral plasma cell granulomas reported in literature are primarily of periodontal origin with varying clinical and radiographic features.\(^15,16\) However the exact incidence of these cases is not known.

The history of tobacco and betel nut chewing with associated clinical features in our case were suggestive of a precancerous lesion. However, the radiographic presentation showed advanced bone destruction which mimicked a malignancy as reported previously.\(^17\) Initial histopathology evaluation however was suggestive of a plasma cell neoplasm which leads to a diagnostic work up to rule out multiple myeloma and extra medullary plasmacytoma. The polyclonal proliferation of plasma cells identified by immunohistochemical stains thus helped us to diagnose the present case as a plasma cell granuloma. The treatment recommended for plasma cell granuloma is surgical resection in order to prevent recurrence; other modalities suggested include cryotherapy, radiotherapy and/or steroid therapy.\(^6,7,3\) The present case was treated surgically with no postoperative recurrence noted for a yearlong follow up.

**Conclusion**

We found the lesion to mimic an epithelial malignancy with clinical and radiographic feature being supported by a positive history of tobacco use. However, the final histopathologic diagnosis was suggestive otherwise. Upon reflection the cause of the lesion in our case may have been chronic inflammation of periodontal origin but the year long follow up did not show any recurrence. These features don’t completely fit into the WHO description of an inflammatory myofibroblastic tumor which convinced us in using ‘plasma cell granuloma’ as our final diagnosis. Thus, plasma cell granuloma still remains enigmatic in their etiopathogenesis and terminology as well.

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References

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