

## Overview of Oral Pyogenic Granuloma

Ashwag S. Noorsaeed<sup>1</sup>, Mohammed A. Al Moslem<sup>2</sup>, Sarah Z. Alghanem<sup>2</sup>, Zuhair M. Al-Khowildi<sup>2</sup>, Hassan A. Alshaban<sup>2</sup>, Zahra H. Alzayer<sup>3</sup>, Ahmed H. Alramadhan<sup>2</sup>, Nour T. Almarhoun<sup>2</sup>, Aamena M. Algheryafi<sup>2</sup>, Hussain Z. Alshakhori<sup>2</sup>, Fahad Hadi A Hadadi<sup>4</sup>.

<sup>1</sup>Consultant Restorative Dentist, KSA.

<sup>2</sup>General dentist, ministry of health, eastern health cluster, KSA.

<sup>3</sup>King Abdullah Hospital, Bisha, Aseer region, KSA.

<sup>4</sup>General dentist, ministry of health, Jazan health affairs, KSA.

### ABSTRACT

A benign vascular tumor is characterized as a pyogenic granuloma (PG), also referred to as a lobular capillary hemangioma. It develops as a result of cutaneous or mucosal inflammation-induced hyperplasia. Its name is misleading because it neither has anything to do with pus generation nor is it histologically made up of real granulomas. The development of PG's neoplastic tumor is thought to be a response to a variety of stimuli, including prolonged localized inflammation, trauma, hormonal effect, and medications. Poor oral hygiene is thought to be the leading cause of its frequent appearance in the oral cavity. Oral PG affects people of all ages, from 4.5 to 93 years old, however, it most frequently affects women than men in their second and fifth decades of life. After the hard plate, the lips, tongue, buccal mucosa, and gingiva were the most common sites. The frenum, tongue, lips, tongue, and palate were additional locations. It can manifest intraorally in a variety of clinical ways, from a sessile lesion to a raised mass. Techniques used for treating oral PG are many and the choice of the appropriate strategy depends on many factors such as the severity of the case.

**Keyword:** pyogenic granuloma, lobular capillary hemangioma, vascular tumor, mouth lesion.

### Introduction

Enlargement of the soft tissues located within the oral cavity frequently provides diagnostic difficulties since they can be caused by a wide range of pathologic diseases. An expansion can be caused by neoplasms, inflammation, cysts, developmental defects, or many types of normal anatomical structures. When a prolonged tissue injury triggers an excessive tissue healing response, reactive hyperplasias develop, which are a subset of these lesions. One of the most typical conditions that result in the enlargement of the soft tissues is pyogenic granuloma [1]. A benign

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**Address for correspondence:** Ashwag Siddik Noorsaeed, Consultant Restorative Dentist, SCFHS Number: 08JD0028070, KSA.

**E-mail:** [ashsns@hotmail.com](mailto:ashsns@hotmail.com)

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About 3.81% to 7% of all biopsy results from lesions of the oral cavity contain oral pyogenic granuloma [4, 5]. Although the lips, tongue, buccal mucosa, and palate can also develop lesions, the gingiva is the most common intraoral location. The best course of treatment is conservative local excision, which has a recurrence rate of 0% to 16%. [6, 7]. It manifests as an inflammatory, pain-free growth of skin or mucous membrane, or as a localized, pedunculated, pleomorphic mass. The gingiva is the most typical intraoral location (almost 75%), however, it can also affect the lips, mucosa, and tongue [8-10]. It primarily affects the mucosal surface of females with elevated levels of steroidal hormones. Female sex hormones are usually thought to be key players in its etiology [11]. A "capillary lobular hemangioma" is referred to histologically when capillary vessels are found to be organized into granulomatous tissue lobes that are encircled by a thin collagen band; however, a "non-lobular capillary hemangioma" is referred to when vascular formations are interconnected in the tissue without obvious order [12]. A study conducted by Saravana [13] In India that included 137 cases diagnosed with oral pyogenic granuloma, showed a strong correlation between socioeconomic and cultural factors and the degree and severity of periodontal disease and gingivitis [14, 15]. Where Dental health appears to be improved by better post-periodontal medication adherence, oral treatment, and awareness. Additionally, the majority of the patients (77% of them) were females. This may be due to the effects of female hormones, whereas other writers only note a modest female inclination (55–58%) [16, 17]. According to the majority of research, the gingiva (83%) was the site most frequently afflicted by this illness. Analyzing 293 cases in a Brazilian population once more [18] revealed that, there was a preference for women, and the ratio of women to men was 2.38:1. The patients were 27 years old on average. The 20th of life showed a significant degree of incidence. The majority of the affected patients (44.7%) were white. The gingiva (83% of the time) was most frequently affected, with the maxilla having a higher incidence. The lesions were categorized as nodules in the majority of instances (73.2%), with layer shapes (62.3%) and a red appearance (71.9%) that also showed bleeding. 8.2% of the cases were reoccurring. Comparable to those seen in investigations of individuals from other nations, the clinical, demographic, and pathologic aspects of oral pyogenic granuloma in the Brazilian population were present., according to all the data that have been mentioned so

far, almost the same results were shown by a study conducted in Jordanians for 108 Cases [19].

### **Epidemiology and etiology**

Although PG can affect anyone at any age, it is most common in young adult females in their probably due to the vascular effects of female hormones, in the second decade of life. This conclusion was supported by studies conducted in Jordanian [20] and Singaporean [21] populations. The peak incidence of occurrence, however, was discovered to occur in the sixth decade of life, according to a recent study. With a mean age of the patient of 52 years [22]. According to some authors, the majority of patients are men under the age of 18, women between the ages of 18 and 39, and elderly patients who are equally split between the sexes. In their investigation, Bhaskar et al. discovered that, excluding caries and gingivitis, About 1.85% of all oral illnesses treated at the US Army Institute of Dental Research were oral pyogenic granuloma [23]. Only 42 out of the total 757 instances were related to pregnancy, according to Daley et al [24]. Oral pyogenic granuloma is reportedly a rather frequent condition. In children, it accounts for 0.5% of all cutaneous nodules. Up to 5% of pregnancies may result in the development of the pyogenic granuloma pregnancy tumor subtype. If you exclude caries, periodontal disease, and periapical inflammatory disorders from your list of oral lesions, Esmeili et al. claim that hyperplastic reactive lesions are the most common oral lesions overall. Peralles et al. discovered that oral pyogenic granuloma and inflammatory gingival hyperplasia were the most frequent diagnoses in their clinicopathologic investigation of gingival and alveolar hyperplastic lesions. In the south Indian population, oral pyogenic granuloma represented 52.71 percent of the 244 gingival lesions, making it the most common lesion. 75.5% of cases were non-neoplastic lesions [25]. Although most experts believe that PG is a benign neoplasm, they generally believe that it is a reactive tumor-like lesion that arises in response to a variety of stimuli, such as prolonged low-grade local irritation, trauma, and hormonal factors [26], or specific types of medicines [27]. Although it was formerly considered to be brought on by pyogenic microbes, new theories suggest that it has no link to the infection. Due to the absence of pus and is not truly a granuloma, the phrase "pyogenic granuloma" is inaccurate. It's critical to remember that infectious agents have been identified, including Bartonella henselae, B. henselae, human herpes virus type 8, and bacillary angiomatosis. However, there is no proof indicating the existence of infectious agents in bigger

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PG groupings [28]. A few medications, including cyclosporine, also play a significant part in the development of PG. Patients receiving cyclosporine reported having 4 cases of oral PG were described by Bachmeyer et al [29] and Lee et al [30]. Additionally, various iatrogenic stimuli in dentistry practices may result in PG. The first case in which PG was connected to tissue regeneration was reported by Fowler et al [31]. Following bone marrow transplantation (BMT), oral problems can arise as a result of infections or the preoperative regimen's toxicity relates to the regimen. Even though oral granulomatous lesions following BMT are uncommon, Kanda et al [32] documented a patient who had one in their tongue after BMT. This lesion has a history of prior trauma, which is not uncommon, particularly for extralingival PGs, where about one-third of lesions do. For many of these people, poor dental hygiene may be a risk factor [33]. Both Aguilo [34] and Milano et al [35] revealed cases of PG connected to aberrant tooth formation. Aguilo [34] explained how PG occurred after a primary tooth was injured. Connective tissue growth factor and vascular endothelial growth factor [36], inducible nitric oxide synthase are among the compounds known to contribute to angiogenesis and the rapid development of PG. Based on the discovery that pregnancy tumors in pregnant women similarly arise from the gingiva and have a similar microscopic appearance, Yung, Richardson, and Krotovich hypothesized a hormonal role [37]. According to clinical data, gingiva may expand throughout pregnancy and atrophy following menopause, according to Hosseini et al. Based on these findings, another "target organ" for the direct effects of progesterone and estrogen is the gingiva [38]. According to a study by Whitaker et al., in oral pyogenic granulomas, the quantity of estrogen or progesterone receptors is not what produces them. Instead, the quantities of circulating hormones may have this role. Ojanotak-Harri et al. have shown that pregnancy inhibits the migration of fibroblasts and inflammatory cells. Thus, it would appear that pregnancy controls both progesterone metabolism and the movement of inflammatory cells inside the tissue. Pregnancy-related gingivitis and granuloma development may be influenced by the amount the "dysfunction" of the inflammatory cells and the active form of progesterone that is present. They proposed that the coexistence of the two elements prevents the acute kind of tissue reaction to plaque which is necessary for keeping the tissues healthy but permits an amplified chronic reaction that clinically manifests

as inflammation that is more pronounced than it is [39].

### Diagnosis

PG comes in 2 histological varieties. Even if the lesion normally does not change in any particular way, such as edema or inflammation of the tissue, the first type is distinguished by developing blood vessels that are grouped in lobular aggregates. The term "lobular capillary hemangioma" (LCH type) was used to describe this histological type of PG [40]. In contrast, the "non-LCH type" describes highly vascular proliferation that resembles granulation tissue. LCH PG is known for having more blood vessels with a narrow diameter of the lumen than in the heart of the non-LCH PG. This variance suggests that there are two distinct histological types of PG. According to Toida et al [41], some pathogenic factors may have an impact on the development of blood vessels with different luminal sizes in the central region of non-LCH PG and the lobular region of LCH PG.

### Clinical presentation

Oral PG affects people of all ages, from 4.5 to 93 years old, however, it most frequently affects women than men in their second and fifth decades of life. After the hard plate, the most frequent locations were the lips, tongue, buccal mucosa, and gingiva. The frenum, tongue, lips, tongue, and palate were additional locations. It can manifest intraorally in a variety of clinical ways, from a sessile lesion to a raised mass. Generally speaking, pyrogenic granulomas are smooth, asymptomatic, and dark crimson to reddish-purple in coloration [42]. Clinically speaking, PG is a sore characterized by a smooth or lobulated form that typically appears as little, red papules on a sessile base, it is mostly subjected to compression, and causes bleeding. The two varieties of PG, according to Epivatianos et al. are clinically distinct. They found that LCH PG frequently manifested as a pedunculated lesion. (77%), nevertheless, non-LCH PG was more frequently a sessile lesion (66%). The size varies in diameter from a few millimeters to several centimeters. Rarely does PG exceed 2.5 cm in size, and it normally reaches its largest diameter within a few weeks or months before remaining there indefinitely afterward. Clinical evolution of the lesion silently, painlessly, and gradually [43, 44]. The surface is typically ulcerated and friable and depending on how old the lesion is, it can be coated in a yellow, fibrous tissue from red to purple are the range of colors the membrane could be found. Young PGs are known for being rich in blood vessels because the majority of their structure is hyperplastic granulation tissue with

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large capillaries. Because of this, slight trauma may result in significant bleeding but older lesions typically develop more collagen and take on a pink color. As described by Goodman-Topper and Bimstein, PG can occasionally result in substantial bone loss [45].

### **Microscopic investigations**

Microscopically, PG shows a highly vascular development resembling granulation tissue. [46]. Multiple channels of different sizes, surrounded by endothelial cells that are flat or protruding, some of which may be mitotically active and inflated with red blood cells, are created [47]. The blood vessels frequently have a clustered or medullary structure, and most pathologists need to see these diagnostic vessels to diagnose lobular capillary hemangioma. Low magnification reveals a lobular pattern where capillary clusters expand and then abruptly terminate. A thin collagen layer surrounds each lobule. This structure is interrupted towards the base, where larger, atypically formed circulatory channels are found and may interact with the proliferation. Another distinguishing characteristic of benign vascular lesions is revealed at higher magnification: the pericytic layer of cells surrounds the tiny capillary endothelial-lined gaps. Other features that could be seen by microscope are the scarring exhibited by the lesions indicating that occasionally the connective tissue repair process may mature. Also as the surface becomes ulcerated, it is replaced by a strong fibrin membrane and eventually a mixture of cells mainly inflammatory cells are seen near the ulcerated tissue, where also fibroblasts are noted to be more active in young cells other than old cells where fewer and more mature cells are the predominant [47]. To conclude the microscopic features we need to set that the lesion has three separate phases; lobules are dense and cellular during the cellular phase, with limited lumen development. Then it becomes vascular during the capillary phase and has an abundance of red blood cells. Finally, during the involutory phase, there is a tendency for intra- and perilobular fibrosis with greater venular differentiation [48].

### **Radiographic and immunohistochemical investigations**

Pyogenic granuloma has no radiographic abnormalities. However, it was reported that in a small number of extremely rare cases of large and chronic gingival cancers, localized alveolar bone resorption can be seen [49]. Angiopoietin-1, angiopoietin-2, ephrinB2, and ephrinB4 as well as antibodies against CD34, alpha SMA, and bFGF all exhibit increased

expression of vascular morphogenesis factors. Additionally, there is an expression of inducible nitric oxide synthase, vascular endothelial growth factor, and Bax/Bcl2 protein with a low apoptotic rate. Polymerase chain reactions have not identified the human herpes virus type or the human papilloma virus [50].

### **Differential diagnosis**

The correct diagnosis is crucial for effective therapy when a mass is discovered in the mouth. The differential diagnosis is based mostly on the results of the biopsy, which plays a crucial and decisive role in making the diagnosis. Pregnancy tumors, metastatic cancer, angiosarcoma, Kaposi's sarcoma, conventional granulation tissue, peripheral giant cell granuloma, and non-Hodgkin lymphoma are the prominent differential diagnoses. Clear involvement of hormones in the pathogenesis of the lesion is indicated by the increasing prevalence of pregnancy epulis when it comes close to the end of pregnancy and the likelihood for this tumor to diminish after birth. Ojanotko-Harri et al. state that there is no clinical or histological difference between pregnancy tumors and PG that affects non-pregnant patients, while some authors believe that pregnancy tumor is typically restricted to the interdental papilla. According to Daley et al., when a PG develops during pregnancy, the diagnosis of a pregnancy tumor is valid clinically since it identifies a distinct lesion based not on histologic traits but rather on the origin, biological behavior, and course of treatment [51]. Sometimes it is impossible to distinguish PG from hyperplastic gingival inflammation histopathologically, therefore, to diagnose a granuloma, the pathologist must rely on the surgeon's description of a distinct clinical mass [52]. Some characteristics of Kaposi's sarcoma from AIDS, such as intracellular hyaline globules and growth, are not present in PG. Kaposi's sarcoma from AIDS exhibits some features which never seen in PG such as intracellular hyaline globules, and proliferation, necessitating microscopic examination of biopsy material for the first diagnosis.

### **Management**

There are numerous methods for treating oral PG, and the selection of the best one depends on many variables, including the severity of the disease. The most common treatment is surgery, which involves a conservative surgical excision and the removal of the irritants that are the cause of the irritation, such as foreign objects. It should be noted, however, that to completely remove the irritant, the excision should extend to the periosteum, and the surrounding teeth

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should be meticulously scaled. A successful alternative to surgery is laser therapy. Powell et al [53] reported on the usage of Nd: YAG laser and said that it is preferable over CO<sub>2</sub> laser due to its greater coagulation power. Due to a lower risk of bleeding, laser use is preferable over surgery. On the other hand, Meffert et al. applied a flash lamp pulsed dye laser to a non-responding mass and reported that this laser led to greater healing after several treatments. Cryosurgery is also another option proposed by Ishida and Ramos-e-Silva [54] which is considered a better option due to the smoothness and humidity of the mucosa of the mouth, but laser and cryosurgery share the problem of causing scars at the site of treatment, so another alternative which is using an injection of absolute "ethanol" tried by Ichimiya et al [55] was a more successful and less invasive one. According to Moon et al. [56], the majority of patients had their lesions eradicated with sodium tetradecyl sulfate (STS) sclerotherapy without experiencing any serious side effects. They believe that this procedure offers a better option for excision due to its simplicity and lack of a scar, despite the requirement for multiple treatment sessions. It primarily exerts its effects by disrupting artery lumina and harming endothelial cells. Care should be taken when pregnant, and treatment focuses mostly on meticulous oral hygiene, plaque removal, and the use of soft toothbrushes. If the bleeding became out of control, numerous operations should be carried out, including supportive therapy including defibrillation of bleeders, localized, firm compression, oral hygiene, blood transfusion, medicines to speed fetal lung development, and even pregnancy termination to preserve the patient's life. And if surgical intervention should be done, it must be in the 2nd trimester. Re-excision is sometimes required since up to 16% of lesions return after excision [57]. It is thought that inadequate excision, failing to remove the etiologic ingredients, or re-injuring the area are the causes of recurrence in some circumstances, the location of a recurrence may be surrounded by several deep satellite nodules. In comparison to lesions from other oral mucosal regions, gingival instances have a substantially higher likelihood of recurring.

### Conclusion

The first line of treatment for oral pyogenic granuloma is the elimination of the trigger, which might include chronic inflammation, trauma, sex hormones, some drugs, and other stressors. Due to the highest similarity between oral PG and other oral disorders, the diagnosis of this condition is crucial in determining the

therapeutic strategy. In the end, it should be noted that the recurrence of oral PG is high, so oral hygiene is important, especially during pregnancy. Surgery is the traditional management technique, but it can cause scars and is an invasive one. Other techniques such as Nd: YAG laser, flash lamp pulsed dye laser, and injection of ethanol are better choices with less invasion and better results.

### Conflict of Interest

None

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None

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