Oral Pyogenic Granuloma and Its Histological Variants: A Review of Case Series

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ABSTRACT

Gingival enlargement is quite common, and occurs as a result of response to varied stimuli and or interactions with the host and the environment. This lesion represents a reactive hyperplasia. Pyogenic granuloma is one of the commonest exophytic lesions found in the oral cavity. Its histological variants are lobular capillary hemangioma (LCH) and non-lobular capillary hemangioma (non-LCH). This growth usually responds well to adequate plaque control, elimination of causative irritants and management of tissue. This case series highlights two cases of localized gingival enlargement, with histologic presentations and its management with emphasis on the importance on patient awareness and motivation.

Conclusion: Awareness of clinical presentations and histologic variants will aid clinicians in arriving at an appropriate diagnosis, as well as reduce the incidence of recurrence, thereby reducing the possibility of a misdiagnosis.

Recommendation: Clinicians should have a good knowledge of the common lesions that occur on the gingiva and be able to distinguish lesions by considering all possibilities before arriving at final diagnosis.

Keywords: Gingival enlargement, pyogenic granuloma, lobular capillary hemangioma, oral exophytic lesion

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INTRODUCTION
Gingival lesions can be localized to certain aspect of the oral cavity or generalized affecting larger areas.¹ Some possible aetiologic factors that have been reported include inflammation, hormonal imbalances or manifestation of a systemic condition.² Other aetiologic factors that have been reported include

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blood dyscrasias, drug induced or genetic origin/predisposition. Inflammatory gingival enlargement can be acute or chronic, with most common form being chronic. The enlargement can cause functional disturbance, aesthetically displeasing and impede tooth cleaning. It may also cause abnormal tooth movement or force the teeth out of alignment.

Pyogenic granuloma (PG) is a form of focal reactive gingival lesions, which was reported to have a prevalence rate of 5.6%, with PG been the most common lesion constituting 57% of the cases. Reactive hyperplasia are the most frequent phenomenon responsible for exophytic lesions. This oral exophytic lesions are pathologic growths projecting above the normal contours of the oral mucosa. There are several underlying mechanisms responsible for oral exophytic lesions such as hypertrophy, hyperplasia, neoplasia, and pooling of the fluid, making it difficult to diagnose such lesions except via decision tree or histologically. Exophytic lesions can be categorized according to the surface texture (smooth and rough), type of base (pedunculated, sessile, nodular, and dome shape), and consistency (soft, cheesy, rubbery, firm, and bony hard). Exophytic gingival lesions represent some of the more frequently encountered lesions in the oral cavity.

Pyogenic granuloma or lobular capillary hemangioma is a tumor-like growth that is considered an exaggerated, conditioned response to minor trauma. Appropriate management depends on accurate diagnosis of the cause of lesion. Treatment in a methodical manner is important and should involve a detailed medical history followed by conventional nonsurgical therapy and surgical therapy may be desirable to preserve esthetics and functional needs. Patient awareness and motivation, along with a timely recall visits is crucial to maintain successful therapeutic outcomes. Often, pyogenic granuloma as a form of exophytic lesion is difficult to diagnose clinically due to the variation of pathogenesis and clinical presentation, thereby yielding diagnostic challenge. Exophytic appearance often provides a greater chance of misdiagnosis as malignant lesions. Clinicians should be aware about the histologic variants of pyogenic granuloma as one of the commonest oral exophytic lesion encountered, so as to manage lesion better and reduce the incidence of recurrence.

Case #1. Description of case
A 22-year-old female business administrator presented in the Periodontology clinic with a slow growing lesion, gradually increasing in size, painless gingiva growth that was present in her left mandibular anterior region. The lesion started as a small nodule one (1) year earlier and gradually increased in size with history of slight bleeding on brushing. Patient did not give a history of trauma, injury or food impaction. No history of pain, discharge, sleep disturbance or headache. Patient was not pregnant, not on any medication.

An intra-oral examination revealed a nodular growth, pinkish red in color, non-tender, firm in consistency, sessile in nature arising on the labial gingival of the interdental papilla of 32 and 33, measuring 1cm by 1cm (Figure 1).

![Figure 1: Preoperative labial view](https://www.njdres.com)

Radiography shows: horizontal bone loss between the 32 and 33, and slight widening of periodontal space 32 and 33. Differential diagnosis of pyogenic granuloma, peripheral giant cell granuloma and peripheral ossifying fibroma was made.

Treatment: After performing oral prophylaxis, patient was placed on warm saline mouth bath for 2 weeks. At the next presentation, gingival enlargement had not resolved and patient wanted it removed due to aesthetic concern. Consent for the surgical procedure was obtained from the patient after proper counseling was done. Under local anesthesia...
the lesion was completely excised with bard paker scalpel handle (no 3) and number 15 blade, with the underlying surface thoroughly curetted up to deepest possible tissue and irrigated with normal saline.

Figure 2: Post operative view

Hemostasis was achieved (Figure 2) and a periodontal dressing was placed. Specimen was sent for histologic diagnosis. Post-operative instruction was given to the patient.

Medications- Analgesic: Tabs Acetaminophen 1000mg Tds X 3/7. Antibiotics: Caps Amoxicillicin 500mg TDS X 5/7, Tabs Metronidazole 400mg TDS X 5/7

Figure 3: Histology slide high magnification

Section of tissue show partly ulcerated epithelium overlying a lesion composed of lobules of small capillaries lined by plump endothelial cells. They are disposed within edematous stroma exhibiting modest inflammatory cells infiltrates (Figure 3).

The patient was recalled after one week for removal of the periodontal dressing and site showed uneventful healing. Correlating clinical findings with histological features, a diagnosis of Lobular capillary hemangioma was confirmed. The patient is still on follow up 8 months after with no evidence of recurrence.

Case #2

Description of case

A 45-year-old female business woman presented in the Periodontology clinic with a slow growing gingival enlargement present in her right maxillary posterior region. The lesion started as a small nodule 8 months ago earlier and gradually increased in size, with pain initially, which was sharp, spontaneous and aggravated by chewing and disturbs sleep. There was associated bleeding, no discharge, no history of toothache, and no trauma from fish bone and brush bristle. Patient medical history was insignificant.

An intra-oral examination, revealed oral hygiene was fair. A nodular growth related to 17, pinkish red in color, well demarcated, tender with firm pressure, soft in consistency, pedunculated in nature arising on the buccal gingival of the interdental papilla of 17 Measuring 2cm x 2cm, with associated mobility of 17 (grade 1), bleeds on probing (Figure 4).
Radiography shows: horizontal bone loss between the 17 and 16, and slight widening of periodontal space of 17
Differential diagnosis of pyogenic granuloma, peripheral giant cell granuloma and gingival epulis was made. Correlating clinical findings with histological features, a diagnosis of pyogenic granuloma was confirmed. The patient is still on follow up 8 months after with no evidence of recurrence.
After performing oral prophylaxis, consent for the surgical procedure was obtained from the patient after proper counseling was done. Under local anesthesia the lesion was completely excised, underlying surface was thoroughly curetted up to deepest possible tissue. Hemostasis was achieved and a periodontal dressing was placed. Specimen was sent for histologic diagnosis. Post-operative instruction was given to the patient.
Medications- Analgesic: Tabs acetaminophen 1000mg Tds X 3/7. Antibiotics: Caps doxycycline 100mg bd X 5/7, Tabs Metronidazole 400mg TDS X 5/7. Patient was recalled after one week for removal of the periodontal dressing and site showed uneventful healing.

DISCUSSION
Localized gingival enlargement usually occurs in the oral cavity. This lesions histologically have been termed epulides, which is a term used to describe pedunculated or sessile swellings of the gingiva. Reactive lesion of the gingiva is often used instead since the word epulide is a topographic term.
Localized reactive gingival enlargements are a distinctive group of epulides that clinically are separate from plaque induced inflammatory enlargements. This distinction allows a clinical diagnosis and defines a treatment protocol made specifically to minimize recurrence. The two distinguishing features is it originates from suprabony fibres of the periodontal ligament and it is primarily a reactive and non-inflammatory lesion. This enlargements are not an enlargement of inflamed interdental papilla, nor does it arise from the gingival surface.
Pyogenic granulomas (PG) of the oral cavity frequently occur in the gingiva. Its name is a misnomer as this condition is not associated with an infection and does not represent a granuloma histologically. Staphylococci and botryomycosis, foreign bodies and localization of infection in walls of blood vessel have been reported as contributing factors in the development of the lesion. The presence of bacilli in oral PG has been demonstrated, this led to the deduction that minimal trauma to the PG causes tissue ulceration which, in turn, encourages colonization of the surface of the ulcer by non-specific microorganisms that may represent contaminants from the oral flora. Based on the histopathologic presentation, it is also called lobular capillary hemangioma (LCH).
It has been hypothesized that trauma can trigger the release of endogenous substances, comprising angiogenic growth factors, from the tumour cells and it may also cause disruptions in the vascular system of the affected area. Angiogenic growth factors such as vascular endothelial growth factor (VEGF) and decorin, transcription factors (pATF2 and pSTAT3), and mitogen-activated protein kinase (MAPK) signal transduction pathway proteins are overexpressed in PGs, but their exact role is undetermined. In addition to trauma, poor oral hygiene, may exaggerate the inflammatory response, further aggravating the lesion. PG represents an exuberant reactive or reparative connective tissue proliferation to a known stimulus or injury, which may be dental plaque or foreign material within the gingival sulcus.
PG is seen predominantly in the second decade of life in females, due to the vascular effects of female hormones.\textsuperscript{46,55} It has been suggested that the gingiva is enlarged during pregnancy and atrophied during menopause due to oestrogen and progesterone acting directly,\textsuperscript{25} and exerting an effect on the endothelium of PG.\textsuperscript{27} On the contrary, Bhaskar and Jacoway established that because PG occur often in males as well as females, it is doubtful that it has any hormonal basis.\textsuperscript{28} It occurs over a wide age range of 4.5–93 years with a slight female preponderance,\textsuperscript{25} but with a peak incidence in second and third decade of life,\textsuperscript{29} as observed in case #1. Both cases seen in this study presented as females.

Pyogenic granuloma may present clinically as a lobulated, exophytic, pedunculated or sessile mass, which is often haemorrhagic and compressible.\textsuperscript{24} PGs generally are soft, painless and deep red to reddish-purple in color and haemorrhagic on slight irritation.\textsuperscript{18} The color may change from pink to red to purple depending on the stage of the lesion.\textsuperscript{23} It has been reported that the LCH PG occurred more frequently (66%) as sessile lesion (as seen in case #1), whereas non-LCH PG mostly occurred as pedunculated (77%)\textsuperscript{28} as seen in case #2. The clinical presentation of the two histological types is essentially the same.

The size of PG differs in diameter from a few millimeters to several centimeters,\textsuperscript{18} reaching its full size within weeks or months and rarely exceeds 2.5 cm in diameter, as observed in both case #1 and case #2. The lesion may grow rapidly, but the common clinical course is slow asymptomatic and painless,\textsuperscript{20} which was observed in case #1. In very rare circumstances, PG has been reported to be associated with significant bone loss and calculus formation in the crypt of the lesion.\textsuperscript{31} Both clinical cases showed a slight horizontal bone loss.

The histologic features of PG include granulation tissues with high vascular proliferation in the stroma and vascular channels engorged with red blood cells and lined by flat or plum endothelial cells that may be mitotically active.\textsuperscript{34} These blood vessels often show a clustered or medullary pattern separated by less vascular fibrotic septa. PG has, therefore, been considered a polypoid form of capillary haemangioma.\textsuperscript{39} The diagnosis of PG as lobular capillary haemangioma is arrangement of the blood vessels in lobular aggregates, which is sometimes observed.\textsuperscript{34,33}

At higher magnification, the lobular arrangement of thin capillaries is often seen at the periphery of the lesion. A thin collagen layer surrounds the lobules. Larger, irregularly shaped vascular channels are seen at the base. These larger channels communicate with the lobulated peripheral vascular channels. A higher magnification, the thin, small capillary endothelial-lined spaces are surrounded by a periepithelial or pericytic layer of cells.\textsuperscript{24} This is an important feature in the classification of PG as a benign vascular lesion.\textsuperscript{24}

Ulceration and surface lined by a thick fibrin purulent membrane is often observed. A mixed inflammatory cell infiltrates of neutrophils is mostly prevalent near the ulcerated surface while chronic inflammatory cells are found deeper in the lesion.\textsuperscript{24} The lesion follows three classic phases of evolution, viz., cellular phase, capillary phase and involutionary phase.\textsuperscript{34}

The two histological variants of PG have been reported are LCH type and non-LCH.\textsuperscript{35} The LCH type is characterized by proliferating blood vessels that are organized in lobular aggregates. In contrast, the second type (non-LCH type) consists of highly vascular proliferation that resembles granulation tissue.\textsuperscript{32,35} The lobular area of the LCH type PG contains a greater number of blood vessels with small luminal diameter than does the central area of non-LCH PG. Biologic behaviors have been suggested as the reason for differences in the two histological variants.\textsuperscript{32} Different pathogenic factors influencing their development has also been suggested to give rise to the different luminal diameter of the blood vessels in the lobular area of LCH PG and in the central area of non-LCH.\textsuperscript{32,35} Foci of fibrous maturation was observed to be present in 15% of non-LCH PG but were totally absent in LCH PG.\textsuperscript{35} Lobular capillary hemangiomas are most of the times clinically similar to peripheral ossifying fibroma and peripheral giant cell granuloma. However, peripheral ossifying fibroma and peripheral giant cell granuloma typically occur only on gingival and alveolar mucosa unlike lobulated capillary hemangioma which can occur on other sites including the gingiva.\textsuperscript{2} Also to be site-specific, peripheral giant cell granuloma is bluish purple and histopathologically it shows the presence of multinucleated giant cells.\textsuperscript{5} Peripheral ossifying fibromas are larger lesions, clinically more than 1.5 cm in dimensions. There is radiographic evidence of ossification (calcification present within the lesion), and histopathologically, it shows minimal vascular component.\textsuperscript{5} Metastatic tumours in the gingiva may resemble PG clinically, but frequently observed in patients in the fifth to seventh decades of life,\textsuperscript{16,37} in
contrast to PG, which is often seen in younger patients. Both case #1 and case #2 in this study occurred in the gingiva, not bluish purple in color, no evidence of calcification on radiograph, histologically no presence of multinucleated giant cells and evidence of vascular component. Management of PG is dependent on considerations such as severity of symptoms, ease of access to the lesion, proximity to dental hard tissues and available resources. A combination of distinct treatment modalities is generally advocated. Surgical excision is indicated for the treatment of PG except when the procedure would produce marked deformity. The excision should extend down to the periosteum and combined with the removal of causative irritants such as plaque, calculus, foreign material and sources of trauma. A conservative management by clinical observation and follow-up is often sufficient when the lesion is small, painless and free of bleeding. Both cases #1 and #2 were initially observed after nonsurgical therapy of scaling and root planing, but lesion did not resolve after 2 weeks, by which time a surgical intervention was billed, especially as patient was concerned about aesthetics. The conventional deep scaling and root planing, in addition to surgical excision of the lesion is still the acceptable treatment option for PG and its histologic variants of LCH and non-LCH. However, there is a need to consider other less aggressive and less morbid methods of treatment such as cryosurgery and laser therapy. Recurrence of lobular capillary hemangiomas in the same location after treatment is common with rates ranging from 3.7% to 43.5%. Both clinical cases seen in this report have been monitored up to 8 months with no signs of recurrence.

CONCLUSION
Gingiva enlargements are frequently encountered in the oral cavity. Pyogenic granuloma (LCH) is a common gingiva enlargement. Thorough diagnosis is crucial to distinguish lesion from other lesions especially vascular lesions. Emphasis should be made on maintaining good oral hygiene. To prevent recurrences of this lesion, surgical excision should be done, along with curettage. Removal of lesion needs to be thorough and based on understanding the lesion. Follow up is required and should be emphasized to ensure that recurrence is detected early.

REFERENCES