Oral Verruciform Xanthoma: A Rare Entity

J.D Sunitha [1], Adusumilli Praveena [1], Ganesh Kulakarni [1], Vaddalapu Hari Priya [1]

Department of Oral Pathology & Microbiology, MNR Dental College & Hospital, Sangareddy, Telangana, India

Key words

Papillary lesions, xanthoma cells, histiocytes, parakeratin

Corresponding author address:

Dr. Adusumilli Praveena MDS

Associate Professor Department of Oral Pathology & Microbiology.

MNR Dental College & Hospital,

Sangareddy, Telangana, India

Email:drpraveenaadusumilli555@gmail.com

ABSTRACT: Verruciform Xanthoma (VX) is a uncommon hyperplastic condition affecting the epithelium, primarily involving oral mucosa. The exact etiology is unknown and numerous hypotheses have been proposed to elucidate the etipathogenesis. Most of the VX resemble papillary lesions and difficult to differentiate clinically but characteristic subepithelial accumulation of lipid -laden macrophages aid in the diagnosis of this rare entity. Here we report a rare case report of VX occurring in an uncommon location.

Introduction:

Verruciform Xanthoma (VX) was first described by Shafer in 1971, is an uncommon reactive papillary growth. It is primarily observed in the oral mucosa and very few cases are reported extra orally. Extraoral occurrence is rare typically linked to systemic conditions like lymphedema, epidermal nevi, and the CHILD syndrome (Congenital Hemidysplasia with Ichthyosiform erythroderma and Limb Defects). [1] Nonspecific reaction to local epithelial trauma or an immune reaction is thought to be etiopathogenesis of VX but the exact underlying mechanism is yet to be fully understood.[2]Most of the oral VXs instigate across in the middle and older persons between 40-70 years with no sex predilection. VX typically manifest as an asymptomatic, solitary growth with rough or a pebbly surface and the lesion is either sessile, or pedunculated and the color varies between white, yellow, and pink influenced by the thickness of the overlying

epithelium.[1,2,3]VX is often clinically diagnosed as papillomas, the definitive diagnosis relies on histopathological features. The key diagnostic feature presence of foamy histiocytes within the elongated connective tissue papillae. The nature and origin of foam/xanthoma cells remain a subject of ongoing debate. [1]Local surgical excision is preferred treatment for VX which is almost always curative with good prognosis.[2,4]

Case report:

A-45- year-old male patient presented to the Department of Oral Medicine and Radiology with the chief complaint of a painless growth on the left buccal vestibule in 38 region for 1 month and he had a history of sharp teeth irritating the buccal mucosa. On clinical examination, there was an exophytic growth is well defined, sessile with a pebbled surface and whitish patch on the centre measuring 2.5 × 2.5 cm in size.(Fig.1) It extends medio-laterally from the marginal gingiva of 38 to the buccal vestibule obliterating the vestibule, anterio-posteriorly from the distal aspect of 37 to the retro-molar area. On palpation, the lesion was non-tender and firm in consistency. Excisional biopsy was done and the histopathological examination showed hyperplastic, parakeratinized stratified squamous epithelium with parakeratin plugging and uniformly elongated retepegs. Underlying connective tissue showed widespread chronic inflammatory cell infiltration, and in the connective tissue papillary areas numerous macrophages with foamy cytoplasm were present suggestive of xanthocytes.(Fig.2, 3,4) On serological examination serum lipid profile was normal based on the clinical, serological and histopathological features a final diagnosis of verrucous xanthoma was established.

Discussion:

VX is an uncommon benign lesion and its first study and description was undertaken by Shafer in 1971. There are no conclusive studies on the incidence of VX but an approximate prevalence of 0.025%–0.094% has been reported.[2] Divergent perspectives exist regarding the etiopathogenesis resulting in the development of VX. Potential etiologic agents in VX include local trauma, inflammation, fungal and viral infections like candida and HPV, carcinoma in situ, have been considered. Tobacco, alcohol, allergy to dental material, and periodontal pathogens can act as triggering agents.[5-8] In some instances, VX has been associated with inflammatory conditions comprising discoid lupus erythematosus, lichen planus, pemphigus vulgaris, epidermal nevus/CHILD nevus, and dystrophic epidermolysis bullosa are reported.[9] These factors

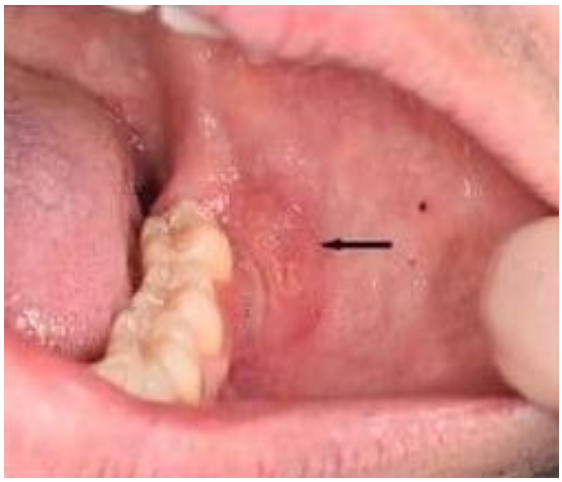

Figure 1: Clinical appearance of VX on the vestibular mucosa showing exophytic growth with a pebbled surface and whitish patch on the centre measuring 2.5 × 2.5 cm in size

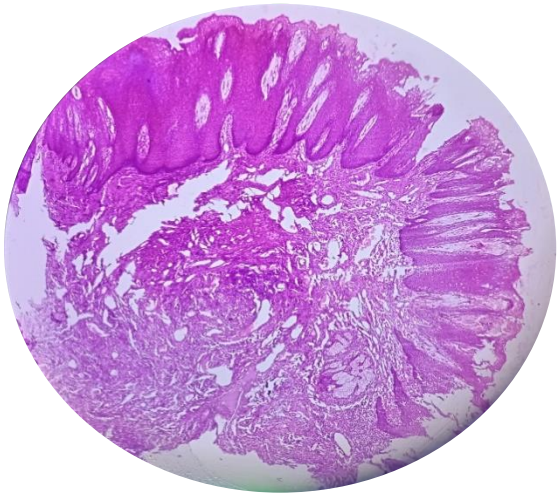

Figure 2: Microphotograph of VX in Scanner view showing hyperparakeratosis, acanthosis, uniform elongated rete pegs

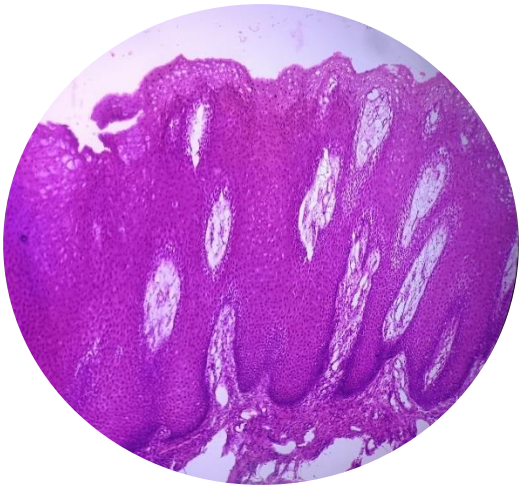

Figure 3: Microphotograph of VX in 100X illustrating foamy macrophages localized within the connective tissue papillae between the elongated rete-ridges.

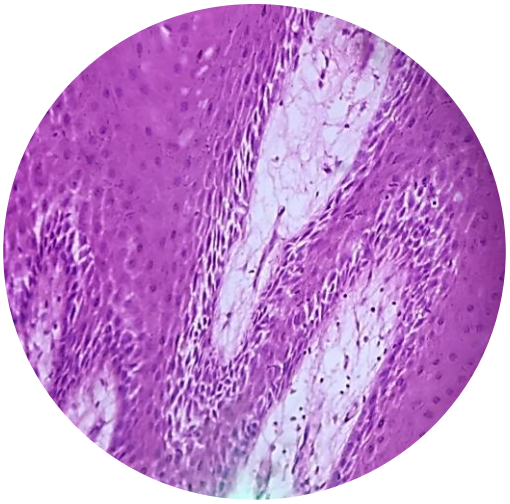

Figure 4: Microphotograph of VX in 400X depicting numerous foam cells with clear cytoplasm

contribute to an increase in the turnover as well as degeneration of squamous cells which in turn leads to an inflammatory response and consequently release the lipid material from the degenerated cells. As former studies stated that the squamous epithelium is an active site of lipid biosynthesis and conditions like chronic inflammation further increase lipid synthesis. [6-8] On analysing the membrane-

bound vacuoles in keratinocytes and foamy macrophages in the epithelium of VX provides additional ultrastructural evidence supporting this.[9]

As a degeneration by-product Lipids scavenged by macrophages, leading to the formation of foam cells in VX.[1] Majority of VX are observed between 40-70 years with no sex predilection. Approximately 57.4% of intraoral lesions are located on the gingiva, with tongue being secondary site at 10.3%, other locations include the hard palate (7.1%), buccal mucosa (6.7%), and floor of the mouth (4.6%). [11,12] In this particular case vestibular mucosa is involved, representing a relatively uncommon site for its occurrence. These lesions are often solitary asymptomatic, and slow-growing and rarely exceed 2 cm in diameter. Clinically, the surface of VX shows three morphological variants they are verrucous warty, papillary, cauliflower-like, and flat. Among them verruciform pattern is more prevalent which shows a papillary or pebbly appearance and the present case also showed pebbled surface. (Fig.1) Colour spectrum ranges from white to red occasionally with a yellowish shade depending on the thickness of the surface epithelium.[11] Current case showed normal surface mucosa with whitish patch in the centre. (Fig.1) Though Clinical features of VXs mimic papilloma they have distinctive histopathological features for diagnosis. They show hyperplastic parkeratotic stratified squamous epithelium with acanthosis, keratin plugging, and thin elongated uniform rete pegs with no evidence of dysplasia. The most important diagnostic feature is the presence of xanthoma cells or lipid-laden foam cells observed in the superficial connective tissue usually restricted to the connective tissue papillae between the elongated rete-ridges. [2]Present case also illustrated similar classic histopathological features. (Fig.2,3,4)There is an ambiguity regarding the cell of origin of these xanthoma cells. Mostafa et al observed strong cytoplasmic positivity for anti-CD68 in their immunohistochemical studies suggesting foam cells in VX derive from monocyte-macrophage lineage. Further studies confirmed this, with positive staining for cathepsin B, another macrophage marker and negative for S-100 eliminating the possibility of dendritic cell origin and confirming the monocytes/macrophages lineage. [8]VX treatment typically involves conservative surgical resection and recurrence or malignant transformation are exceptionally rare. Nonetheless recurrence occurred when the probable cause for chronic irritation was not removed.[11,13]

Conclusion: Clinical features of Verruciform xanthoma presents challenges

in definitively distinguishing from papillary lesions like papilloma, verruca vulgaris, verrucous carcinoma,
and occasionally squamous cell carcinoma. Nevertheless, the distinctive histopathological features like a hyperplastic para keratinized epithelium with elongated rete ridges of relatively uniform depth, parakeratin plugging between the epithelium projections, and numerous large foamy macrophage which are the hallmark of this lesion and their typical location in the connective tissue papillae helps in arriving at a definitive diagnosis. Although the VXs are rare lesions, the oral pathologist must be aware of these cases as the diagnosis is entirely depends on the histological features.

References:

1. Hegde U, Doddawad VG, Sreeshyla HS, Patil R. Verruciform xanthoma: A view on the concepts of its etiopathogenesis. Journal of oral and maxillofacial pathology: JOMFP. 2013 Sep;17(3):392.
2. Balasundaram T, Chattopadhyay PK, Desai AP, Semi RS, Kamalpathey K. Rare case of large verrucous xanthoma of oral cavity managed with nasolabial flap and review of literature. Oral and Maxillofacial Surgery Cases. 2020 Sep 1;6(3):100170.
3. Tamiolakis P, Theofilou VI, Tosios KI, Sklavounou-Andrikopoulou A. Oral verruciform xanthoma: Report of 13 new cases and review of the literature. Medicina oral, patologia oral y cirugia bucal. 2018 Jul;23(4):e429.
4. Garcia AS, Pagin O, da Silva Santos PS, Oliveira DT. Verruciform xanthoma in the hard palate: a case report and literature review. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2016 Dec;42(6):383.
5. Khaskhely NM, Uezato H, Kamiyama T, et al. Association of human papillomavirus type 6 with a verruciformxanthoma. Am J Dermatopathol 2000;22(5): 447–52.
6. Mohsin SK, Lee MW, Amin MB, et al. Cutaneous verruciform xanthomna: a report of five cases investigating the etiology and nature of xanthomatous cells. Am J Surg Pathol 1998;22:479–87.
7. Philipsen HP, Reichart PA, Takata T, Ogawa I. Verruciform xanthoma: biological profile of 282 oral lesions based on a literature survey with nine new cases from Japan. Oral Oncol 2003;39
8. Rawal SY, Kalmar JR, Tatakis DN. Verruciform xanthoma:

immunohistochemical characterization of xanthoma cell phenotypes. J Periodontol 2007;78(3): 504–9.

9. Farahani SS, Treister NS, Khan Z, Woo S-B. Oral verruciform xanthoma associated with chronic graft-versus host disease: a report of five cases and a review of the literature. Head Neck Pathol 2011;5(2):193–8.
10. Ide F, Obara K, Yamada H, Mishima K, Saito I, Kusama K. Cellular basis of verruciform xanthoma: Immunohistochemical and ultrastructural characterization. Oral Diseasaes 2008;14:150-7.
11. Neville B. Epithelial pathology. In: Neville B, Damm D, Allen C, Bouquot J, editors. Neville Text Book of Oral and Maxillofacial Pathology. 2nd ed. United States of America: Saunders; 2005. p. 324-6
12. Gannepalli A, Appala A, Reddy L, Babu DB. Insight into verruciform xanthoma with oral submucous fibrosis: Case report and review of literature. J Oral Maxillofac Pathol 2019;23:43-8
13. Lalawat S, Tomar N, Chaudhary A, Reddy V. Oral verruciform xanthoma: The great imitator. Journal of Indian Academy of Oral Medicine and Radiology. 2020 Apr 1;32(2):196-8.