Clinicopathological Study of Oral Plasma Cell Granuloma

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Abstract:

Objective: To identify the characteristic clinical and Histopathologic features encountered in the oral lesions of PCG; thus clarifying the variability nature of the studied oral plasma cell granulomas (OPCGS). **Materials and Methods:** A sample of 25 retrospective paraffin blocks of OPCGS was thoroughly investigated histopathologically. **Results:** the studied OPCG was mainly represented as a gingival swelling, there was a female tendency in most of the studied OPCGS (92%), ranging from 11-73 years with a mean of 42.40. the majority of the current OPCG (64%) did not express any bone changes. the OPCGS of the present work were characterized by their variable histopathological features, thus creating a marked histological diversity **Conclusions:** Oral plasma cell granuloma (OPCG) is a benign inflammatory lesion that requires biopsy and Histopathological examination to be differentially diagnosed from other lesions irrespective of the clinical features and clinical diagnoses. this is important to rule out possible neoplastic and plasma cell dyscrasias, and other similar diseases such as multiple myeloma.

Introduction:

Plasma cells (pcs) are terminally differentiated B lymphocytes that 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. A plasma cell's main function is to produce immunoglobulin's or antibodies.[1]Plasma cell granuloma (PCG) is a rare benign tumor-like condition that showed proliferation of spindle cells with marked inflammatory infiltrates composed predominantly of pcs and small lymphocytes. Although it occurs most commonly in the lungs, [2] extra pulmonary presentation of PCG was reported to affect other organs such as the vagina, bladder, and the abdominal cavity.[3]The occurrence of PCG in the head and neck region is also rare. Oral plasma cell granuloma has been reported to be rarely seen in the oral cavity, as a single unilateral swelling seen primarily on the periodontal tissue, mainly the gingiva,[4] followed by the tongue,[5] lips,[6] buccal and oral mucosa.[1]These lesions have been observed to have no gender predilection and might occur at any age. [7] The reported cases of OPCG were in the wide range of 19 months to 63 years old, but most of the reported cases are observed in the fourth and fifth decades of life with female predominance. Most of these are in the form of single case reports.[8,9] The etiology of OPCG is controversial and not yet defined. [10] The clinical gross appearance of OPCG has been reported to take at least two morphologic Forms in the oral mucosa: epiphytic/tumor-like or unilateral ulcerative.[11] Histologically, OPCG has been characterized by fascicles of spindle mesenchymal cells admixed with chronic inflammatory cells, predominantly pcs which are arranged in sheets and aggregates.

The pcs are intermixed with a few other cellular elements, namely lymphocytes, or/ and eosinophil's. The stroma is collagenous and/or myxoid. All these components are arranged in varying proportions thus creating a marked histological diversity.[7]

Histopathological examination of these lesions has been reported to be a must to decide the exact nature of these lesions and to rule out other potential plasma cell dyscrasias and neoplasms. Thus this study is designed to describe the characteristic histopathologic features encountered in the oral lesions of PCG and to throw a beam of light on the obscure nature of these lesions.

Material and methods:

The current work was carried out as a retrospective study of 25 subjects of OPCG. Available clinical data were also added and possibly radiographic ones. All data were retrieved from the Oral Pathology Department of the Faculty of Dentistry of Mansoura University.

Clinico-radiological data: All OPCGS were subjected to:

Complete history: Present history including (age, sex and site).Interpretation report of radiographs if included in patients' data sheets. **Histopathological study:** The retrieved Paraffin blocks of the study cases were serially cut into 4µ thickness sections to perform the following: Hematoxylin and Eosin (H&E) staining for thorough histological examination and diagnosis: With the aid of the light microscope, the hematoxylin and eosin (H&E) sections were thoroughly investigated and rediagnosed histopathologically. According to The WHO classification of head and neck tumors, 2017 listed non-laryngeal PCG (including the oral cavity) as a synonym for IMT and OPCG.[12] **Statistical analysis:** Data were tabulated, coded, and then analyzed using the computer program SPSS (Statistical package for social science) version 24.0.

Descriptive data: Descriptive statistics were calculated in the form of Mean ± standard deviation (SD), median, and frequency (number-percent).

Analytical statistics: In the statistical comparison between different groups, the significant differences were tested using the Chi-square test. The significance of the obtained results was judged at the 5% level **(**$p < 0.05$) was

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Table 1: The relation between clinical and radiological data of bone involvement of OPCGs

		Bone involvement								P value
		Without		Slight		Severe		Total		
		n	%	n	%	n	%	n	%	
Age	<25 n=4	3	75%	1	25%	0	0	4	100%	3.61 0.460
	25-50 n=11	7	63.6%	4	36.4%	0	0	11	100%	
	>50 n=10	6	60%	2	20%	2	20%	10	100%	
Sex	Male	2	100%	0	0	0	0	2	100%	1.223 0.543
	Female	14	60.7%	7	30.4%	2	8.9%	23	100%	
Site	Upper Anterior gingiva	3	50%	3	50%	0	0%	6	100%	12.033 0.061
	Upper posterior gingiva	0	0	0	0	2	100%	2	100%	
	Lower anterior gingiva	5	83.4%	1	16.6%	0	0	6	100%	
	Lower posterior gingiva	8	72.7%	3	27.3%	0	0	11	100%	

Data expressed as frequency (n=number of OPCG -%=percent). P: Probability. Significance where P value <0.05. Test Data used: Chi-square test.

considered statistically significant.

Results:

Clinical findings of OPCGS:

The relation between clinical data (age, sex and site) and radiological data of bone involvement among the current OPCGS: Current study results revealed that age groups were ranging from 11-73 years with a mean of 42.40. There was a female tendency in all studied OPCG subjects (92%). Almost all subjects were reported as having a gingival lesion. Interestingly, the radiographic data, revealed that the majority of the current OPCG subjects (64%) Didn't express any bone changes. Bone involvement of the current OPCG was observed among the studied OPCG of the age group above 50 years (20%), equally divided, between slight and severe bone loss. Noticeably they were exclusively among females. No statistically significant difference was demonstrated between clinical data (age, sex, and site) and radiological data on bone involvement, (Table1).

Histopathological findings of the current OPCGS:

The H&E stained sections of the studied OPCGS showed a surface of keratinized hyperplastic stratified squamous epithelium (showing no epithelial dysplastic changes), with elongated rete processes (52%).

Although pseudo epitheliomatous hyperplasia was evident in 48% of the studied OPCGs, alternating fields of the atrophic epithelium were also detected in 28% of OPCGs. Meanwhile, ulceration was occasionally detected in 20% of OPCGs. The underlying connective tissue was mainly fibrovascular entrapping variable populations of PCs and other inflammatory cells; mainly lymphocytes, and histiocytes with scarce neutrophils and eosinophils. No atypical changes were detected in the examined PCs. In most of the studied OPCGs (72%), the PCs showed a grouping pattern of distribution. This grouping was detected between fibrous and collagen bundles of the stroma of the current OPCGs. (Figure 1).Most of the stroma revealed high vasculature (92%), also the perivascular aggregation of PCs was observed among 68% of the current OPCGs, The relation between clinical data (age,sex and site) and distribution pattern of PCs among OPCGs.

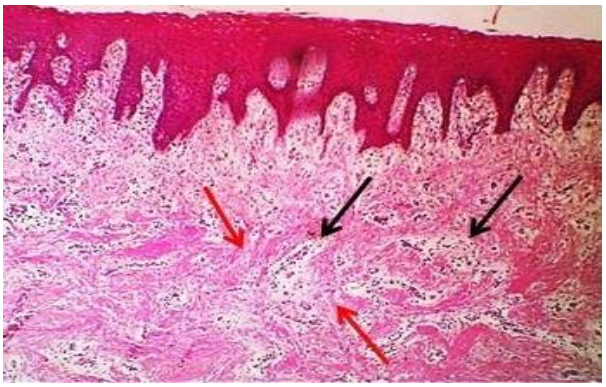

Figure 1: Photomicrograph of OPCG shows groups of PCs (black arrows) surrounded by dense collagen bundles (red arrows). (H&E x40).

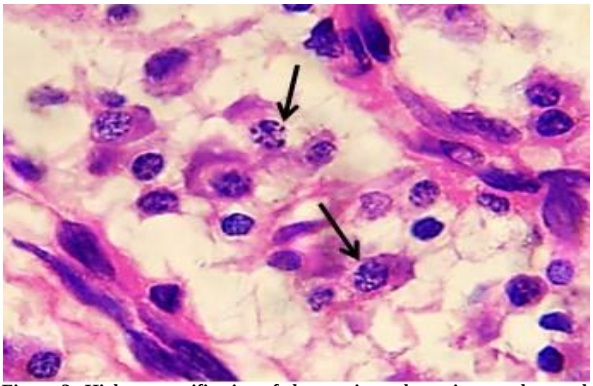

Figure 2: Higher magnification of the previous photomicrograph reveals PCs nuclei with (cart-wheel) appearance (black arrows). (H&E x1000 oil lens)

The pattern of distribution of PCswas noticed to be arranged in the form of groups among studied OPCGs that of age <25 years and of less incidence among other age categories. Among all OPCGs of upper anterior and posterior, PCs were noticed to be arranged in groups. However, no statistically significant difference was demonstrated between clinical data (age, sex, and site) and the distribution pattern of PCs of OPCGs, (Table 2).

The characteristic microscopic features of PCs were uniform, small, and mature with basophilic cytoplasm and eccentric nuclei giving the characteristic of (cart-wheel) pattern and perinuclear clear zone (Hof) with no signs of atypia seen among current OPCGs, (Figure2).

Discussion:

Plasma cell granuloma was defined as a plasma Cell lesion consisting predominantly of PCs and other inflammatory cells such as lymphocytes and/or eosinophil's in a fibroblast- rich stromal background. These lesions mainly occur in the lungs. [13] However, they can arise in any organs as well as in the head and neck region, the most commonly involved regions have been reported in the orbit,[14] as well as in the tonsils, and ears.[15]Findings of this lesion in the oral cavity were found to be very rare and were diagnosed as OPCG. Mostly, they have been recorded as single case reports. Oral plasma cell granuloma has been represented in the tongue,[5] lip,[6] oral mucosa,[1] and gingiva.[7, 16] The demographic data analysis of the current study groups of OPCG revealed that the ages were found to range from 11 to 73 years with a mean of 42.40 years. This was in agreement with many other researchers.[16, 17] This might be related to that the aging process is accompanied by alterations in the function of the immune system. This has been reported to be associated with weakened adaptive immunity (plasma cells), leaving older individuals susceptible to infection and unprotected from chronic tissue inflammation.[18, 19]Presently, it was interestingly obvious that female predilection was observed among almost all current studied OPCGs, showing similarities with other case reports.[8, 20] Meanwhile, few case reports were found to be among males. [16, 17] This female predominance might be interpreted by the influence of the levels of Circulating sex hormones; estrogen or progesterone. Estrogen has been reported to be A Regulator of inflammation, hence, the deficiency of ovarian steroidal hormones potentiates the pro-inflammatory state.[21] Almost all OPCGs were currently reported in the gingiva. This was following most of the previous study case reports.[16, 20] Additionally, it was observed that mandibular gingiva was more affected (68%) than maxillary ones (32%) among the current studied OPCGs. This might be explained as that the maxilla has been reported to have a significant collateral blood flow, thin cortical bones, and bone marrow with struts which make it less prone to infection and granuloma formation.[22] Hence this specific OPCG.More than half of the studied OPCGs (64%), showed only soft tissue involvement without any radiologic changes. This was in agreement with Bhagawati, Sharanamma, and Kanwar, 2018 .Meanwhile, bone involvement was currently variably observed in the other 36% of

Table 2: The relation between clinical data and distribution pattern of PCs among OPCGs

		Histologic PC distribution pattern						P value
		Diffuse		Grouped		Total		
		n	%	n	%	n	%	
Age	<25 n=4	0	0	4	100%	4	100%	
	25-50 n=11	**4**	36.3%	7	63.7%	11	100%	1.364 0.506
	>50 n=10	**3**	30%	7	70%	10	100%	
Sex	Male	**0**	0	2	100%	2	100%	
	Female	**7**	30.5%	16	69.5%	23	100%	0.543 0.633
Site	Upper Anterior gingiva	**0**	0	6	100%	6	100%	
	Upper posterior gingiva	**0**	0	2	100%	2	100%	3.030 0.387
	Lower Anterior gingiva	**2**	33.3%	4	66.7%	6	100%	
	Lower Posterior gingiva	**3**	27.3%	8	72.7%	11	100%	

Data expressed as frequency (n=number of OPCG -%=percent). P: Probability. Significance where P value <0.05. Test used: Chi-square test. PC:Plasma cells.

OPCGs, mostly noticed with slight bone resorption in a saucer shape pattern. This was in agremment with other previous reports. [23]The bone loss might be explained as a result of inflammatory causes that might be related to bad oral hygiene such as the formation of plaque or calculus. Moreover, the severity of the subsequent bone loss may directly depend on the lesion's etiology and chronicity.Interestingly, marked vascularity in the connective tissue stroma was observed in most of the current Studies OPCG (92%). A finding that might be related to the vasodilation of the small vessels, occurs during inflammation leading to an increase in blood flow, Which could be more suggestive for the nature of OPCG.[24]On a statistical basis, no significant difference was found between clinical data and both radiological data and histopathologic features of OPCGs in the present research. This finding might declare the absence of any clinical impact or histopathologic changes among present studied OPCGs.

Conclusions:

- Oral Plasma Cell Granuloma (OPCG) was mainly represented as a gingival swelling. Therefore, OPCG should be considered one of the differential diagnoses of gingival swellings.

- There was a female tendency in most of the studies OPCGs (92%) ranging from 11-73 years with a mean of 42.40.

- OPCG despite being a benign inflammatory lesion, it requires biopsy and histopathological examination to rule out possible neoplastic and plasma cell dyscrasias, such as multiple myeloma, irrespective of the clinical features and clinical diagnoses.

- Further studies for understanding the histogenesis of the OPCG lesion are recommended. It is necessary to perform routine laboratory investigations, and microbiological culture for patients with OPCG based on the medical history and clinical features to exclude local and systemic factors.

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