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CASE REPORT

Verruciform Xanthoma-Histopathologically: A Distinct Entity

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ABSTRACT

Verruciform xanthoma (VX) is an uncommon benign muco-cutaneous lesion of unknown etiology. It is essential to diagnose this lesion as a varied entity of utmost importance as clinically their appearance could range from a simple leukoplakia or papilloma to as grave as squamous cell carcinoma SCC. Although this lesion is of multifactorial pathogenesis, a viral etiology like human papilloma virus (HPV) has been suggested in some cases. This rare, harmless lesion usually presents as a sessile or pedunculated, pale yellowish-to-red, papillary, granular or verrucous mucosal growth. Histopathologically, VX is characterized by the presence of parakeratinzed epithelium showing papillary or verrucous growth with thin rete ridges and connective tissue papillae extending up to the surface. The papillae characteristically consist of foam cells, also called xanthoma cells. We report two cases of VX of varied clinical appearance but very similar and characteristic histopathological presentation to be diagnosed as VX. The clinical diagnosis, though may be challenging; the histopathological features are diagnostic and well-defined. It is also noteworthy that in an improper biopsy, xanthoma cells may be scanty and their presence can be missed, especially if one is unfamiliar with the existence of this lesion.

Keywords: Verruciform xanthoma, Foam cells, Masticatory mucosa.

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INTRODUCTION

Verruciform xanthoma (VX) is an uncommon benign, hyperplastic lesion primarily of the oral mucosa, first described by Shafer in 1971.[1] Verruciforms xanthomas are usually asymptomatic, solitary and slow-growing lesions. Verruciforms xanthoma appears as a well-defined, sessile growth having smooth margins with papillary, granular or verrucous appearance.[2,3] Males are affected slightly more than females and the most frequently affected intraoral sites are gingiva, alveolus and hard palate.[2-4] The lesion probably represents an unusual reaction or immune response to localized epithelial trauma or damage. The hypothesis of an unusual reaction or immune response to localized epithelial trauma is supported by cases of VX that have developed in association with disturbed epithelium like lichen planus, lupus erythematosus, epidermolysis bullosa, epithelial dysplasia, pemphigus vulgaris, warty dyskeratoma, graft-*vs* host disease.[5] Clinically, it is seen as a well demarcated, soft, painless, sessile, elevated mass with papillary or roughened surface with an average size of 2 cm.[4] Histopathologically, foam cells are the characteristic of the lesion along with hyperplastic parakeratinzed squamous epithelium with elongated rete ridges of relatively uniform depth.[3,4]

Here, we report two cases of VX of varied clinical appearance but very similar and characteristic histopathological presentation.

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CASE REPORTS

Case I

A 30-year-old male patient complained of gingival growth in his upper front region of the jaw since 2 to 3 months. Patient was apparently normal 2 to 3 months back after which he developed a painless small triangular gingival growth on the labial aspect of interdental papilla of 11 and 21 which had gradually increased to the present size. There was no pain, bleeding or trauma associated with the gingival growth. No aggravating or relieving factors were associated with the growth. Root canal treatment was done with 11 and 21 and porcelain fused metal bridge given from 14 to 22, 4 to 5 years back. All vital signs were within the normal range. Medical history was noncontributory. Intraorally, on inspection a localized gingival enlargement was present in the interdental papilla of 11 and 21 region approximately 1 × 2 cm in size and reddish-pink in color (Fig. 1). The localized gingival enlargement was well-defined, sessile having smooth margins and rough pebbly surface. On palpation, the enlargement was nontender, soft to firm in

consistency and was clearly demarcated from the adjacent apparently normal attached gingiva. There was no bleeding on probing, pockets or any other secondary changes. Considering the clinical features, a provisional diagnosis of papilloma, pyogenic granuloma, peripheral giant cell lesion, fibrous epulis and VX was made. An excisional biopsy was performed and sent for histopathological analysis.

H & E stained soft tissue section shows parakeratinized stratified squamous epithelium with papillary surface (Fig. 2). The connective tissue stroma comprises collagen fibers, blood vessels and numerous foam cells which are restricted to papillary layer of lamina propria. Moderate degree of chronic inflammatory cell infiltration is also seen (Fig. 3). Correlating the clinical and histopathological features, we arrived on the diagnosis of VX.

Case II

A 37-year-old male patient complained of growth in his upper left back region of the jaw since 1 to 2 months. Patient was apparently normal 1 to 2 months back after which he noticed a growth in left posterior palatal region involving the palatal gingiva and extending onto the hard palate. The growth had not increased in its size since its first appearance. Patient also experienced mild, intermittent type of pain since 15 days. No aggravating or relieving factors were associated with the growth. All vital signs were within the normal range. Medical history was noncontributary. Intraorally, on inspection, a well-defined, sessile nodular growth was present on palatal gingiva in relation to 26, extending on to the hard palate, with rough and pebbly surface measuring about 1 × 2 cm in size and reddish in colour (Fig. 4). On palpation, lesion was soft, tender with rough surface texture. Considering

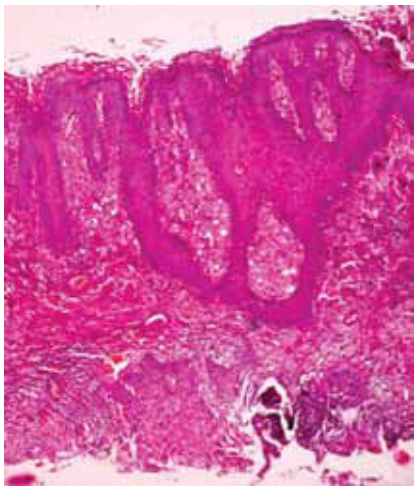

Fig. 1: Intraoral view shows localized gingival enlargement in the interdental papilla of 11 and 21 regions

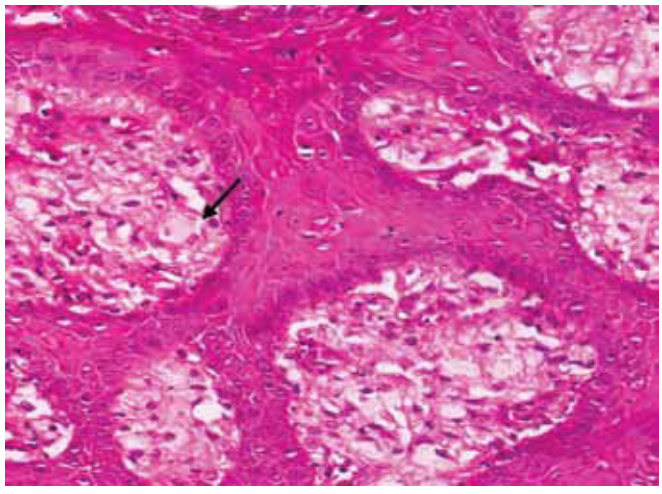

Fig. 2: H & E (40x) stained soft tissue section shows parakeratinized stratified squamous epithelium with papillary surface along with connective tissue papillae of variable length and thickness

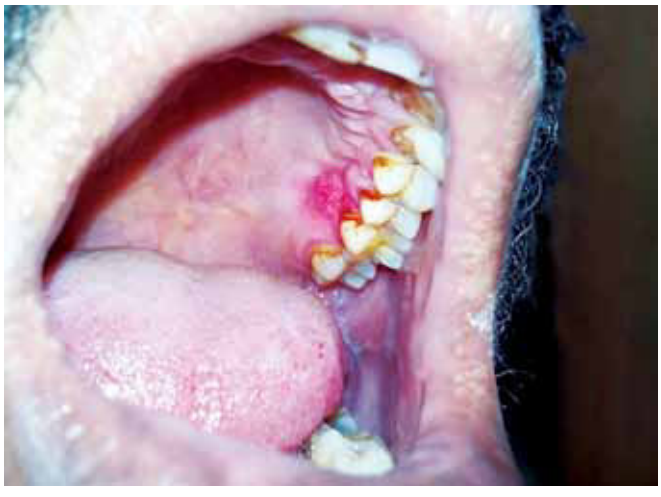

Fig. 3: H & E (400x) stained soft tissue section shows foam cells with clear-to-granular eosinophilic cytoplasm and eccentrically placed nuclei. Moderate degree of chronic inflammatory cell infiltration is also seen

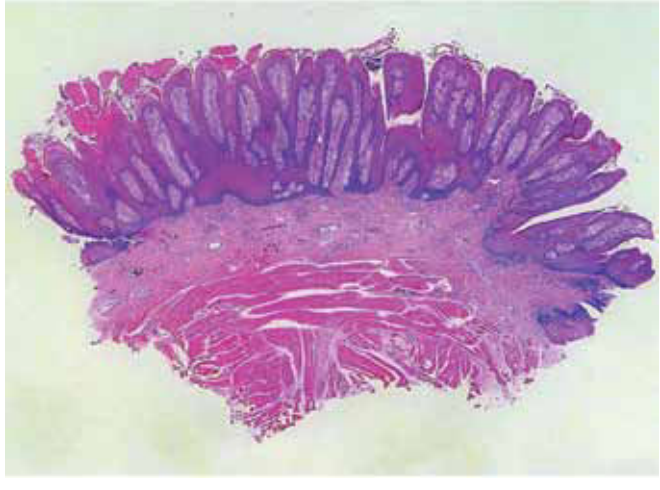

Fig. 4: Intraoral view shows well-defined, sessile nodular growth present on palatal gingiva in relation to 26 and extending onto the hard palate

the clinical features, a provisional diagnosis of non-homogenous leukoplakia, mucocutaneous lesion and VX was made. An excisional biopsy was performed and sent for histopathological analysis.

H & E stained soft tissue section shows parakeratinized stratified squamous epithelium with papillary surface (Fig. 5). Shallow clefts filled with parakeratin are seen between the epithelial projections. Uniform and elongated reteridges with foam cells entrapped in the connective tissue papillae are evident (Fig. 6). The sparse connective tissue shows few blood vessels and scanty inflammatory cells. Clinicopathologically, the diagnosis of VX was made.

DISCUSSION

Verruciform xanthoma manifests as a solitary, asymptomatic, slow-growing plaque or nodule with a papillary, granular or verrucous surface and sharply delineated margins that may appear pink, red, yellow, or white in color.[6] Approximately 75% of all oral VX lesions occur on the masticatory mucosa of the palate, gingiva or alveolar ridge. In the largest series of 282 cases of oral VXs reported by Philipsen et al, the most commonly affected site was the gingiva (57.4%), followed by the tongue (10.3%), hard palate (7.1%), buccal or vestibular mucosa (6.7%), floor of the mouth (4.6%), and soft palate (3.2%). Oral lesions of VX are mostly seen in males, with a male-to-female ratio of 1.1:1. Both our cases are in accordance with the literature as VX appeared in male patients and presented on the masticatory mucosa.

The etiopathogenesis of VX is unclear but appears to be associated with localized inflammation. Immunologic factors and viral etiologies have been also suggested. The prevailing theory is that epithelial tissue damage results in the breakdown of the phospholipid-rich cell membranes releasing lipids that are then taken up by the macrophages within the connective tissue that become lipid-laden or foamy in appearance. An immunologic pathogenesis has been suggested because of the predominant T cells infiltrate and decreased number of Langerhans cells in oral VX compared to normal tissue. Human papillomavirus (HPV) has not been demonstrated in VX lesions and viral particles have not been identified ultrastructurally.[7]

Based on light and electron microscopic studies, Zegarelli et al proposed that foam cells are lipid-laden macrophages and oral VX may develop as a consequence of epithelial entrapment with subsequent degeneration and lipid accumulation.[8] They suggested a local irritant as the initiator of the disease process, because oral VX is frequently found on masticatory mucosa where localized trauma is very common. The predominant cells in the inflammatory infiltrate were T cells (51.8 ± 2%), and (43.3 ± 2)% were positive for human leukocyte antigen DR antigens. They suggested that an immune response may play a role in VX pathogenesis.[7,8] Zegarelli et al introduced the concept that the cause of accumulation of lipid-containing macrophages is epithelial degeneration. The products of epithelial breakdown elicit an inflammatory response which is manifested by a predominant neutrophil infiltrate in the epithelium and a subsequent release of lipid material through the epithelium which finally is scavenged by the macrophages. They also suggested that a 'local irritant' could act as the initiator of this process. The fact that 70% or more of all VXs are located on the masticatory oral mucosa which is constantly subjected to trauma from mastication as well as to the sensitizing agents of foodstuffs, this theory seems quite plausible.[8,9]

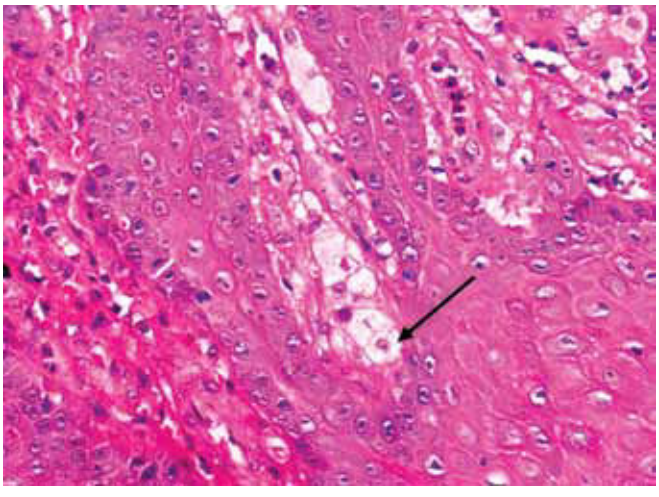

Fig. 5: H & E (40x) stained soft tissue section shows parakeratinized stratified squamous epithelium with papillary surface and elongated rete ridges uniformly extending into the underlying connective tissue

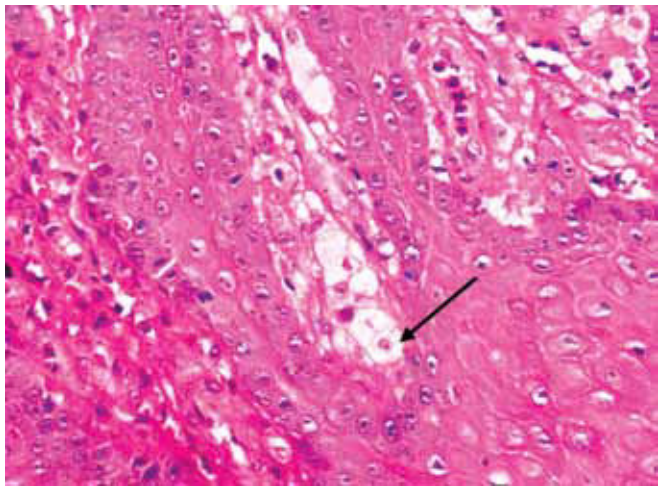

Fig. 6: H & E (400x) stained soft tissue section shows uniform and elongated rete ridges with foam cells entrapped in the connective tissue papillae are evident. The sparse connective tissue shows few blood vessels and scanty inflammatory cells

The differential diagnosis of VX includes: squamous papilloma, verruca vulgaris, condyloma acuminatum, verrucous carcinoma (VC) and squamous cell carcinoma (SCC). The presence of foamy macrophages, distinctive papillary epithelial proliferation, brightly eosinophilic parakeratin with keratin squames and neutrophilic infiltration are the characteristic features of VX that would help it in distinguishing from the above mentioned lesions.[10] Histologically, the differential diagnosis from VC is clearly an important one. The marked acanthosis with minimal or no atypia, and the presence of keratin-filled crypts are among the shared features. Squamous papilloma does not contain lipid-laden macrophages (foam cells) like VX, thus can be differentiated histologically. Xanthoma cells are also not a feature of either verruca vulgaris or condyloma acuminatum. The vacuolation of epithelial cells in the upper epidermis that is prominent in verruca vulgaris and condyloma acuminatum, is either absent or inconspicuous in VX. Presence of invasive epithelial proliferation, parakeratin plugging, pushing border and the lack of foamy histiocytic infiltrate would help in distinguishing VC from VX. Absence of cellular architectural atypia and breach in basement membrane as in SCC, exclude the possibility of VX.[3]

Surgical excision is treatment of choice for VX. The prognosis for VX is excellent and recurrence is extremely rare.

CONCLUSION

We report two cases of VX of varied clinical appearance but very similar and characteristic histopathological presentation. The clinical diagnosis, though may be challenging; the histopathological features are diagnostic and well-defined. It is also noteworthy that in an improper biopsy, xanthoma cells may be scanty and their presence can be missed, especially if one is unfamiliar with the existence of this lesion.

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