Aggressive Pyogenic Granuloma: A Case Report
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Abstract
The pyogenic granuloma is an exuberant tissue response to local irritation or trauma. Pyogenic granuloma is relatively common, soft tissue tumor of oral cavity that is believed to be reactive and not neoplastic in nature. The young lesions are highly vascular, red or reddish purple, often elevated and ulcerated, and bleed easily. Older lesions tend to be more collagenized and pink in appearance and histologically it resembles an angiomatous lesion rather than a granulomatous lesion. Some believe that the older lesion will develop into a peripheral ossifying fibroma or peripheral fibroma over time through fibrous maturation and ossification. In this paper, we present a case of pyogenic granuloma with large size and bone loss occurring on the posterior mandibular gingiva in a 44 years old female patient.

Keywords: Aggressive;Angiomatous;Inflammatory Hyperplasia;Pyogenic Granuloma;Reactive

Introduction
The pyogenic granuloma (PG) is an exuberant tissue response to local irritation or trauma. It is known by a variety of names such as Crocker and Hartzell's disease, granuloma pyogenicum, granuloma pediculatum benignum, benign vascular tumor and during pregnancy as granuloma gravidarum. PG is relatively common, soft tissue tumor of oral cavity that is believed to be reactive and not neoplastic in nature.1 Pyogenic granuloma typically occurs on the mucosal surfaces, particularly the mouth and the skin. These lesions may be seen at any age and tend to occur more commonly in females than in males. The young lesions are highly vascular, red or reddish purple, often elevated and ulcerated, and bleed easily. Older lesions tend to be more collagenized and pink in appearance. Some believe that the older PG will develop into a peripheral ossifying fibroma or peripheral fibroma over time through fibrous maturation and ossification.2,3

The PG can often exhibit rapid growth, appearing on the gingiva in 75% of reported cases with a female predilection. The histological appearance is characterized by vast numbers of endothelium lined vascular spaces infiltrated with lymphocytes, plasma cells and neutrophils. There is extensive fibroblastic proliferation with a diffuse, often dense chronic inflammatory infiltrate. The lesion is covered by a thin, often ulcerated layer of stratified squamous epithelium.4,5 In this paper, we present a case of pyogenic granuloma with large size and bone loss occurring on the posterior mandibular gingiva in a 44 year old female patient.

Case Report
A 44 year old female patient presented with a rapidly growing lesion on the gingiva of the lower posterior teeth causing an inability to achieve plaque control and eat properly. The growth started two months ago, as a small sessile painless growth progressively increased to attain the size of 1.5×3cm at the time of presentation. The growth was associated with profuse bleeding on provocation and there was hindrance in mastication. There was no contributory past medical history. Examination of the head and neck revealed no cervical and submandibular lymph node enlargement.

Intraoral examination revealed full complement of teeth. However there was a pedunculated growth arising from the gingiva in relation to 47 and 48 on the buccal aspect extending distal to 48 and to the occlusal surface also (Figure 1a). Palpatory findings revealed swelling measuring 1.5×3 cm which was soft to firm in consistency. There was also mobility seen in relation to 47 and 48. Intra oral periapical radiograph in relation to 47 and 48 revealed loss of alveolar crestal bone interproximally. With the above said findings, provisional diagnosis of pyogenic granuloma on the buccal gingival in relation
to 46 was established. Peripheral giant cell granuloma and peripheral fibroma were considered in the differential diagnosis. Since the growth was causing hindrance in mastication, an excisional biopsy was carried out under antibiotic coverage of amoxicillin 500 mg 3 times daily for 5 days.

The macroscopic examinations showed soft tissue measuring 1.5x1.5cm, yellowish in color and soft in consistency (Figure 1b). The microscopic examination showed a band of connective tissue made up of fibro-vascular reactive tissue consisting of abundant young proliferating blood capillaries, filled with red blood cells, numerous plump active fibroblasts densely infiltrated with both acute and chronic inflammatory cells (Figure 1c & d). A histopathological diagnosis of pyogenic granuloma was given. With regular follow up at one monthly interval showed no evidence of recurrence.

**Figure 1:** The Intraoral examination (a) revealed a pedunculated growth arising from the buccal aspect of tooth #47 till distal to 48 and extending to the occlusal surface. The gross examination (b) of the excised tissue was soft to firm in consistency, 1.5x1.5cm in size and yellowish in color. The photomicrograph of H and E stained section under low (c) power showing a band of connective tissue made up of fibrovascular tissue and at high power (d) consisting of abundant young proliferating blood capillaries covered by fibrino-purulent membrane.

**Discussion**

Originally, pyogenic granulomas were believed to be botryomycotic infection which was transmitted from horse to man. Subsequently it was proposed that these lesions are caused due to some pyogenic bacteria like streptococci and staphylococci. However there is no evidence of any infectious organisms isolated from the lesions confirming the unlikely relation to any infection and hence the name is a misnomer. It is now largely agreed that pyogenic granuloma arises as a result of various stimuli such as low grade chronic irritation, trauma, hormonal imbalances or certain kinds of drugs. The tissues react in a characteristic manner resulting in overzealous proliferation of a vascular type of connective tissue. The growth rate of tumor depends upon the proliferative capability and the rate of cell death. Nakamura (2000) described cells in pyogenic granulomas have low apoptosis influenced by the anti apoptotic proteins like bcl-2 family proteins. Thus even pyogenic granulomas can behave aggressively by causing bone loss and leading to tooth mobility. According to Shafer et al., oral pyogenic granuloma arises as a result of infection by either staphylococci or streptococci, partially because it was shown that these microorganisms could produce
colonies with fungus-like characteristics. The tissues respond in a characteristic manner to these organisms of low virulence by the overzealous proliferation of a vascular type of connective tissue. They explain the mechanism by suggesting that tissue response reiterates the well-known biologic principle that any irritant applied to living tissue may act either as a stimulus or as a destructive agent or both. Regezi et al. suggest that pyogenic granuloma represents an exuberant connective tissue proliferation to a known stimulus or injury like calculus or foreign material within the gingival crevice. According to Cawson et al., pyogenic granuloma represents vascular proliferations and do not represent a stage in the development of fibrous nodules or merely inflamed fibrous nodules. Regarding the pregnancy pyogenic granuloma, they state that like pyogenic granulomas in a non-pregnant women, pregnancy tumor may show minimal or no inflammation, but vascular proliferation is occasionally very active so as to suggest a neoplasm.

Certain kinds of medications are considered to be the etiology of PG. Some medications such as cyclosporine have an important role in the genesis of PG. Bachymer et al. and Lee et al. reported four cases of oral PG in chronic graft-versus-host disease in patients who were receiving cyclosporine. In a study of PG among patients, who were receiving carbamazepine individuals reported to have side effects? Among them, two patients (0.02%) had PG. Approximately one-third of the lesions develop after trauma particularly those occurring on the extragingival sites. Trauma from adjacent sharp teeth, ill fitting dentures, accidental biting and tongue piercings are most common. Poor oral hygiene may be another precipitating factor. Additionally some drugs, like cyclosporine may be involved in the genesis of the pyogenic granulomas. In a study done by Skinner et al. (1973) described that pyogenic granulomas are more common in females in the third decade of life with a predilection of 3:2 over males possibly because of vascular effect of female hormones.

Although pyogenic granuloma can be diagnosed clinically, atypical presentations lead to inappropriate diagnosis and should be further investigated by biopsy to rule any other serious lesions. Differential diagnosis of pyogenic granuloma includes parulis, peripheral giant cell granuloma, peripheral ossifying fibroma, hemangioma, peripheral fibroma, leiomyoma, hemangioendothelioma, hemangiopericytoma, bacillary angiomatosis, kaposi sarcoma, metastatic tumour, and post extraction granuloma. Thus definitive diagnosis of pyogenic granuloma can only be made by histopathologic examination of biopsied tissue.

Histologically, pyogenic granulomas are classified as the Lobular capillary haemangioma (LCH) type and the non-Lobular capillary haemangioma type. The LCH type has proliferating blood vessels organized in lobular aggregates; no specific changes such as edema, capillary dilation or inflammatory granulation were noted. The non-LCH type consisted of a vascular core resembling granulation tissue with foci of fibrous tissue. The lobular area of the LCH type has a greater number of blood vessels with small luminal diameter than that in a non-LCH type of pyogenic granuloma. In the central area of the non-LCH pyogenic granuloma a greater number of vessels with perivascular mesenchymal cells non-reactive for alpha smooth muscle actin (SMA) is detected as compared with the lobular area of the LCH type pyogenic granuloma, thereby Epivatianos et al., suggested that the LCH and the non-LCH pyogenic granulomas have different pathways of evolution.histologically, Apostosis et al., used CD34, a-SMA, MSA to compare LCH and non-LCH PG and suggested that the two histological types of PG represent distinct entities. A CD31 positive cell in non-LCH PG was higher than the LCH. Regarding the role of CD31 in diapedesis, the high percentage of CD31 positive cells in the non-LCH type can represent the inflammatory or reactive nature of this type of PG. Lower density of CD31 positive endothelial cells can be due to lower differentiation in the endothelial cells of the LCH type compared to the non-LCH PG.

Our present case appears to be one of the few cases of large sized pyogenic granuloma behaving aggressively by causing bone loss and tooth mobility in a 44 year old female patient. Treatment of pyogenic granuloma involves complete excision of the lesion down to the peristeme or periodontal ligament and removal of local irritants. This can be difficult due to the hemorrhagic nature of the lesion and may be better accomplished
through laser eradication than the scalpel.\textsuperscript{5} Other conventional surgical modalities for the treatment of pyogenic granuloma reported is cryosurgery in form of either liquid nitrogen spray or a cryoprobe, which has been used for eradication of the lesion.\textsuperscript{16} It is safe, easy and inexpensive technique suited for out patient’s clinic setting. Nd: YAG and CO and flash lamp pulsed dye lasers have also been used for the treatment for oral pyogenic granuloma. Lasers have shown to be a successful option for the excision of pyogenic granuloma with advantages of minimal pain and invasiveness and the lack of need for suturing or packing. A recurrence rate of 16% however has been reported.\textsuperscript{17}

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