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CASE REPORT

EXTRAGINGIVAL PYOGENIC GRANULOMA: REPORT OF AN UNUSUAL CASE WITH REVIEW OF LITERATURE

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ABSTRACT:
Pyogenic granuloma is a reactive tumor-like lesion commonly affecting the oral cavity. These lesions usually appear as localized solitary nodule with a sessile or pedunculated base and color varying from red, purplish, or pink, depending on the vascularity of the lesion. Pyogenic granuloma shows predilection for gingiva and is usually slow growing, but at times it shows rapid growth. On rare occasion, it can be found extragingivally on lips, tongue, buccal mucosa, and palate which may mimic more serious pathological conditions such as malignancies. This article reports an unusual case of extra gingival pyogenic granuloma occurring on the right buccal mucosa in a male patient and discusses the features that distinguish this lesion from other similar oral mucosal lesions.
Keywords: Granuloma gravidarum, Hyperplasia, Pregnancy tumor, Pyogenic granuloma

INTRODUCTION

Pyogenic granuloma is also known as a "Granuloma gravidarum," and "Pregnancy tumor". Pyogenic granuloma represents an exuberant connective tissue proliferation to a known stimulus or injury.[1] Pyogenic granuloma is an inflammatory hyperplasia seen as a response to underlying irritating factor. The name pyogenic granuloma is a misnomer since the condition is not associated with pus and does not represent a granuloma histologically. It is a reactive inflammatory process associated with proliferating vascular channels, immature fibroblastic connective tissue, and scattered inflammatory cells. The surface usually is ulcerated, and the lesion exhibits a lobular architecture.[2]

The incidence of pyogenic granuloma has been described as between 26.8% to 32% of all reactive lesions. Although it has been reported in all age groups, it occurs mainly between the ages of 11 and 40 years, with peak incidence in the third decade. Females are more susceptible.[3] Oral sites of pyogenic granuloma can include the gingiva, lips, tongue, buccal mucosa, and palate. It is more common in the maxilla than in the mandible and in anterior as opposed to posterior areas.[4] The first case was reported in 1844 by Hullihen and the term "pyogenic granuloma" or "granuloma pyogenicum" was coined only in 1904 by Hartzell.[2]

The lesion usually appears as a localized elevated lump with a sessile or pedunculated appearance. The surface may be smooth or lobulated, and when exposed to traumatic irritation it becomes ulcerated. The color may range from pink to red or purple. The

lesion is well vascularized (hyperplastic response), with a tendency for bleeding in response to even minor injury.[3] These may be seen in any size from a few millimeters to several centimeters.[5] The course of the lesion can be described as "early," "established," and "healing" type. The color of the lesion also varies and is dependent on the vascularity of the lesion in relation to its clinical course. The early lesions are usually pinkish in color and resemble the normal mucosal color. Established lesions are reddish to purplish due to the increased vascularity whereas the late healing type presents as pinkish to whitish mass.These different phases of pyogenic granuloma can be appreciated on the microscopic level as well. The natural course of this lesion can be categorized into three distinct phases, namely, (i) cellular phase, (ii) capillary phase/vascular phase, and (iii) involutionary phase. Histopathologically, pyogenic granuloma is classified into lobular capillary hemangioma (LCH) &and non-lobular capillary hemangioma (non-LCH).[6] The purpose of this article is to report a rare case of extra gingival pyogenic granuloma occurring on the right buccal mucosa in a male and to distinguish this lesion from other similar lesions of the buccal mucosa, with special emphasis on the diagnosis and treatment of this condition.

CASE REPORT

A 50-year-old male patient reported to the Department of Oral Medicine and Radiology, Jabalpur, with the chief complaint of growth on the inner aspect of right cheek with one-year duration. History of presenting illness revealed that the growth was gradual in onset, initially small in size and has increased to attain the present size. There was also a history of occasional bleeding from the growth during chewing. The patient's medical and family histories were insignificant. The patient cleans his teeth once daily using a toothpaste and brush using a horizontal stroke. Extra oral examination showed no swelling or facial asymmetry. Intraoral examination revealed a solitary, nodular, exophytic, pedunculated growth (Figure 1). The growth was in right side of buccal mucosa extending to edentulous site on the right lower quadrant where the molars were missing. The growth measured about 2cm×2cm in dimension, which was soft to firm in consistency and bleeded on provocation. The growth was roughly oval in shape, color varied from pinkish to red, and surface was smooth. There was no evidence of pus discharge from the lesion. Regional lymph nodes were not palpable. Based on the history and clinical appearance of the lesion, provisional diagnosis of benign exophytic growth of right buccal mucosa was considered and the differential diagnosis included traumatic fibroma, pyogenic granuloma, and capillary hemangioma. The treatment procedure was explained to the patient and informed consent was obtained. Routine Blood examination revealed values within normal range. The treatment comprised of oral prophylaxis and an excisional biopsy under local anesthesia along with histopathologic evaluation. Histopathological examination of H and E stained sections showed parakeratinized stratified squamous type epithelium with numerous blood vessels, chronic inflammatory cells like lymphocytes and plasma cells in connective tissue (Figure 2.). Extravasated RBCs were also seen confirming the diagnosis of pyogenic granuloma (Figure 3). The patient was recalled after a week and the excised area was evaluated. Healing was satisfactory (Figure 4).

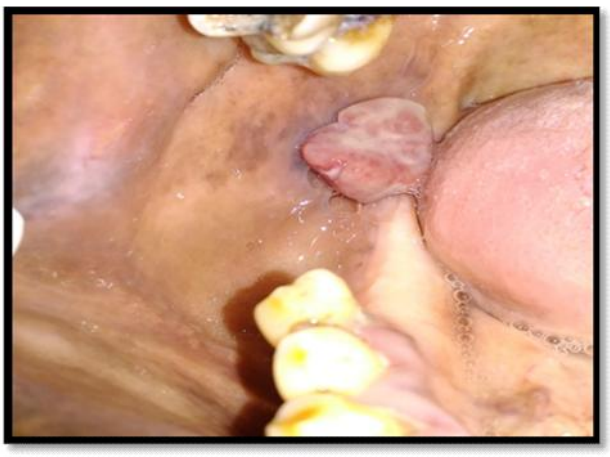

Figure 1: Solitary growth

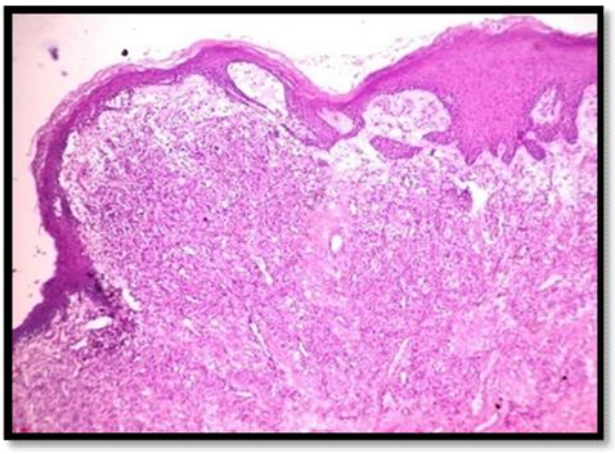

Figure 2: Showing hyperplastic parakeratinized stratified squamous epithelium overlying delicate inflammatory stroma

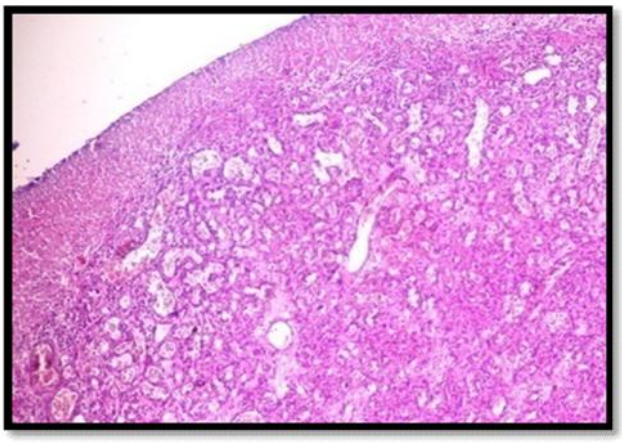

Figure 3: Showing connective tissue with dense fibrous stroma

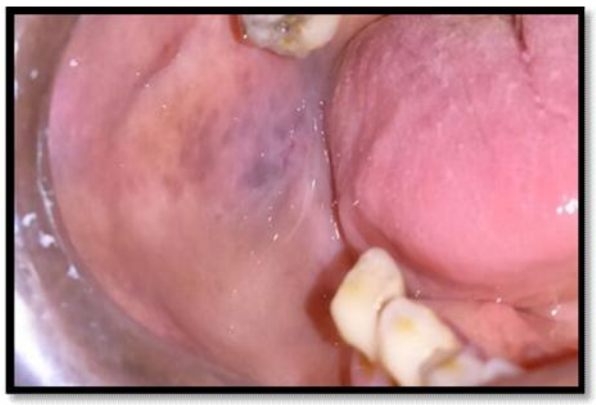

Figure 3: After 1 week of follow up

DISCUSSION

Hullihen (1844) was first to define pyogenic granuloma in the English literature. In 1897, pyogenic granuloma in man was designated as botryomycosis hominis. Hartzell (1904) was credited with giving the current term of pyogenic granuloma or granuloma pyogenicum. It was also called as Crocker and Hartzell's disease. Angelopoulos histologically defined it as hemangiomatous granuloma due to the presence of frequent blood vessels and the inflammatory nature of the lesion. The incidence of pyogenic granuloma is 26.8 to 32% of all reactive lesions.[7]

The term pyogenic granuloma is misleading because the lesion is not pus producing, as 'pyogenic' implies and it is not a true granuloma. In actuality it is a capillary hemangioma of lobular subtype, quite prone to bleeding.[8] Pyogenic granuloma originates from a response of the tissues to various stimuli such as low-grade chronic irritation, trauma, and hormonal imbalances are said to be the main etiology for pyogenic granuloma which results in the overzealous proliferation of vascular type of connective tissue. Poor oral hygiene leading to accumulation of plaque and calculus and overhanging restorations are said to be the most common precipitating factors.[6] Pyogenic infection of the gingiva occurs in up to 5% of pregnant women, generally appearing in the second to third month of pregnancy.[9] The levels of estrogen and progesterone are markedly elevated in pregnancy and could therefore exert a greater effect on the endothelium of oral pyogenic granuloma. Ojanotak-Harri *et al*. (1991) stated that it has been shown that pregnancy inhibits the migration of inflammatory cells and fibroblasts. Hence, it seems that pregnancy regulates both the metabolism of progesterone and also influences migration of inflammatory cells in tissue. The level of progesterone available in the active form and "dysfunction" of the inflammatory cells may have a role in development of pregnancy gingivitis and granuloma formation.[10] Recently at the molecular level Kuo Yuon et al reported that an imbalance between the angiogenesis enhancers and inhibitors, i.e over expression of vascular endothelial growth factor (VEGF) and Basic fibroblast growth factor (bFGF), which are the angiogenesis enhancers and decreased amount of angiostatin which is a angiogenesis inhibitor plays a role.[11] Vascular morphogenesis factors Tie-2, angiopoietin-1, angiopoietin-2, ephrinB2, and ephrinB4 were found upregulated in pyogenic granuloma compared to healthy gingiva. The importance of decorin, vascular endothelial growth factor, basic fibroblast growth factor, or connective tissue growth

factor particularly in angiogenesis associated with a profound inflammation has been proved by some investigators.[10] Other etiological agents includes use of certain immunosuppressive drugs and oral contraceptives. Nonspecific bacterial infection is thought to be a secondary involvement rather than being the main etiology of this lesion.[6]
Oral pyogenic granuloma occurs over a wide age range of 4.5 to 93 years with highest incidence in second and fifth decades as with our parent case and females are slightly more affected than males.[10]The tissue overgrowth varies from small growths of only a few millimeters in size to larger lesions that may measure 2 to 3 centimeters in diameter.[11] In the oral cavity, pyogenic granuloma has site preference for the gingival (75% of the cases) specifically, interdental papillae. On rare occasion, it can be found extragingivally in the area of frequent trauma, such as lower lip, tongue, palate and buccal mucosa as with our present case.[7] In the present case, it arised extragingivally from right buccal mucosa. Extra-oral sites have also been described; the skin of the upper and lower extremities, scalp, face, mucous membrane of the nose, eyelids, and genitalia.[12] Pyogenic granulomas generally are deep red to reddish‑purple in color as also seen with our present case.[10] Color of the lesion changes from pink to red and from red to purple depending on the age of the lesion. Young PG's are highly vascular in appearance because of increased number of capillarie.[11] Pyogenic granuloma is usually a smooth or lobulated exophytic lesion with a pedunculated or sessile base. Occasionally they may become ulcerated because of secondary trauma.[13] It is usually painless and soft in consistency, although older lesions tend to be firm and fibrotic. The surface may be smooth or occasionally ulcerated with a tendency for hemorrhage either spontaneously or upon slight trauma.[12] Pyogenic granuloma is highly vascularized lesion with high propensity for bleeding after light probing or any minor injury. The surface of pyogenic granuloma may undergo secondary or nonspecific changes which include ulceration, capillary dilation, stromal edema, inflammation and granulation tissue reaction.[14]
Pyogenic granuloma can be diagnosed clinically with considerable accuracy, radiographic and histopathological investigations aid in confirming the diagnosis and treatment. Radiographs are advised to rule out bony destructions suggestive of malignancy or to identify a foreign body.[7] Radiographic findings are usually absent However, Angelopoulos concluded that in some cases long standing gingival pyogenic granulomas caused localized alveolar bone resorption.[5] Moreover, the radiographs help in determining the alveolar bone erosion leading to mobility and tooth loss.[7]
Differential diagnosis included peripheral giant cell granuloma, peripheral ossifying fibroma, metastatic cancer, hemangioma, pregnancy tumor, conventional granulation tissue hyperplasia, Kaposi's sarcoma, bacillary angiomatosis and non‑Hodgkins lymphoma. Peripheral giant cell granuloma can be histologically identified due to the presence of multinucleated giant cells and lack of an infectious source. Ossifying fibroma or peripheral odontogenic fibroma occurs exclusively on the gingiva, however it has a minimal vascular component unlike a pyogenic granuloma. Due to the proliferating blood vessels differential diagnosis of pyogenic granuloma from a hemangioma is made histologically in which hemangioma shows endothelial cell proliferation without acute inflammatory cell infiltrate, which is a common finding in pyogenic granuloma.[5] Metastatic tumors of the oral cavity are rare and attached gingiva is commonly affected, clinically they resemble reactive or hyperplastic lesions such as pyogenic granuloma, but microscopically they usually resemble the tumor of origin, which usually is distant from

the metastatic lesion seen in the oral cavity. Kaposi's sarcoma can mimic a number of intraoral lesions such as pyogenic granuloma. Non-Hodgking's lymphoma is usually found to be an asymptomatic gingival enlargement or mass resembling a pyogenic granuloma. Non-Hodgking's lymphoma is usually found to be an asymptomatic gingival enlargement or mass resembling a PG. The established diagnosis depends on biopsy.[15]
Therefore, all clinically suspected pyogenic granuloma must be histopathologically examined to rule out other benign and malignant conditions. Differentiation is done on clinical and histological features which also help in adequate treatment and good prognosis. The histopathological picture of the extragingival pyogenic granuloma is similar to the gingival pyogenic granuloma. Histopathologically, it consists of many dilated blood vessels in a loose edematous connective tissue stroma. Sometimes, these vessels are organized in lobular aggregates and called as lobular capillary hemangioma.[7]
Histologically, the pyogenic granuloma are characterized by vascular proliferation, which may take the form of either solid sheets of endothelial cells with little evidence of canalization or numerous small vessels and large, dilated, thin-walled vascular spaces.[9]
Pyogenic granuloma is partly or completely covered by parakeratotic or non‐keratinized stratified squamous epithelium. Major bulk of the lesion is formed by a lobulated or a non lobulated mass of angiomatous tissue. Usually, lobulated lesions are composed of solid endothelial proliferation or proliferation of capillary sized blood vessels.[10]
Cawson et al. have described two variants of pyogenic granuloma depending on the rate of proliferation and vascularity, namely, (i) lobular capillary hemangioma (LCH) and (ii) non-lobular capillary hemangioma (non-LCH). However, it should be remembered that these terms have been used to describe pyogenic granuloma based on its histopathological variations only and it is not a true hemangioma in the real sense. Hemangiomas are benign tumors consisting of endothelial cell lined blood vessels which can occur within the oral cavity and should be considered as a differential diagnosis for pyogenic granuloma which is actually a reactive lesion. The LCH type of pyogenic granuloma is characterized by proliferating blood vessels organized in lobular aggregates whereas the non- LCH type shows high vascular proliferation resembling granulation tissue. Sternberg et al. suggested three distinct phases to describe the course of pyogenic granuloma.The "early phase" reveals a compact cellular stroma with little lumen formation. The next phase described as the capillary phase reveals lobules which are highly vascular with abundant intraluminal red blood cells. The final phase referred to as "involutionary
phase" shows intra- and perilobular fibrosis. This phase is suggestive of healing phase of pyogenic granuloma. Clinical correlation should be done for various phases of pyogenic granuloma, with younger lesions being red to purple due to high vascularity whereas older lesions become collagenized and appear pink. Depending on the different stages of pyogenic granuloma, certain lesions come in as differential diagnosis. Younger lesions may be mistaken for conventional granulation tissue histopathologically or hemangioma, Kaposi's sarcoma, and bacillary angiomatosis clinically. Hemangioma generally presents in extragingival locations and is devoid of any inflammatory components, points which help it in differentiating from pyogenic granuloma. Histopathologically, the absence of atypical cells and bizarre vascular channels helps to differentiate pyogenic granuloma from Kaposi's sarcoma whereas absence of any granular bacterial material differentiates it from bacillary angiomatosis.[6]

Sangueza and Requena stated that immunohistochemical investigations of pyogenic granuloma lesions express factor VIII – related antigen positivity in the endothelial cells lining large vessels, but are negative in the cellular areas, whereas Ulex europaeus I lectin binds to endothelial cells in both large vessels and cellular aggregates. Enhanced expression of the bFGF, Tie-2, anti-CD34 and anti alpha SMA antibodies, and vascular morphogenesis factors such as angiopoietin-1, angiopoietin-2, ephrinB2, and ephrinB4. There is also expression of inducible nitric oxide synthase, increased expression of vascular endothelial growth factor, low apoptotic rate expression of Bax/Bcl-2 proteins and strong expression of phosphorylated mitogen activated protein kinase. Polymerase chain reaction investigations for human papilloma virus and human herpes virus type have yielded negative results.[10]

Management of pyogenic granuloma is conservative surgical excision, after thorough oral prophylaxis. If the lesion is small, painless and free of bleeding, oral prophylaxis and removal of causative irritants is advised. If the lesion is of large size, a thorough oral prophylaxis followed by surgical excision using gingivectomy or flap surgery procedures is done.[7] Rapid healing can be observed within a few days of treatment, and as blood vessels are sealed, there are both a reduced need for post-surgical dressings and improved haemostasis and coagulation. It also depolarizes nerves, thus reducing post-operative pain and also destroys many bacterial and viral colonies that may potentially cause infection. Reduced post-operative discomfort, oedema, scarring and shrinkage have all been associated with its use.[16] Other treatment protocols have also been proposed such as cryosurgery which is safe, easy and inexpensive; and also Nd: YAG and CO2 and flash lamp pulsed dye lasers. Lasers have advantage of minimum pain and invasiveness and the lack of need for suturing or packing. Moon *et al.* reported that sodium tetradecyl sulfate sclerotherapy successfully cleared the lesions in most patients without major complications. Parisi *et al.* used a series of intralesional corticosteroid injections for the treatment of recurrent pyogenic granuloma.[7] Other treatment modalties includes cryosurgery, elctrodessication, sodium tetradecyl sulphate sclerotherapy, steroid injections and ultrasonic scissors.[17] Treatment considerations during pregnancy are very important. During this period, careful oral hygiene, removal of dental plaque, and use of soft toothbrushes are important to avoid occurrence of a pregnancy tumor. If uncontrolled bleeding occurs, management should be based on the individual condition and should range from supportive therapy such as desiccation of bleeders; local, firm compression and oral hygiene to blood transfusion, as well as medication to accelerate fetal lung maturity or even termination of pregnancy to save the patient's life, as with treatment of uncontrollable eclampsia. Lesions removed during pregnancy may have a higher recurrence rate.[18] Recurrence of pyogenic granuloma after excision is a known complication but can be prevented. The recurrence rate for pyogenic granuloma is said to be 16% of the treated lesions and so re-excision of such lesions might be necessary.[19] Recurrence is believed to result from incomplete excision, failure to remove etiologic factors, or re-injury of the area.[18] Some recurrences manifest as multiple deep satellite nodules that surround the site of the original lesion Warner-Wilson Jones syndrome.[20] It should be emphasized that gingival cases show a much higher recurrence rate than lesions from other oral mucosal sites.[18]

This paper presents a case of a pyogenic granuloma managed by surgical intervention. On clinical examination, moderate supragingival and subgingival calculus was detected.

So a thorough scaling and root planning was performed before the surgical excision of the lesion. Satisfactory healing was seen after 1 week of surgery without any sign of recurrence and patient discomfort. There was no recurrence seen after 6 months of follow up.

CONCLUSION

A pyogenic granuloma is an exuberant growth of granulation tissue secondary to irritation. Individuals with poor oral hygiene and chronic oral irritants most frequently are affected. This article thus attempted to the occurrence of pyogenic granuloma in extra gingival sites is unusual, this case report emphasizes the importance of the correct diagnosis of this lesion and review the main theories of etiopathogenesis and the basis for such observations. As Subsequently, the oral physicians should be aware of occurrence of these type of lesions on uncommon sites and there proper management.

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