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Case Report

Dentistry Section

An Insight into Pyogenic Granuloma with Ossification: Exploring a Unique Association

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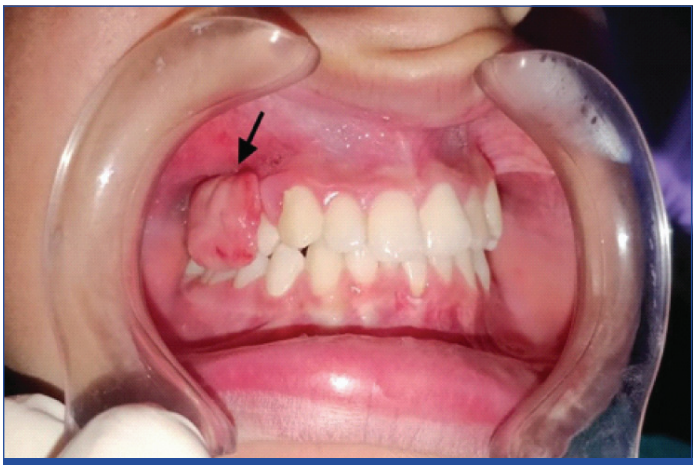
ABSTRACT

Pyogenic Granulomas (PG) are reactive hyperplastic lesions that are formed in relation to some chronic irritation, physical trauma or hormonal factors. The PG may present in various clinical and histological forms. These often present as a smooth lobulated exophytic lesions and at times may show a marked resemblance to Peripheral Ossifying Fibroma (POF). However, the characteristic histologic presentation helps in differentiating both the lesions. Microscopically, presence of ossification in pyogenic granuloma is not common and could possibly indicate an altered response of the connective tissue stroma. The present case report shows occurrence of pyogenic granuloma in a 12-year-old female which on histological examination not only exhibited proliferating blood vessels, endothelial cells and inflammatory cells which are typical features of pyogenic granuloma but also exhibited areas of ossifications which are not frequently encountered in PG. It is important to explore the underlying aetiological factors that could lead to formation of such ossifications. It has been suggested that pyogenic granuloma and peripheral ossifying fibroma could represent part of same spectrum of focal reactive lesions. However, it is still considered that these two lesions are separate clinical entities and the histologic presentations are different and unique to both of them.

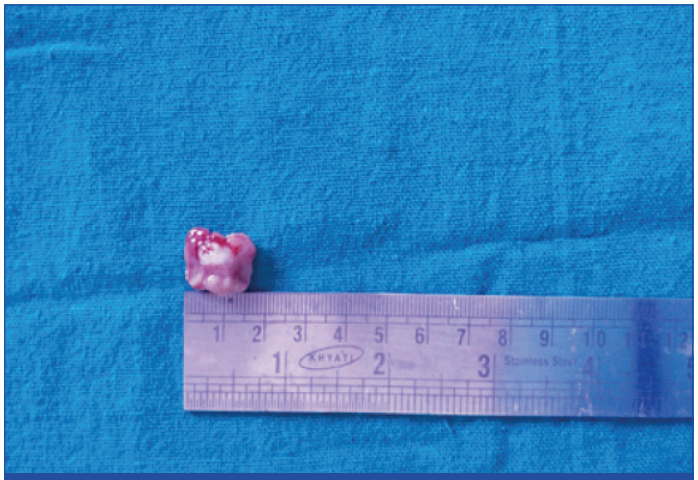
Keywords: Gingiva, Hormonal, Osteoid, Reactive lesions

CASE REPORT

A 12-year-old female patient, reported with a chief complaint of soft tissue overgrowth from the gums in the upper right back tooth region. The patient noticed the growth two months back. Though the growth was small initially, but it gradually increased to the present size. On clinical examination, it was found to be pedunculated, painless and was soft to firm in consistency. The growth measured around 2.0×1.5 cm in size extending from distal surface of 14 to mesial surface of 16 arising from interdental papilla [Table/Fig-1]. Periodontal evaluation did not reveal periodontal pockets but plaque was observed. There was no remarkable finding seen in the Intraoral Periapical Radiograph (IOPA). On the basis of clinical and radiographic examination a provisional diagnosis of pyogenic granuloma was made. Differential diagnosis included peripheral ossifying fibroma, peripheral giant cell granuloma, irritational fibroma as these lesions mimic each other clinically, but histopathology can confirm the diagnosis. Oral prophylaxis was performed followed by an excisional biopsy of the lesion which was carried out with scalpel followed by curettage and through scaling of the involved tooth. Excised tissue was sent to the Department of Oral Pathology for histopathological examination [Table/Fig-2].



[Table/Fig-1]: Gingival overgrowth extending from distal surface of 14 to mesial surface of 16.

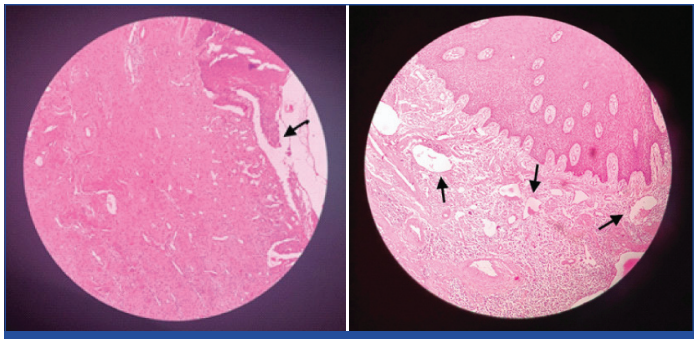


[Table/Fig-2]: Gross specimen.

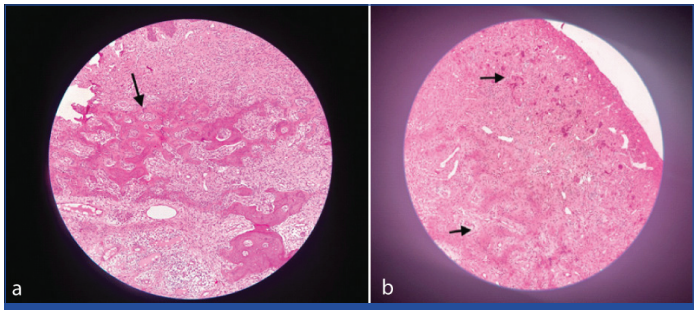
Microscopically, the excised tissue exhibited proliferative hyperplastic stratified squamous epithelium which was ulcerated in one area [Table/Fig-3]. The underlying connective tissue stroma showed presence of numerous blood vessels, proliferating endothelial cells, dense chronic inflammatory cell infiltrate, and areas of calcification [Table/Fig-4]. Calcifications were in the form of bony trabeculae exhibiting osteocytes and osteoblastic riming. In a few areas, acellular basophilic calcifications were also noted [Table/Fig-5a,b]. Based on the presence of numerous blood vessels, proliferating endothelial cells and the dense inflammatory infiltrate a diagnosis of pyogenic granuloma was made. Since areas of ossification were additional findings, the lesion was diagnosed as pyogenic granuloma with ossification. The patient was followed-up and no recurrence was reported.

DISCUSSION

Benign growths are often observed in oral cavity. These could be developmental in origin, an inflammatory lesion, a reactive or a hyperplastic lesion or could be some cyst or a neoplasm [1]. The PG is one of the reactive lesions that may be encountered in oral cavity. The term PG or granuloma pyogenicum was given by



[Table/Fig-3]: Haematoxylin and Eosin stained microscopic picture exhibiting ulcerated epithelium and connective tissue stroma (20x); **[Table/Fig-4]:** Haematoxylin and eosin stained section exhibiting stratified squamous epithelium and connective tissue stroma showing numerous proliferating blood vessels and moderately dense chronic inflammatory cell infiltrate (20x) (Images from left to right).



[Table/Fig-5]: a) Haematoxylin and eosin stained section exhibiting areas of ossification within connective tissue stroma (20x); b) Microscopic picture exhibiting areas of ossification and areas of dystrophic calcification within connective tissue stroma (10x).

Crocker in 1903 though some researchers believe that the term was coined by Hartzell in 1904 [1,2]. The lesion has been referred to as granuloma pediculatumbenignum, pregnancy tumour, vascular epulis, and Crocker and Hartzell's disease [3]. Since, it is associated with abundant blood vessel proliferation it was referred as hemangiomatous granuloma by Angelopoulos AP and Granuloma Telangietacticum by Cawson RA et al., [4].

Clinically, pyogenic granulomas are usually asymptomatic, slow growing, painless lesions and of size ranging from few millimeters to several centimeters. These lesions present as a pedunculated or sessile mass. Depending on the course of lesion and vascularity the colour may vary from pinkish to reddish in appearance [5]. In the present case, the lesion presented as a pinkish pedunculated lesion. The PG has a predilection to occur on gingiva and is more common in maxillary anterior region than posterior region [6]. In the present case, the lesion was located in maxillary posterior region extending from distal surface of 14 to mesial surface of 16. Extra gingival location of oral pyogenic granuloma has also been reported where lesion can occur on buccal mucosa, lips, tongue, palate [1]. The PGs are considered as reactive lesions. These are often associated with exuberant connective tissue proliferation and usually develop as a result of some chronic low grade irritation, hormonal imbalance or may be due to some injury to that issue [7]. It has also been suggested that frequent trauma from tooth brushing can also cause formation of such lesion [8]. In the present case, the girl was in early adolescence period which is often associated with fluctuating hormonal levels [9]. Even a slight trauma in any form could possibly contribute to the formation of a reactive lesion.

Hormonal influence on gingiva is a well documented fact. It is believed that female sex hormones play a significant biological action on oral cavity and have a role in in the pathogenesis [8]. Oestrogen and progesterone fluctuations are observed during puberty and this could be the reason that PG are seen in young females as it was seen in the present case where the lesion occurred in a 12-year-old female [10].

On microscopic examination, proliferating blood vessels, dense inflammatory cells within the connective tissue stroma were observed which are characteristic histopathological features of PG [6]. It has been suggested that gingiva may function as target organ for oestrogen and progesterone [11,12]. Receptors for oestrogen and progesterone have been demonstrated in gingiva indicating their action on gingival tissue. Female steroid hormones tend to increase expression of angiogenic factors in the local tissue which is responsible for increased vascularity of the lesion and also prevents the apoptosis of activated macrophages [13]. Elevated levels of progesterone lead to increased vascular dilation of the gingival tissues, increased production of prostaglandins, and are also responsible for the movement of polymorphonuclear leukocytes. These changes results in an exaggerated inflammatory response of the tissue and conversion of an inflammatory tissue in granuloma [14]. Further enlargement of granuloma could be influenced by angiogenesis and hormone dependent.

In the present case, in addition to characteristic histopathological presentation of PG areas of calcification in form of bony trabeculae and basophilic calcifications were also noted. Calcifications in form of bony trabeculae are not frequently seen in pyogenic granuloma and are not a characteristic finding of pyogenic granuloma, rather such calcifications are seen in peripheral ossifying fibroma [14]. Possibility of calcifications can be attributed to varying levels of progesterone seen in prepubertal phase. Progesterone has been seen to have an influence on osteoblast to lay down osteoid tissue [15]. Kim ES et al., observed calcifications in cutaneous pyogenic granuloma [16]. It has been suggested that inflammation or low oxygen environment leads to osteoblast differentiation and formation of bone. Another possibility for ossification which has been suggested is that a local tissue injury favours formation of dystrophic calcification which subsequently ossifies. Local factors in terms of calcium and phosphorus ions, pH also influence ossification [16]. In a study by Elanagai R et al., stromal fibroblast within the pyogenic granuloma shows expression of osteopontin [14]. Osteopontin has a high calcium binding potential. This could be a contributing factor for ossification in pyogenic granuloma. Narwal A and Bala S has proposed that inflammation in pyogenic granuloma induces release of cytokines which further stimulate osteogenic differentiation of the cells and thereby contribute to ossification or the mineralisation process. They observed a positive osteopontin expression around the blood vessels and in stroma which justifies the occurrence of calcifications [17].

Sridhar R et al., have proposed that pyogenic granuloma and peripheral ossifying fibroma are interconnected wherein a long standing pyogenic granuloma undergoes maturation and converts into peripheral ossifying fibroma [18]. It has been suggested that PG and POF could be lesions of same spectrum of the disease, where as some consider POF as a separate clinical entity [19].

In the present case the clinical and histological presentation could be attributed to the possibility of fluctuating hormonal levels that can be seen in younger females. Zia A et al., have also proposed that hormonal imbalance during puberty could play a contributory role in development of PG [20]. However, it is uncommon to see pyogenic granuloma to be associated with ossifications or calcifications [21]. Whether inflammation plays a role in osteogenic differentiation of cells in pyogenic granuloma or ossification is representation of a reaction of tissue to some irritation or such association of ossification in pyogenic granuloma is to be considered as a transition stage of development and conversion of pyogenic granuloma into peripheral ossifying fibroma needs to be explored [21].

Management of pyogenic granuloma includes complete surgical excision with deep curettage and removal of aetiologic factors. Recurrence may occur in cases of incomplete excision or failure to eliminate aetiologic factor necessitating the need of a follow-up [1,20].

CONCLUSION(S)

Pyogenic granulomas are reactive lesions which can exhibit a varied clinicopathological presentation. Local grade irritation, trauma is often associated with development of lesion however it is important

to understand that female sex hormones also play a significant role in modifying the response of gingival tissue to the local irritant there by contributing to the development of the lesion. Surgical excision with deep curettage is the treatment of choice in minimising the recurrence of lesion.

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