Clinicopathological analysis of 80 cases of oral lobular and non lobular capillary hemangioma (pyogenic granuloma): A Retrospective study

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Abstract: Background: Oral pyogenic granuloma (PG) is a clinicopathological entity that could develop due to the reaction to a variety of stimuli, such as low-grade local irritation, traumatic damage, and hormonal stimulation. There are two histopathological types of pyogenic granuloma; lobular type -capillary hemangioma (LCH) and non-lobular type; with PG,LCH has highly vascular, diffuse capillary growth while non- lobular variant mimicking granulation tissue with heavily inflamed stroma. The study aims were to review the clinical and histopathological spectrum of an oral pyogenic granuloma from different intraoral sites in order to avoid diagnostic pitfalls associated with similar morphological lesions and to determine whether lobular and non-lobular histopathological subtypes being distinct entities.

Materials and Methods: A retrospective review of eighty formalin-fixed paraffin-embedded tissue blocks (40 cases each of males and females) were retrieved from the archives of Oral & Maxillofacial Pathology at the University of Baghdad, from 1979 to 2017. According to Mills et al., criteria for lobular capillary hemangioma description, the diagnosis of each case was confirmed by the examination of Hematoxylin and Eosin stained sections by an expert pathologists.

Results: The present result revealed that patients with oral pyogenic granuloma were with age range from 12 to 59 years, with a mean of 30.57 years. Forty nine cases (61.25%) out of eighty were of lobular pattern and 31 cases (38.7%) of non-lobular pattern type PG. The most common site of LCH was in the buccal mucosa, 12 cases (75%), while higher case numbers were observed in the 21-30 year age group. There were non-significant differences between lobular and non-lobular histopathological subtypes regarding age groups and between other studied variables.

Conclusions: It has been proposed that LCH and non-LCH subtypes reflect distinct phases in the development of a single lesion, which exhibits variable degrees of proliferative, angiogenic, and inflammatory activities.

Keywords: Lobular capillary hemangioma, pyogenic granuloma, Oral cavity, histopathological differences.

Introduction

Pyogenic granuloma (PG) is a relatively frequent type of vascular growth on the mucosal surface epithelium and skin. For the first time in 1904, Hartzell used the word “pyogenic granuloma” which is a misleading phrase since the lesion does not contain pus, as the name suggests (1,2). The oral Pyogenic granuloma is a clinicopathological entity that could result from the tissues reaction to a variety of stimuli such as low-grade local irritation, traumatic damage, and sex hormones. It is a painless growth comonly occurs in maxillary gingival area, particularly on the gingiva’s labial side as well as; the prebence incidence for the pregnant female, tumor that sometimes grows at an accelerating rate. Lesions are more prevalent intra-orally in the anterior and younger age groups, are believed to be due to a hormonal impact on the vasculature. However, a few infections, such as Bartonella henselae, have been linked to recurring pyogenic granuloma(3). Oral PG is described clinically as a solitary soft mass that may be smooth or lobulated, sessile or nodule-like, or it can be a pedunculated growth. The color of the lesion varies from

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pink to red that changes according to its vascularity and tumor progression. There may be some blood
flowing spontaneously or as a result of a trauma\(^2,4\).

Two common histopathological variants of PG were reported in previous studies. The first variant
consists of lobular architecture including several small-sized capillaries lined by plump endothelial sep-
ated by fibrous septa with a paucity of the inflammatory stromal cells called lobular-capillary heman-
gioma (LCH). Non-lobular type PG (non-LCH) is the second histopathologic type characterized by
highly vascular, diffusely arranged capillary proliferation resembling granulation tissue with heavy in-
flammatory stroma\(^5,6\). Numerous studies have previously investigated the clinicopathologic and immu
nopathological characteristics of PG, but distinctions between PG’s two histological variants are
uncommon.

To avoid diagnostic pitfalls associated with similar morphological lesions and to determine whether
lobular and non-lobular histopathological subtypes are two distinct entities, the study aims were to re-
view the clinical histopathological spectrum of an oral pyogenic granuloma from different intraoral sites.

**Materials and Methods**

A retrospective review of eighty formalin-fixed, paraffin-embedded tissue blocks reported as pyo-
genic granuloma of the oral cavity were retrieved from the archives of the department of Oral & Maxil-
lofacial Pathology/College of the Dentistry/University of Baghdad; from 1979 to 2017. Clinical and De-
mographic data, including the patient’s age, gender, and intraoral site of occurrence of PG, were ob-
tained from the relevant histopathological reports that were available with the tissue specimens. Ac-
cording to Mills, et al., 1980 criteria for lobular capillary hemangioma description, the diagnosis of each
case was confirmed by the examination of H & E sections by an expert pathologists. The statistical anal-
ysis was performed as follows: SPSS Version 23 was used to perform statistical analysis. A chi-squared
test was applied to test statistical differences. Differences between studied variables were set as not sig-
nificant P>0.05, significant P≤0.05, or highly significant (P≤0.01).

**Results**

A total of eighty cases (40 cases of males and 40 cases of females) of oral pyogenic granuloma were
evaluated. The age ranges of patients with oral PG were from 12 to 59 years, with a mean age of
30.57 year. There were no significant differences in the mean age of patients with PG between males
(29.77 years) and females (31.37); Figure (1). Regarding the site, in the present study, equal numbers
were collected in both males and females (16 cases from each: gingiva, buccal mucosa, tongue, palate,
lips). Histopathological study of oral pyogenic granuloma cases revealed that 49 cases (61.25%) out of 80
were of lobular pattern, and 31 cases (38.7%) out of the 80 were of non-lobular pattern type PG. The
higher number of cases and percentage of lobular pyogenic granuloma cases were detected in females,
25 cases (62.5%), at a young age (less than 15 years old and age (30-40) receptively, 10 cases (83.33%),
and the most common cases were in the buccal mucosa12 cases (75%) While the number and of cases
percentage of non-lobular pyogenic granuloma cases showed higher case numbers in the 21-30 years of
age group, 12 cases (66.67%), and higher cases of non-LCH occurred in the palate, 9 cases (56.25%)
There were non-significant differences between lobular and non-lobular pattern prevalence regarding age groups, gender; Table (1). Microscopically, both groups had two distinct components: an ulcerated surface and a deep section. In both groups, the ulcerated surface was equivalent, consisting of inflammatory granulation tissue covered by a fibrinopurulent membrane. The deep part of the LCH group had lobular zones of tiny capillaries lined by plump endothelial cells separated by fibrous stroma with little or no inflammatory cell infiltration; Figures (2,3). The non-LCH type pyogenic granuloma in the deep part showed many dilated capillaries with a dispersed pattern comparable to that of the granulation tissue, which was more infiltrated by chronic inflammatory cells than the LCH type figures (4, 5).

**Table (1):** Demographic description of studied cases (lobular and non-lobular pyogenic granulomas) concerning gender, age, and intraoral sites.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Lobular</th>
<th>Non-lobular</th>
<th>Total</th>
<th>P-value</th>
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<tr>
<td>Gender</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>24(60%)</td>
<td>16(40%)</td>
<td>40</td>
<td>0.818</td>
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<tr>
<td>Females</td>
<td>25(62.5%)</td>
<td>15(37.5%)</td>
<td>40</td>
<td>ns</td>
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<tr>
<td>Age groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤15</td>
<td>10(83.33%)</td>
<td>2(16.67%)</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>16-20</td>
<td>10(66.67%)</td>
<td>5(33.33%)</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>6(33.33%)</td>
<td>12(66.67%)</td>
<td>18</td>
<td>0.097ns</td>
</tr>
<tr>
<td>31-40</td>
<td>10(71.43%)</td>
<td>4(28.57%)</td>
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<td>41-50</td>
<td>7(58.33%)</td>
<td>5(41.67%)</td>
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<tr>
<td>&gt;50</td>
<td>6(66.67%)</td>
<td>3(33.33%)</td>
<td>9</td>
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<tr>
<td>Site</td>
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<tr>
<td>Gingiva</td>
<td>9(56.25%)</td>
<td>7(43.75%)</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Palate</td>
<td>7(43.75%)</td>
<td>9(56.25%)</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Lip</td>
<td>11(68.75%)</td>
<td>5(31.25%)</td>
<td>16</td>
<td>0.477ns</td>
</tr>
<tr>
<td>Tongue</td>
<td>10(62.5%)</td>
<td>6(37.5%)</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Buccal mucosa</td>
<td>12(75%)</td>
<td>4(25%)</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>49(61.25)</td>
<td>31(38.75)</td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

χ² test, P<0.05 was selected to improve significant differences
Figure (1): mean age of studied patients Independent t-test, ns = non-significant

Figure (2-A): Photomicrograph lobular

Figure (2-B): Photomicrograph lobular PG 10x

Figure (3-A): Photomicrograph lobular PG 40x

Figure (3-B): Photomicrograph lobular PG 40x
Discussion

Because the oral mucosa is continuously being influenced by external and internal factors, which could be lead to developmental disorders, irritants, inflammatory responses, as well as benign and/or malignancies. These lesions mimic benign and/or malignant clinically. Early identification and treatment of such lesions by clinicians may minimize dentoalveolar consequences.

This better understanding could help practitioners improve diagnoses and provide appropriate management (7). Pyogenic granuloma is a vascular growth that occurs quite often on the mucosal surface epithelium and subcutaneous tissue. The term granuloma pyogenicum (pyogenic granuloma) was coined by Hartzell in 1904; while in 1980, the name "lobular capillary hemangioma" (LCH) was published as the synonym for pyogenic granuloma according to histological characteristics (5,8).

The prevalence of oral PG varied across investigations, ranging from 1.85 percent to 37 percent of reported oral lesions in previous research (9). The clinicopathological findings of the present study revealed that the mean age for the occurrence of pyogenic granuloma was 30.57 years, and a higher number of cases and percentage of lobular pyogenic granuloma cases were detected in females, 25 cases (62.25%). These findings concur with previous studies (10,11). This may reflect a hormonal impact on mucosal lesions (10,12,13). The gingiva was found to be the most often seen intraoral site of PG incidence. Following common sites intraorally were the lips, tongue, buccal mucosa, and palate (13).
Although our study involved 16 cases from the gingiva, buccal mucosa, lips, tongue, and palate equally. As well as for both genders. The most striking histopathological feature was detected in all examined oral PG cases was the presence of significant capillary development inside the hyperplastic granulation tissue, indicating the presence of robust angiogenic activity in both histological subtypes (lobular and non-lobular). The histological types of PG have been studied in many prior clinicopathological investigations, some of which included both LCH and non-LCH histopathological subtypes. Some of these studies have shown clinical, histological, and immunohistochemical distinctions between LCH and non-LCH PG. which agrees partially with our study findings that showed statistically clinicopathological differences between lobular and non-lobular subtypes. However, this study did not include immunohistochemical (IHC) makers to support our results. Even though immunohistochemistry may help exclude some alternative diagnoses and identify growth features, no immunohistochemical marker was specific for LCH, and diagnosis is often made using morphologic criteria.

In addition, it is still not obvious how the many etiological factors contribute to the various histological types of PG. Accordingly, The oral PG may appear differently, creating a diagnostic challenge for the treating surgeon. As a consequence of an overactive tissue repair reaction, it's a begin vascular tumor. The diagnosis is confirmed by a histopathological assessment, which also excludes out other soft tissue lesions that seem similar. The most significant differential diagnoses are as follows: Hemangioma, peripheral giant cell granuloma, peripheral ossifying fibroma, Hodgkin’s lymphoma, and conventional granulation as well as, for capillary-type vascular tumors.

The presence of giant cells or scattered ossifications inside the tumor stroma assists in ruling out peripheral giant cell granuloma, peripheral ossifying fibroma, or both to rule out are Kaposi sarcoma and low-grade angiosarcoma. Lobular capillary hemangioma endothelial cells may be somewhat spindle. However, in Kaposi sarcoma, the spindle cells are elongated and organized in a slit-like pattern, forming pseudo-vascular blood-filled areas. Unlike capillary hemangioma and its variations, Kaposi sarcoma lacks conspicuous endothelial cells. Human herpesvirus type 8 (HHV8) has been detected in Kaposi sarcoma and, if present, may help confirm the diagnosis, Additionally, nuclear atypia and pleomorphism are required for the diagnosis of angiosarcoma. While mitotic figures may be observed throughout the proliferative phase of lobular-capillary hemangioma in children and adults, the mitotic index is much increased in angiosarcoma, and the mitoses often take on unusual configurations. Neither angiosarcoma nor Kaposi sarcoma has an overall lobular architecture; rather, they develop infiltrating.

The preferred method of cure is surgical excision. After surgical excision, recurrence is very uncommon. According to the results, this study proposed that LCH and non-LCH subtypes reflect distinct phases in the development of a single lesion (PG), which exhibits variable degrees of proliferative, angiogenic, and inflammatory activities. Our suggestion is the usage of the descriptive term "lobular capillary hemangioma" as a suitable alternative term (PG) in the oral cavity. Further research with larger sample size and molecular methods is suggested to confirm or refute this study assumption.

Conflict of interest: None.
References


التحليل السريري المرضي لـ 80 حالة من الشعيرات الدموية الفموية المصصية وغير المصصية ورم وعائي (ورم حبيبي قيحي): دراسة بأثر رجعي

كارار ناجح شريف (1) ، بشار حامد عبدالله (2)

المستخلص:

التحليل السريري المرضي الالكلينيكي لـ 80 حالة من الورم الوعائي الحبيبي الشعري المفصص في الفم (ورم حبيبي قيحي): دراسة بأثر رجعي العلقي: الورم الحبيبي القصحي المصص (PG) هو كيان إكلينيكي يمكن أن يتطور بسبب تفاعل الأنسجة مع مجموعة متنوعة من المحفزات مثل التهيج المناعي والاضطرابات المناعية والتهاب التهابي. هناك نوعان من الورم الحبيبي القصحي - النوع المفصص (PG) - الورم الوعائي LCH - النوع غير المفصص PG.LCH. في الورم الحبيبي القصحي LCH، الورم الوعائي يتم التعبير عنه في بعض الحالات كورم حبيبي قيحي في الفم. الورم الحبيبي القصحي PG له تطور حيوي متغير والتشخيص مع وجود تفاعلات مع الأنسجة الأخرى. الورم الحبيبي القصحي PG مرتبط بالورم الوعائي LCH غير المصص.

المادة والطرق العمل: تم تجميع 80 عينة من الخلايا المثلثية المجموعة في كلا الجنسين من أرشيف أمراض الفم والوجه والفكين في جامعة بغداد من الفترة 1979 إلى 2017. تم تقييم الخلايا المثلثية المجموعة في كلا الجنسين باستخدام تقنيات الميلز بأطراف معينة للورم الحبيبي القصحي PG/LCH.

النتائج: المرضى الذين يعانون من الورم الحبيبي القصحي PG/LCH تتراوح أعمارهم من 12 إلى 59 سنة، بمتوسط 30.57 سنة. من الناحية العددية، 61.25% من النمط الفصيصي، في حين أن 38.7% من النمط غير الفصيصي. الأورام الأكثر شيوعًا في الفئة العمرية 21-30 عامًا، حيث تم الاكتشاف في أكثر من 80% من الحالات.

الاستنتاجات: ينصح بإجراء المزيد من الدراسات الجد لتحديد الأسباب والعوامل المضافة في تطور الورم الحبيبي القصحي PG/LCH. عملياً، يتطلب الدراسة المزيد من الأبحاث لفهم الطبيعة المتغيرة في الورم المفصص وغير المفصص.