Intra-oral Plasma Cell Granuloma: A Rare Clinico-pathological Entity-Report of Two Cases with Review

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Abstract

Plasma cell granulomas (PCGs) or inflammatory pseudotumors are non-neoplastic lesions that consist of predominantly antibody-producing plasma cells and innate immune cells such as neutrophils, macrophages, and eosinophils. Unlike in multiple myeloma, the plasma cells are polyclonal and proliferate in a fibroblast-rich stromal background. These lesions are predominantly reported in the lungs; however, they may involve other organs too. Very few cases are reported regarding the presence of PCG in the oral cavity and a confirmatory diagnosis is crucial for further management. A critical and careful examination from a pathological point of view is obviously necessary to rule out other plasma cell neoplasms. We present here two cases of intra-oral PCGs; one in the gingiva & another within the jaw; both showing a polyclonal staining pattern in immunohistochemistry confirming a diagnosis of plasma cell granuloma.

Introduction

Plasma cell granuloma (PCG), also known as inflammatory pseudotumor is a tumor-like lesion, and most cases are reported in the lungs [1]. But this tumor can involve other sites like the orbit, head and neck, liver, and rarely the oral cavity. Gingival Plasma cell granulomas are extremely rare. These are non-
neoplastic reactive lesions of idiopathic nature and predominantly comprise of polyclonal plasma cells. Intraoral PCG have been reported in a wide range from pediatric to geriatric groups, but most of the cases of gingival PCG manifest in the 4th and 5th decades of life with slight female predominance [2]. Confirmation depends on clinical, radiographic, morphologic and immunophenotypic evaluation. These tumors contain an increased number of plasma cells that are expressed with CD138 and are polyclonal for kappa and lambda light chains, confirming the non-neoplastic nature. Here we report two cases of intra-oral plasma cell granuloma and discuss the pathology and diagnosis in general context of PCGs.

**Case Presentation**

**Case 1**

An 80-year-old female patient reported to our department with the chief complaint of a painless growth in the lower right back teeth region for the last three months. The growth was small initially but increased gradually to attain the present size over the period. Extraoral examination revealed nothing significant. Cervical lymph nodes were not palpable. Her medical history revealed hypothyroidism, controlled by medication. A general physical examination showed a moderately built, nourished female with a steady gait and satisfactory vital signs.

Intraoral examination revealed the presence of a well-circumscribed, solitary, pale pink, multi-lobulated growth measuring about 3.5 cm × 1.5 cm over the alveolar ridge in the region of teeth from 42 to 46. The growth was situated surrounding teeth 43 & 44, which were found periodontally compromised and mobile. No other teeth were present in that segment. On palpation, the growth was soft to firm in consistency, non-tender, and non-pulsatile.

**Figure 1:** Intra-oral photograph showing solitary, pale pink, multi-lobulated growth over the alveolar ridge.

The growth was pedunculated with a broad stalk attached to the inter-proximal gingiva of the associated teeth. The overlying mucosa was smooth, non-ulcerated, and without any vascular prominence. (Figure
1) Panoramic radiographic examination showed spiking root resorption of the involved teeth and loss of alveolar bone too. (Figure 2)

**Figure 2:** Photograph of panoramic radiograph showing spiking root resorption of the involved teeth and loss of alveolar bone.

Based on the clinical examination and history given by the patient, the growth was thought to be a benign neoplasm and a provisional diagnosis of “peripheral giant cell granuloma” was made. Other clinical differential diagnoses included fibroma, pyogenic granuloma, neurofibroma, schwannoma, fibrous histiocytoma, and granular cell tumor.

The patient’s routine haemogram was found to be within normal limits, except for raised ESR. After receiving informed consent from the patient, an excisional biopsy was performed under local anesthesia with concomitant extraction of regional teeth. A per-operative striking feature was excessive hemorrhage from the biopsy site. The gross specimen was well-circumscribed, brownish white, and lobulated mass measuring about 3.5 cm × 1.5 cm in dimension. The cut surface was homogenous, white, firm, and without any evidence of hemorrhage or necrosis.

Histopathological examination of the sections stained with hematoxylin & eosin revealed the presence of connective tissue stroma which is characterized by diffuse sheets of plasma cells in a relatively eosinophilic background along with non-specific lymphocytic infiltrates. No epithelium was found in the sections. Based on these histopathological features, a Plasma cell neoplasm was thought. Further immunohistochemical analysis revealed the kappa lambda expression ratio of approximately 1:2, confirming a reactive plasma cell proliferation. (Figure 3)

Overall histopathological & IHC features were suggestive of “Plasma cell granuloma”.

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Figure 3: Composite image showing histopathology stained with H & E (A), Immunohistochemistry with lambda (B), and Kappa (C) positivity.

The patient was advised for a PA view chest X-ray, which showed no focal lesion in the lungs. Presently the patient has been kept under close watch through regular follow-ups.

Case 2

A 15-year-old female patient reported the chief complaint of a painless growth in the lower anterior teeth region for the last three months. Extraoral examination revealed small lobulated swelling below the lower lip on palpation. Her medical history revealed nothing significant. A general physical examination showed a moderately built, nourished female with a steady gait and satisfactory vital signs. Intraoral examination revealed the presence of soft, nodular growth obliterating GB sulcus in relation to 31,32,41,42 region which was mild tender on palpation. (Figure 4)

The teeth were vital without any mobility. On palpation, the growth was soft to firm in consistency and non-pulsatile. IOPA radiograph showed a round-shaped radiolucent lesion with an appreciable margin along with a widening of the lamina dura of the involved teeth. (Figure 5)

Based on the clinical examination and history given by the patient, the growth was thought to be a benign neoplasm and a provisional diagnosis of “central giant cell granuloma” was made. Other differential diagnoses included odontogenic cyst, neurofibroma, schwannoma, fibrous histiocytoma and granular cell tumor.
Figure 4: Intra-oral photograph showing soft, nodular growth obliterating GB sulcus.

Figure 5: Photograph of IPA radiograph showing a round-shaped radiolucent lesion along with widening of lamina dura.

In routine hemogram, ESR was found raised and Hb% was 7.9 gm/dl; anisocytosis and hypochromic RBCs with a total count of 2.6 million/cu mm; other parameters were found within normal limit. After written informed consent from the patient, an incisional biopsy was performed under local anesthesia. Histopathological examination of the section stained with hematoxylin & eosin revealed the presence of
connective tissue stroma which is characterized by diffuse sheets of plasma cells in a relatively eosinophilic background along with non-specific lymphocytic infiltrates. Based on these histopathological features, a plasma cell neoplasm was thought. Further immunohistochemical analysis revealed the kappa lambda expression ratio approximately 1: 2, CD 138 was positive, and cytokeratin was negative; confirming a reactive plasma cell proliferation. (Figure 6) Overall histopathological & IHC features were suggestive of “Plasma cell granuloma”.

Figure 6: Composite image showing histopathology stained with H & E (A), Immunohistochemistry with lambda (B), and Kappa (C) positivity.

The patient was referred to the Oral Surgery department for further surgical management and was advised for regular follow-ups.

Discussion
The incidence of plasma cell infiltrate was first enunciated by Zoon in 1952 while describing balanitis plasmacellularis [3]. The first use of the term PCG came into practice during the 1950s and was first reported as a gingival lesion in 1968 and described as an inflammatory pseudotumor in 1973 by Bahadori and Liebow. The other names are inflammatory myofibrohistiocytic proliferation, inflammatory myofibroblastic tumor, and xanthomatous pseudotumor [4]. The exact etiology of oral cavity PCG is obscured. The factors like reactive and associated periodontitis, peri-radicular inflammation due to the presence of the foreign body or the presence of viral antigens such as EBV and HHV-8 are responsible for its occurrence [5]. Amlodipine and cyclosporine have been reported as causative drugs for plasma cell granulomas [6]. Though the patients in our cases had no such drug history. Kim et al. observed that interleukin-6 (IL-6) and phospholipase C-γ1 might stimulate the
plasma cells to infiltrate in case of cyclosporine-induced gingival overgrowth [7]. The microscopic diversity has led to different opinions regarding the inflammatory or neoplastic nature of this lesion. The plasma cells in PCG show polyclonality in lambda and kappa light chains favoring its inflammatory nature. The three microscopical variants of PCG viz. plasma cell predominant type (PPT), mixed inflammatory cell type (MICT), and sclerosed fibrosis type (SFT) have also been postulated by Kim et al [7].

Though PCG most commonly arises from the lungs; it accounts for less than 5% of all extrapulmonary cases in orofacial regions [8]. The disease involves generally the orbit; followed by the meninges, infratemporal fossa, paranasal sinuses, and other soft tissues. Very rarely the oral cavity gets affected, commonly the maxillary and mandibular gingiva with an equal rate of distribution [9]. There could be the presence of multiple simultaneous lesions, but solitary lesion was found in the majority of cases, which were the cases for both patients reported here.

Histopathologically, the polyclonal population of plasma cells is seen as a sheet of inflammatory cells; along with polymorphonuclear neutrophils and lymphocytes. The plasma cells have the classic eccentric nuclei; with clear, perinuclear Hoff’s and numerous cytoplasmic Russell-Fuchs bodies [10]. Plasma cells are terminally differentiated B-lymphocytes that are typically found in the red pulp of the spleen, tonsils, medulla of the lymph nodes, lamina propria of the entire gastrointestinal tract, mucosa of the nose and upper airway, and at the sites of inflammation. The main function of plasma cells is to secrete Igs or antibodies and PCG is a plasma cell-rich lesion that merits discussion because it is neither a neoplastic process nor is associated with a monoclonal proliferation of a single plasma cell; rather this is a reactive inflammatory lesion. Immunohistochemical studies show that the plasma cells in PCG express CD138 & are polyclonal as illustrated by positive immune reactivity for both kappa and lambda light chains by immunohistochemistry or in situ hybridization [11]; which were the findings in immunohistochemical evaluation in our cases.

In our cases, the predominant presence of plasma cells primarily led to the diagnosis of plasmacytoma or PCG. As in plasmacytoma, there is the presence of diffuse sheets of variably differentiated neoplastic monoclonal plasma cells. Other differential diagnoses of plasma cell lesions in the oral cavity include plasma cell mucositis, plasma cell gingivitis, solitary myeloma & multiple myeloma. Multiple myeloma and solitary myeloma frequently present as solitary bone tumors, whereas plasmacytoma and plasma cell granulomas primarily affect the soft tissues [12]. Plasma cell gingivitis is usually not a localized nodular lesion but presents as generalized oedematous and erythematous overgrowth [13]. As plasma cell granuloma is a benign growth while plasmacytoma has got potential to form multiple myeloma, which is a malignant proliferation of plasma cells & requiring a different treatment strategy, proper diagnosis of the soft tissue tumor is mandatory. The polyclonality of plasma cells in our cases went in favor of PCG.
Dimension and associated symptoms will guide the treatment plan and outcome of the disease. It includes oral prophylaxis, excision of the lesion, and possible extraction of the involved tooth. As the tumors are unencapsulated, surgical excision by keeping healthy margins is necessary to prevent recurrence [14]. In a few cases, regression of the lesion with the usage of corticosteroids and nonsteroidal inflammatory agents had been reported, though the mainstay of treatment remains surgery [15]. In our cases, the short-term follow-up of 6 months showed no recurrence.

**Conclusion**

Abundant plasma cell infiltration as a histopathological finding primarily leads to the diagnosis of PCG as a differential diagnosis; after conditions such as infections and plasmacytoma have been eliminated. Immunohistochemistry plays a key role in accurate diagnosis. The clinical nature and microscopic features of intra-oral PCG / inflammatory pseudotumor remain the principal facet for a conclusive diagnosis of the lesion. At the same time, it is prudent to recognize this entity as a reactive inflammatory lesion to avoid unnecessary invasive radical surgery. Our case reports validate the occurrence of such types of inflammatory pseudotumors within the oral cavity as well as the need for further research to determine its idiopathic nature and etiology.

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