Histopathological variations in Pyogenic Granuloma: A Case Series

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Citation
Gautam D, Bajracharya D, Ojha B, Bhandari P. Histopathological variations in Pyogenic Granuloma: A Case Series. J Kantipur Dent Coll. 2022;3(2): 35-7.

ABSTRACT

Pyogenic granuloma is a reactive tumor-like lesion commonly affecting the oral cavity. These lesions usually appear as localized solitary nodule with predilection for gingiva. The natural course of this lesion can be categorized into three distinct phases; cellular phase, capillary/vascular phase and involutionary/healing phase. In this series, three cases of pyogenic granuloma showing varying histological phases has been described. Hence, knowledge of the various histopathological presentation of pyogenic granuloma is necessary for proper understanding of the lesion along with clinical correlation and also to rule out various soft tissue lesions with similar appearance.

Keywords: histopathology; oral cavity; pyogenic granuloma

INTRODUCTION

Pyogenic granuloma is benign, soft, solitary, non-neoplastic vascular proliferation of the skin and oral cavity.[1] The term "pyogenic granuloma" or "granuloma pyogenicum" was stated by Hartzell in 1904.[1] It occurs as a result of chronic irritation or trauma. The common clinical presentation is a smooth or lobulated mass that can be either sessile or peduculated.[2] Gingiva is most frequently involved site in the oral cavity and presents as a nodular growth which may be slow growing or rapid in nature.[3] The natural course of this lesion can be categorized into three distinct phases namely; cellular phase, capillary/vascular phase and involutionary /healing phase.[4] In this series, three cases of pyogenic granuloma showing varying histological phases has been described and the clinical descriptions are given in Table 1.

CASE PRESENTATION

Case 1: Microscopic evaluation showed parakeratinized stratified squamous epithelium. The underlying connective tissue was composed of loosely arranged collagen fibers with mixed inflammatory cells and few proliferating capillaries features resembled the features of Pyogenic Granuloma (cellular phase), Figure 1.

Case 2: Microscopic evaluation showed parakeratinized stratified squamous epithelium with the underlying connective tissue showing loosely arranged collagen fibers. Large sinusoidal spaces with extravasated RBCs and areas of multiple proliferating small endothelial lined blood vessels with dense inflammatory infiltration. Histopathological features were suggestive of Pyogenic Granuloma (capillary phase), Figure 2.

Case 3: Microscopic evaluation showed parakeratinized stratified squamous epithelium.The underlying connective tissue revealed dense bundle of collagen fibers with plump fibroblasts arranged in streaming fascicles. Areas of large sinusoidal spaces with extravasated RBCs and areas of multiple proliferating small endothelial lined blood vessels with scanty inflammatory infiltration. The Histopathological features resembled the features of Pyogenic Granuloma (involutionary phase), Figure 3.

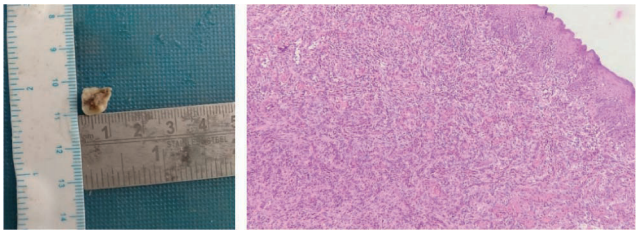

Figure 1:(a) Gross specimen (b) Parakeratinized epithelium and underlying cellular stroma with mixed inflammatory cells and few proliferating capillaries (10X)

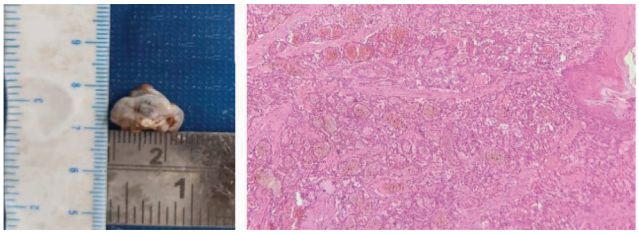

Figure 2: (a) Gross specimen **(b)** Parakeratinized epithelium and underlying connective tissue shows large sinusoidal spaces with extravasated RBCs(10X)

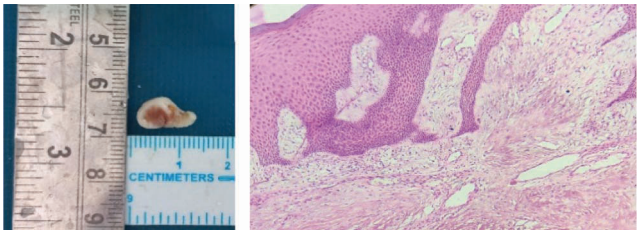

Figure 3: (a) Gross specimen **(b)** Parakeratinized epithelium and underlying connective tissue shows dense bundles of collagen fibers (10x)

Table 1. Clinical Descriptions of the cases of Pyogenic Granuloma

S.N	Age	Gender	Site	Size	Histopathological Category
Case 1	33	Female	Gingiva	1cm×0.9cm	Cellular phase
Case 2	12	Female	Gingiva	1.3cm×1cm	Capillary phase
Case 3	28	Male	Gingiva	1.4cm×0.8cm	Involutionary phase

DISCUSSION

Pyogenic granuloma is also termed as lobular capillary hemangioma, telangiectatic granuloma, and "pregnancy tumor" as it has been frequently found in pregnant females.[4]

Bhaskar et al. reported that Pyogenic granuloma accounts for 1.85% of all oral biopsies.[2] Pyogenic granuloma is a type of reactive inflammatory lesion, which results in overgrowth of granulation tissue in response to various stimuli such as chronic low-grade local irritation, trauma, hormonal factors, or certain kind of drugs.[5,6] Reported incidence of pyogenic granuloma has been found between 26.8% and 32% of all reactive lesions.[4] Regezi *et al.* explained that foreign material is the known stimulant or injury as the etiological factor for pyogenic granuloma which results in exaggerated proliferation of connective tissue.[4,7] Ainamato *et al.* stated the cause of the lesion to be repetitive tooth brush trauma to the gingiva and trauma can cause release of various endogenous substances including angiogenic factors which may also lead to disturbances in the vascular system of the affected area.[4,7] Elevated levels of estrogen and progesterone can modify the vascular response to local irritants which leads to the occurrence of this lesion during pregnancy.[3,7] Increased production of vascular endothelial growth factor, the basic fibroblast growth factor and decreased amounts of angiostatin, thrombopsondin-1, and the estrogen receptor are known to be involved during angiogenesis of the lesion.[1,4,7]

According to Sternberg *et al*, there are three phases of pyogenic granuloma described; namely, 1. Cellular phase 2. Capillary/vascular phase 3. Involuntary/healing phase.[4] The cellular phase consists of little lumen and compact cellular stroma.[3] The capillary phase has high vascularity in the form of lobules and intraluminal RBC's.[3] The involuntary/healing phase mainly represents healing of the lesion and intra and perilobular fibrosis.[8] These phases can be correlated with the clinical presentation of the lesion. In the initial phase the mass appear as reddish blue whereas in late phase the lesion appears pale to pink.[4] Depending upon the rate of proliferation and vascularity, there are two histopathological types of pyogenic granuloma; lobular capillary hemangioma (LCH type) and non-lobular capillary hemangioma (non- LCH type).[9,10] According to Neychev *et al*. LCH type clinically presents as sessile lesion in 66.4% of overall cases and the non-LCH type presents as pedunculated lesion in 77% of all cases.[2] The lobular region of the LCH is characterized by proliferation of capillaries in a loose lobular configuration, imparting a glomerulus-like appearance whereas the non-LCH type shows high vascular proliferation resembling granulation tissue.[2,7,11] Diagnosis of pyogenic granuloma can often be challenging because of the similarities in the clinical presentation with many other intraoral hemangiomatous lesions.[2] Usually, such lesions can be clinically diagnosed and confirmed following histopathology. The differential diagnosis of pyogenic granuloma includes irritation fibroma, hemangioma, benign salivary gland tumors and metastatic tumors of the oral soft tissues, Kaposi's sarcoma, fibroma, angiomatosis, angiosarcoma, non-Hodgkin's lymphoma, conventional granulation tissue, hyperplastic gingival inflammation, peripheral giant cell granuloma and peripheral ossifying fibroma.[6,7,12] Due to the presence of proliferating blood vessels, cavernous hemangioma can be differential diagnosis of pyogenic granuloma before histologically hemangioma shows endothelial cell proliferation without the infiltration of acute inflammatory cell.[5] Histopathologically, the absence of atypical cells and abundant vascular channels helps to differentiate

pyogenic granuloma from Kaposi's sarcoma.[3] Bacillary angiomatosis consists of dense extracellular deposits of pale hematoxyphilic granules representing a bacterial material.[8] This features differentiates it from pyogenic granuloma. The late phase pyogenic granulomatous lesions can be mistaken for oral fibroma, peripheral giant cell granuloma, or peripheral ossifying fibroma due to the presence of extensive fibrosis in the connective tissue stroma.[3] However, the increased vascularity and the inflammatory components are suggestive of pyogenic granuloma which helps in differentiating it from these lesions.[3] Also, a prior history of bleeding from the granulomatous growth would be suggestive of the involutionary/healing phase.[3]

Conventional granulation is also considered as another differential diagonosis.[8] Despite the close association between pyogenic granuloma and conventional granulation tissue, pyogenic granuloma shows clinically different behaviour in comparison to conventional granulation tissue such as rapid growth and frequent recurrence.[8] Hyperplastic gingival inflammation can also be considered which on histopathology may be difficult to differentiate from pyogenic granuloma therefore in such cases pathologist must rely on the surgeons description of a distinct clinical mass to diagnose pyogenic granuloma.[8]

Peripheral giant cell granuloma(PGCG) clinically cannot easily be differentiated from pyogenic granuloma.[9] PGCG appears as a bluish to purple compared to red colored pyogenic granuloma.[9] Radiographically PGCG is more likely to produce bone resorption compared to pyogenic granuloma.[9] Histopathologically, PGCG differs from pyogenic granuloma in having multinucleated giant cells.[9] Peripheral ossifying fibroma can be differentiated from pyogenic granuloma by its firm and light pinkish colour.[9] Another characteristic feature of peripheral ossifying fibroma is alveolar bone involvement.[9] Hence, a careful clinical and histopathological correlation is of utmost importance in identifying pyogenic granuloma.

CONCLUSION

Pyogenic granuloma is a benign inflammatory lesion resulting from an exaggerated response to chronic low-grade irritation. Despite various treatment options, recurrence rate is frequent. The patient follow-up is a must in preventing the recurrence of pyogenic granuloma. Hence, knowledge of the various histopathological presentation of pyogenic granuloma is necessary for proper understanding of the lesion in terms of diagnostic accuracy along with clinical correlation and also to rule out various soft tissue lesions with similar appearance.

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