10.5005/jp-journals-10037-1128

CASE REPORT

Verruciform Xanthoma: An Unusual Lesion of Tongue—A Case Report and Review of Literature

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ABSTRACT

Verruciform xanthoma (VX) is a rare entity and we could procure only very few publications in the literature. This innocuous lesion with a sessile or pedunculated base is normal, reddish in color but occasionally pale or hyperkeratotic with rough or pebbly surface; 75% of VX occurs in masticatory mucosa, gingiva, and palate and very few occurs in buccal mucosa, floor of the mouth, and rarely in the tongue. Our case on the tongue exhibited papillary or verrucous proliferation of squamous epithelium associated with hyperkeratosis and with copious foamy cells confined to lamina propria papillae. The hallmark of VX is the presence of vacuolated foam or xanthoma cells. The xanthoma cells have been shown to be cells of the monocyte/macrophage lineage. The exact etiopathogenesis of VX is not fully known, but various concepts have been postulated. Recurrence is unusual after surgical removal.

Keywords: Recurrence, Verruciform xanthoma, Xanthoma cells.

How to cite this article: Rajalakshmi G, Vinod S, Anjana R, Mathews PP, Rajan R. Verruciform Xanthoma: An Unusual Lesion of Tongue—A Case Report and Review of Literature. Oral Maxillofac Pathol J 2018;9(1):42-46.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Verruciform xanthoma was first described by Shafer.[1] It occurs mainly in the oral mucosa, with spasmodically extraoral cases being reported, inclusive of those on penis,[2] scrotum,[3] and vulva.[4] The term xanthoma is derived from the Greek word xanthos, meaning yellow. Originally, xanthoma was used to define a yellowish, slightly raised or flat lesion occurring on the skin, propounding an underlying illness. Oftentimes, lipid material accumulates in reticuloendothelial cells in various sites of the body. The phenomenon of xanthoma occurs beneath the epithelial surface, thus giving a yellow tan hue to the cutaneous lesions.[5] Most VX have been misdiagnosed clinically as papillomas and occasionally as verrucous carcinomas or squamous cell carcinomas.[6] Histologically, VX is characterized by papillary or verrucous proliferation of squamous epithelium associated with hyperparakeratosis and numerous foamy cells.

These xanthoma cells are confined within lamina propria papillae and do not extend below rete pegs tips level.[1,7,8] Zegarelli et al[9] validated the presence of macrophages containing lipid in VX. The macrophagic nature of foamy cells has been confirmed by immunohistochemical studies.[8,10] The etiology and pathogenesis of VX still remain enigmatic. The presence of S100-positive Langerhans cells in the epithelium and connective tissue of lesions suggests that VX is at least relatively mediated by immune mechanism.[8,11]

CASE REPORT

A 35-year-old male patient presented with a white patch on the left side of his tongue which he spotted since 3 days. There was no associated pain, difficulty in mouth opening and chewing or articulating. He had history of smoking for 2 to 3 years back and later ceased. He also had a habit of keeping hans (a smokeless tobacco product) in the upper anterior gingiva and vestibule for the past 8 months. On intraoral examination, a white plaque-like lesion of approximate size 1.5 × 1.5 cm was noticed on the left posterolateral aspect of tongue irt 36, 37 (Fig. 1). Shape and borders were irregular, the surrounding area was nonerythematous. On palpation, the lesion was nontender, nonscrapable, and was slightly firm in consistency with irregular borders. No induration was present, and the surface of the lesion was raised from adjacent normal mucosa. Based on history and clinical examination, we framed a provisional diagnosis of homogeneous leukoplakia. Later, an excisional biopsy was performed (Fig. 2). Histopathology revealed areas of parakeratinized stratified squamous epithelium with elongated rete ridges at a uniform level (Figs 3 and 4). Epithelium also showed areas of koilocytic changes, dyskeratosis, and loss of cohesion. Subepithelial areas showed sheets of large foamy macrophages (xanthoma cells; Fig. 5). The cytoplasm of these cells seemed to be granular and the nuclei either

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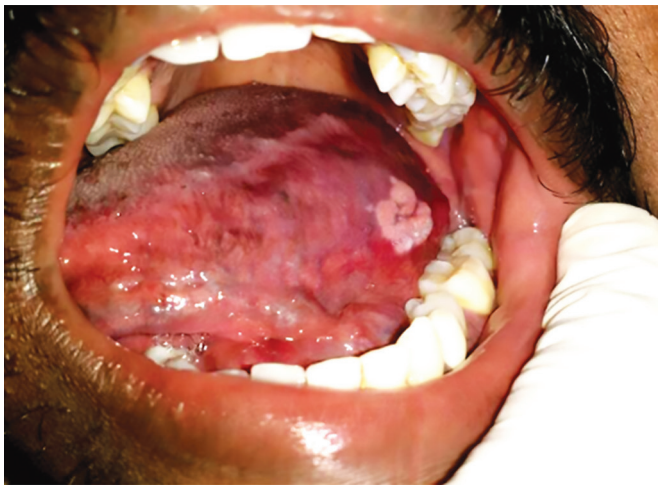

Fig. 1: Plaque-like lesion on the left posterolateral aspect of the tongue

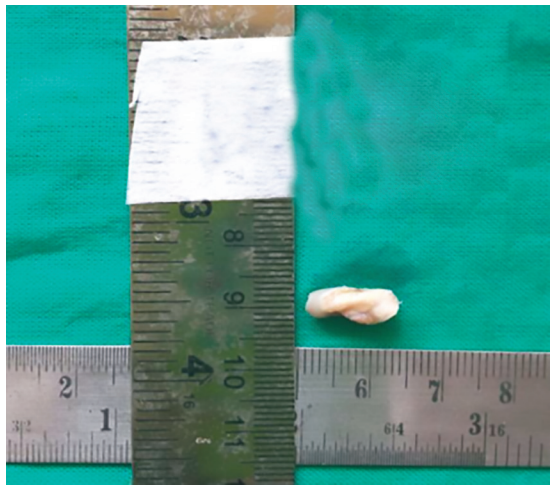

Fig. 2: Excisional biopsy specimen

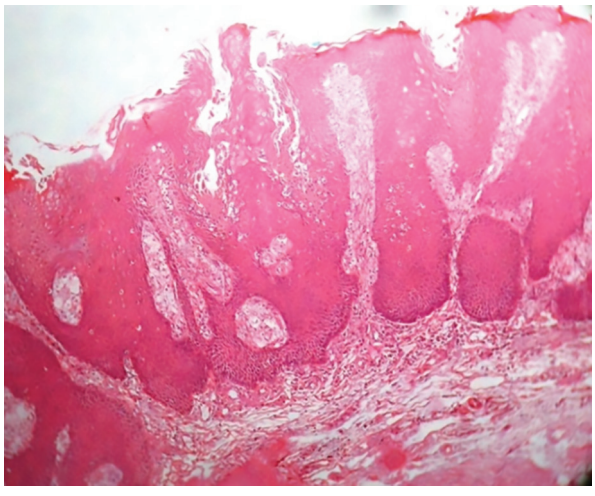

Fig. 3: Papillary or verrucous proliferation of squamous epithelium associated with hyperkeratosis (10× view)

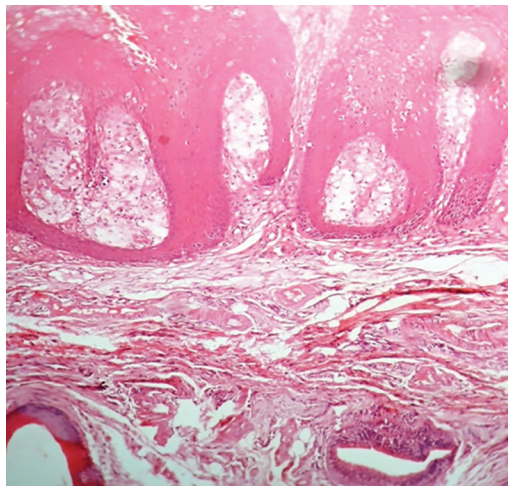

Fig. 4: Numerous foamy cells confined to lamina propria papillae (10× view)

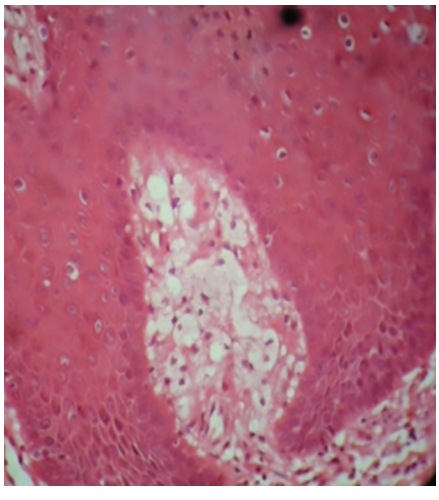

Fig. 5: Xanthoma cells (40× view)

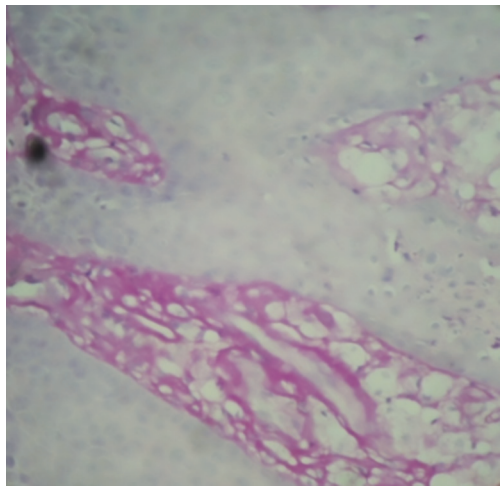

Fig. 6: Large eosinophilic granular cells showing PAS positivity

small round or were eccentrically placed. The connective tissue stroma showed a moderate subepithelial chronic inflammatory infiltration. The granules of foam cells were slightly periodic acid–Schiff (PAS) positive (Fig. 6).

DISCUSSION

Data regarding the prevalence or incidence of oral VX are unexceptionally little. Verruciform xanthoma is a rare entity accounting for 0.025 to 0.095% of all cases with an

unknown etiopathology.[12] From the available epidemiological data, oral VX is present in males below the age of 50, with a female-to-male ratio of 1:1.6 and the ratio reverses to 1:0.8 after the age of 50 years. Concerning the ethnic origin, oral VX is more common in Caucasians and rare in Asian population. The duration of lesion varies from a few weeks to 10 years.[13] Clinically, VX has been variously described, but principally, the oral lesions are described as asymptomatic, roughened, papillary or cauliflower-like lesions with sessile or rarely pedunculated base, and the size ranges from 0.2 to 4 cm.[14]

Etiology and pathogenesis of oral VX are still far from being clarified, though reactive, immunological, infectious, and genetic mechanisms have been considered. The prominent accumulation of lipid-laden cells within the lesions has strongly suggested the association with systemic lipid abnormality.[14] But van der Waal et al[15] suggested that the lesion does not seem to be associated with systemic abnormality of lipid metabolism. Its association with the underlying inflammatory disorders of oral mucosa, such as blisters, lichen planus, pemphigus vulgaris supports that VX is a reactive process initiated by inflammatory reaction rather than a true neoplasm. But Travis et al[16] have reported a case associated with systemic unknown lipid storage disease.

Zegarelli et al[9] put forward the concept that the cause of accumulation of lipid-containing macrophages was epithelial degeneration. The products of epithelial breakdown elicit an inflammatory response which is manifested by a predominant neutrophil infiltrate in the epithelium and the subsequent release of lipid material through the epithelium which is finally scavenged by macrophages. He also suggested that local irritant acts as an initiator in this process. Based on the fact that 70% or more of all VXs are located in the masticatory oral mucosa which is constantly subjected to the trauma of mastication as well as to the sensitizing agents of foodstuffs, this theory may seem quite plausible. The presence of inflammatory cells and colonies of microorganisms points toward an inflammatory response.

Cobb et al[17] recommended that VX is inflammatory in origin as the lesion is predominantly present in masticatory mucosa.

However, many authors suggest that VX is less common secondary to inflammation or irritation and foam cell deposition may be abundant where epithelial breakdown is limited.[16]

Many authors substantiate that damage to squamous cells due to trauma, irritation, or infection can cause increased epithelial turnover results in epithelial breakdown, leading to inflammatory response and subsequent release of lipid material from the degenerated cells.[18] But VX has been reported in the oral regions, such as the floor of mouth and soft palate where trauma is minimal. The VX occurs in patients using snuff or indulging in the habit of chewing tobacco, possible etiological factors that Buchner et al could not subscribe to, as they denied the VX being inflammatory in nature.[19,20]

Rowden et al[11] demonstrated dendritic cells among the mononuclear inflammatory infiltrate of VX lesions. These Langerhans cells were located at the base of the lesions and to a lesser extent among the foamy cells. Thus, they suggested that VX belongs to a new category of non-X histiocytosis in which the presence of Langerhans cells suggests an immunologic pathogenesis.

Mostafa et al[8] validated the presence of macrophage marker (CD68) in the foamy cells of VX, thus determining the macrophagic nature of these cells.

Mohsin et al[21] betokened human papillomavirus (HPV) as a putative pathogen because of the condyloma-like architectural appearance of VX. However, most investigators have not found any evidence for the presence of HPV in oral VX. But only recently, Khaskhely et al[22] described an association of HPV with extraoral VX. Thus, a possible relationship between VX and HPV is not fully clarified. Neville and Weathers[19] noticed PAS-positive fungal hyphae compatible with *Candida albicans* in parakeratotic layers.

Recently, four cases of VX occurring within lichen planus of the oral mucosa have been reported. Based on their data, the authors recommended that the condition of altered epithelial turnover, as in repeated epithelial desquamation, would give rise to the VX.[23] Furthermore, VX and oral lichen planus may occur concomitantly without having a specific causal relationship between them.[24] Missense mutations in exon 6 of 3-beta hydroxysteroid dehydrogenase have been reported in solitary VX.[25]

Histopathologically, oral VX is characterized by a squamous epithelial surface of varying morphology covered with parakeratin, showing elongated rete pegs of relatively uniform depth. The most pathognomonic feature of this lesion is the presence of large swollen "foam cells" or xanthoma cells, which fill the connective tissue papillae between the rete pegs.[1] A variable degree of parakeratosis is observed that is usually marked in verrucous and papillary forms of VX with hyperparakeratosis present in the crypts in between papillae, although no increase in mitosois is observed. Pseudoepitheliomatous hyperplasia is not usually seen, but connective tissue papillae are of variable length and thickness and often extend close to the surface.[26]

Nowparast et al[5] demonstrated three different architectural appearances of oral VX on low-powered microscopy. Pattern A, a wart or verrucous appearance which

is usually elevated, is well circumscribed but does not show thick stratum granulosum like verruca vulgaris. There is hyperparakeratosis, acanthosis, and elongation of rete ridges. Pattern B papillary or cauliflower architecture, which has many finger-like projections composed of stratified squamous epithelium containing connective tissue core, forming crypt-like spaces covered by parakeratin, often extends above the mucosal surface. Pattern C flat type, epithelial proliferation is seen below the surface with variable elongation of rete ridges which may be slender or of uniform depth. The connective tissue papillae extend almost to the surface only separated from the outer surface by a few parakeratotic cell layers. There is only a thin layer of parakeratin, although a wedge-shaped plugging phenomenon may often be recognized. Parakeratosis is more intense in verrucous and papillary form.

Neville and Weathers[19] suggested that parakeratin exhibits an orange color in hematoxylin and eosin staining which sharply demarcates the remaining epithelium.

Mostafa et al[8] suggested that elongation of epithelial rete ridges is illusory and is not a proliferation of epithelial cells with downgrowth of rete pegs, but rather results from the upward pushing effect of macrophages toward the epithelium. The side pressure exerted by the macrophages leads to the thinning of rete ridges through the compression of epithelial cells which may display a relatively spindle cell appearance rather than a polygonal one. Collections of microorganisms may present upon the epithelial surface and within the parakeratin invaginations. Neville and Weathers[19] noticed PAS-positive fungal hyphae compatible with *C. albicans* in the parakeratotic layers. A slight to moderate degree of chronic inflammatory cell infiltration consisting mainly of lymphocytes is observed in the subepithelial connective tissue. However, the hallmark feature of VX irrespective of intraoral or extraoral location is the presence of vacuolated foam cells or xanthoma cells. The PAS stains show many xanthoma cells to contain tiny PAS-positive granules in cytoplasm. Scharlach and Sudan III stains reveal an abundance of cytoplasmic lipid. No mucicarminophilic or alcinophilic material has been noted.[9]

In most ultrastructural studies, these cells demonstrated oval or elongated irregular nuclei with peripheral condensation of chromatin and intense nucleoli, and a variable number of lipid droplets and lysosomal structures. Plasma membrane showed long thin filamentous processes.[9,17] Mostafa et al[5] suggested that the foam cells were stained intensively with monoclonal antimacrophage antibodies (CD68, KP1 and PG-M1), moderately with antileukocyte common antigen, faintly with antilysosome and alpha-1-antichymotrypsin antibodies. Some studies showed S100 positive dendritic cells in the lesional connective tissue.[11]

However, as yet unrecognized factors may play a role in the development of VX, thus more comprehensive studies are needed to illustrate the nature of lesion.

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