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Assessment of estrogen receptor marker and smooth muscle actin marker in oral pyogenic granuloma

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***Abstract*---**Soft tissue enlargement of the oral cavity usually existent a diagnostic challenge because many group of pathologic activity can cause these lesions. An enlargement may display a variation of normal anatomic structure, cyst, inflammation, developmental anomalies and neoplasm. These lesions included a group of reactive hyperplasia which arises in response to recurring; chronic tissue injury that provokes vigorous or extreme tissue repair response .so pyogenic granuloma is one of the many common entities in charge of soft tissue enlargement. Objective: The current study aimed to detect the immunohistochemical expressions of ER and alpha smooth muscle actin (α-SMA) for lobular capillary hemangioma (pyogenic granuloma). Material and Methods: fifty cases of confirmed diagnostic pyogenic granuloma were subjected to immunohistochemically assessment by using ER marker and Smooth Muscle Actin marker. Result: The immunohistochemically finding appeared that all 50 cases were positive for SMA marker while only 14 cases were positive for ER marker. So there is no significant difference between ER marker in relation to clinical parameters (age, gender and location) and intensity. Conclusions: High expression rate of Smooth Muscle actin in pyogenic granulomas so it can be regarded as highly sensitive diagnostic marker, so it's useful to use this marker for diagnosis of pyogenic granuloma. The positive result of ER marker may affect the treatment choice.

***Keywords*---**Pathogenesis, expression, diagnosis, tissue specimen.

Introduction

Pyogenic granulomas are small, elevated, and red humps on the skin. The humps have a wet smooth surface. They bleed easily due to the higher number of blood

vessels at this area [1]. It is a noncancerous (benign) thickening. Medicals terms for this conditions is lobular capillaries hemangioma [2]. People used to refer to pyogenic granulomas as an exaggerate granulomatous reactions to an infections or pyogenic insult, hence the term granuloma pyogenic and pyogenic granuloma. Even so, this nomenclature is misleading [3,4]. Several factors have been linked to the etiopathogenesis of this condition, but the exact etiology has yet to be determined. Several research on signal transduction pathways and particular angiogenic factors have been unsuccessful in identifying a single cause in the lesion's development [5]. Pyogenic granuloma can occur in people of all ages [6]. There are different reports about the diseases epidemiological pattern [7,8]. The prevalence peaked in the 2nd decade of life, with some studies indicating a slight male preponderance. [9]. Females were more likely than males to have mucosal lesions in their fourth decade of life. Another study discovered a male-to-female ratio of 1:1.2. [10]

Material and Methods

The study was conducted at the Department of Pathology and Forensic Medicine/Faculty of Medicine/University of Kufa. Immunohistochemistry was carried out in paraffin –embedded tissue specimen. This study included (33) women, (17) men, the cases collected from different location of oral cavity. The immunohistochemically procedure used in this study includes dewaxing of formalin fixed paraffin embedded tissue followed by 2 changes in xylene then rehydration in decreased grade of alcohol. Then use diluted retrieval solution and place the jars in heated water bath. Let the slides cool and then wash with wash buffer before and after adding the peroxidase blocking reagent. Primary antibody now is added and incubate for ½ hour to 24 hours then washed with wash buffer. The next step is incubation with HRP for ½ hour, then wash with wash buffer. The following step is incubation with chromogen for 15 minutes then washed with distill water, and incubation with hematoxylin then distill water for washing. Dehydration, xylene then cover the slides.

Results

Age, Gender and Site Distribution of Studied Samples.

In the present study, paraffined blocks of fifty patients with oral pyogenic granulomas were evaluated and Age, Gender and Site distribution of patients were presented in Table 1.

Table 1: Age, Gender and Site Distribution of Studied Samples.

		Sites					**Total**
		Buccal mucosa	**Gingiva**	**Lips**	**Palate**	**Tongue**	
Age	<34 years	9 (18%)	6 (12%)	4 (8%)	2 (4%)	4 (8%)	25 (50%)
	≥34 years	4 (8%)	4 (8%)	5 (10%)	2 (4%)	10 (20%)	25 (50%)
Gender	Female	7 (14%)	7 (14%)	6 (12%)	2 (4%)	11 (22%)	33(66%)
	Male	6 (12%)	3 (6%)	3 (6%)	2 (4%)	3 (6%)	17(34%)
Total		13	10	9	4	14	50 (100%)

ER Expression According to Sites

The results declared that immunostaining of ER was accumulated in the nucleus of diseased cells. ER recorded in (14 cases out of 50) (28%) and (36 out of 50 cases), (72%) was negative for ER. Assessment of ER expression in pyogenic granuloma from different sites revealed that, palate (3 out of 4 cases), (75%) were negative for ER marker, only (1 out of 4), (25%) were positive. Lips (5 out of 9) (55.6 %) were negative and (4 out of 9), (44.4%) were positive, gingiva (8 out of 10), (80%) were negative only (2of 10) (20%)were positive, buccal mucosa (11out of 13),(84.6%) were negative while only (2 out of 13) (15.4%)were positive , tongue (9 out of 14), (64.3%) were negative and only (5 out of 14)(35.7%) were positive .The expression of ER marker did not significantly differ among various sites (p>0.05), (table 4.4).

Table 2: Relation. Between ER Expression and Sites of Lesion in Studied Samples.

		ER		Total	P
		Positive (n=14), No. (28%)	Negative (n=36), No. (72%)		
Site	Buccal m	2 (15.4%)	11 (84.6%)	13 (100%)	0.6
	Gingiva	2 (20%)	8 (80%)	10 (100%)	
	Lip	4 (44.4%)	5 (55.6%)	9 (100%)	
	Palate	1 (25%)	3 (75%)	4 (100%)	
	Tongue	5 (35.7%)	9 (64.3%)	14 (100%)	

ER Expression According to Age Group and Gender

Assessment of age group in ER expression revealed that (7), (28%) were positive and 18 (72%) were negative in both age group (<34years) (≥34 years), that's mean the expression of ER marker did not significantly differ among age group (p value >0.05).

The assessment of gender in ER expression revealed that 9 (27.3%) were positive and 24 (72.7%) were negative in female, while 5 (29.4%) were positive and 12 (70.6%) were negative in male. There were no significant differences between ER expression with age and gender (p value > 0.05) (**Table** 4.5).

Table 3: Relation Between ER Expression with Age and Gender in Studied Samples.

		ER		**Total**	**P**
		Positive (n=14)	**Negative (n=36)**		
Age group	<34	7 (28%)	18 (72%)	25 (100%)	0.99
	≥34	7 (28%)	18 (72%)	25 (100%)	
Gender	Female	9 (27.3%)	24 (72.7%)	33 (100%)	0.9
	Male	5 (29.4%)	12 (70.6%)	17 (100%)	

Smooth Muscle Actin Immunohistochemical Expression

The results clarify that immunostaining of SMA was accumulated in the cytoplasim of diseased cells. SMA recorded in (50 cases out of 50) (100%) and no case was negative for SMA stain.

SMA Expression According to Age, Gender and Site of Disease

Assessment of age group in SMA expression revealed that (25) (100%) were positive and (0) (0%) were negative in both age group (<34years) (≥34 years), that is, SMA expression did not significantly differ by age group (p value NA).

The assessment of gender in ER expression revealed that (33) (100%) were positive and 0 (0%) were negative in female, while 17(100%) were positive and 0 (0%) were negative in male .There were no significant differences between SMA expression and gender (p value NA). (Table 4.8). Assessment of SMA expression in pyogenic granuloma from different sites revealed that , palate (0 out of 4 cases)(0%) were negative for SMA marker , (4 out of 4)(100%) were positive .

Lips (0 out of 9)(0%) were negative and (9 out of 9)(100%) were positive , gingiva (0 out of 10)(0%) were negative , (10 of 10) (100%)were positive , buccal mucosa (0out of 13)(0%) were negative while (13out of 13) (100%)were positive , tongue (0 out of 14)(0%) were negative and only (14 out of 14)(100%) were positive. The expression of SMA marker was not different between various sites (p Value NA) (table 4.8)

Table 4: Relation between SMA Expression with Age, Gender and Sites in Studied Samples.

		SMA		Total	P
		Positive (n=50)	Negative (n=0)		
Age group	<34	25 (100%)	0 (0%)	25 (100%)	NA
	≥34	25 (100%)	0 (0%)	25 (100%)	
Gender	Female	33 (100%)	0 (0%)	33 (100%)	NA
	Male	17 (100%)	0 (0%)	17 (100%)	
Site	Buccal m	13 (100%)	0 (0%)	13 (100%)	NA
	Gingiva	10 (100%)	0 (0%)	10 (100%)	
	Lip	9 (100%)	0 (0%)	9 (100%)	
	Palate	4 (100%)	0 (0%)	4 (100%)	
	Tongue	14 (100%)	0 (0%)	14 (100%)	

Discussion

Pyogenic granulomas are a common vascular tumor. Trauma, infection, drugs, or pregnancy-related hormonal changes can cause pyrogenic granulomas [1]. Immunohistochemically detection of estrogen receptor and angiogenesis markers are considered as a most important diagnostic way for pyogenic granuloma .so in this research we investigated the immunohistochemically detection rate of estrogen receptor and smooth muscle actin were done to determine the sensitivity of such markers. Moreover, the correlation of collected data assuming different clinicopathological parameters regarding age, site and gender in the presented

patients was done in an attempt to find any correlated diagnostic significance between these markers in pyogenic granuloma in relation to clinicopathological Parameters.

Clinicopathological Analysis

Age Distribution

The age range throughout this study was 3-80 years, which was consistent with previous study which ranged from 3 to 84 years [3,11].

The average age in this study was 34 years, which was similar to the average age of presentation in other studies 31–35 years [3,4,11]. But compared to Epivatianous A. was 46.3 years [12]. So, the mean age for included patients was close for peoples in other regions.

Gender Distribution

The current study found a 66 % female predominance, which is consistent with others researches, record the 62.96– 77% [13]. However, certain study have reveals only slight predilection 55–58% of female [4,5]. Pyogenic granuloma was significant in females with the upper gingivae (50.23%) [14].

The hormonal influence on the vasculature is thought to be the reason for the preference for females and patients in their younger age groups [15]. Females were more susceptible among the patients previously analyzed [16].

Site Distribution

In this study, (28%) of cases were taken from tongue, (26%) were from buccal mucosa, (20%) were from gingiva, (18%) were from lips and (8%) were from palate. Gingiva is common site of oral pyogenic granuloma, about 75% of the cases. It can also appear as a pedunculated, elevated, or sessile tumor with a lobulated or smooth surface that is occasionally ulcerated on the tongue, buccal mucosa, and lips. Pyogenic granulomas are most frequent in the maxillary area (anterior), primarily on the facial gingiva's aspect [9,15]. The gingiva is the most common site for pyogenic granuloma, according to the majority of studies. Current study found 20% of the gingiva cases, which was significant lower than in other studies. Al-Khiateeb [13], Lawyoin [3]**,** Vilmann [17] and Shraavana [11] revealed 44.4%, 74%, 76%, and 83%, respectively.

ER Immunohistochemical Expression

In this study, In Pyogenic granuloma, ER expression was not significantly higher. Estrogen receptor expression in Pyogenic granuloma was positive of 14(28%) cases and negative for 36 (72%) patient samples.

These results are much higher than those reported by other reports. Although, Estrogen may play a role in the pathogenesis of pyogenic granuloma that isn't detected by receptor expression; estrogen stimulates the production and signaling of growth hormone [18]**.** This sex hormone promotes neovascularization, which facilitates tumor growth [19].

Demir *et al.* show that ER expression is positive in pyogenic granuloma, implying that estrogens may play a role in the progression of pyogenic granuloma during pregnancy [20]. According to a current study, the steroid hormone receptors absence have not rule out a hormonal function in the development of these lesions [20]. The number of cases in the current study is one of the study's

limitations. The findings didn't show a relation between receptor expression and pathogenesis of pyogenic granuloma. Immunohistochemically protocol have been reported to given negative results in patients with low ER expression levels because they are below the immunohistochemically detection threshold [20]. As a result, it's possible that this study didn't have enough power to use immunohistochemically methods. Additionally, even though pyogenic granulomas were likely to display growth hormone receptors, this observing may be an association, and not physiologically relevant.

SMA Immuonhistochemical Expression

Our research had shown that 100% of studied cases (50 out of 50 cases) were expressing smooth muscle actin in their histological section. These discrepancy of reported rates of SMA expression may be due to differences in applied scoring criteria for the analysis of SMA expression. Many of cases 48% were exist with moderate (score +2) SMA expression. These results clarify that there were no significant association between SMA expression and site of pyogenic granuloma.

Conclusions

High expression rate of Smooth Muscle actin in pyogenic granulomas so it can be regarded as highly sensitive diagnostic marker, so it's useful to use this marker for diagnosis of pyogenic granuloma. The positive results of ER marker, such result may affect the treatment choice.

Acknowledgments

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