

Oral Verruciform Xanthoma: A Case Report

ABSTRACT:

Verruciform xanthoma is a benign growth found on the oral mucosa and occasionally may affect the skin. Clinically, verruciform xanthoma is an asymptomatic lesion. Depending on the amount of keratin present on the surface of the oral mucosa, it can appear as a reddish-gray papillary, flat or a slightly raised, rough lesion. The verrucous structure and exophytic properties of these lesions are similar to those of malignant lesions; therefore, histopathological assessment is mandatory for definitive diagnosis. Herein, we report a case of oral verruciform xanthoma on the lower right labial vestibule and to confirm the diagnosis immunohistochemistry (IHC) was done which showed positive CD 68 macrophages.

Keywords: Xanthoma, immunohistochemistry, CD 68

INTRODUCTION:

Verruciform xanthoma [VX] is an uncommon benign lesion primarily of the oral mucosa with an incidence rate of 0.025-0.05% of all the pathology cases. In 1971, Shafer first described the entity "Verruciform Xanthoma"¹. The etiopathogenesis of verruciform xanthoma is unknown, though been identified in several parts of the body. Most frequently encountered sites for oral lesion are gingiva, alveolus and hard palate². It is most commonly presented with a verrucous appearance, however in some instances it may appear polypoid, papillomatous, or sessile. It occurs as a small (0.2–2 cm), solitary, asymptomatic, slow growing, white or yellowish red lesion with no sex predilection^{3,4}. Histopathological examination is the gold standard for the diagnosis of verruciform xanthomas. Microscopically, these lesions are characterized by the presence of parakeratinized stratified squamous epithelium having papillary or verrucous growth with connective tissue papillae extending up to the surface. The papillae characteristically contain foam cells called xanthoma cells⁵. The treatment of the VX lesion involves local surgical excision and recurrence is rare⁴. The aim of this report is to present a rare case of oral verruciform xanthoma on the lower right labial vestibule of a 52-year-old male along its clinical and pathologic features and treatment modalities.

CASE REPORT:

A 52-year-old male patient presented with the chief complaint of a painless growth on the right labial vestibule for 4-5 months (Figure 1). He had a habit of tobacco chewing for the past 15 years. On clinical examination, whitish pink, exophytic lesion, measuring 1 x 1 cm approx. in size, was found over lower right labial mucosa. The lesion was asymptomatic and soft in consistency. Lymph nodes were not palpable. A provisional diagnosis of verrucous hyperplasia was made. After clinical examination an excisional biopsy was done to rule out malignancy. Grossing examination showed verrucous projections with pebbly surfaces (Fig 2). On histopathological examination, the hematoxylin and eosin (H&E) stained sections showed parakeratinized stratified squamous epithelium with underlying fibrocellular connective tissue stroma. Epithelium showed varying degrees of exophytic proliferation with thin rete ridges and entrapped connective tissue core. Mild dysplastic features such as nuclear hyperchromatism and increased nuclear cytoplasmic ratio were evident. Adjacent papillary connective tissue showed presence of large foam cells. Mild degree of chronic inflammatory cell infiltrate and vascularity was evident throughout connective tissues (Figures 3 and 4). Deeper section showed salivary gland acini, transverse section of muscle fibers and nerve bundles. Overall features suggestive of verrucous hyperplasia with mild dysplasia. To eliminate Verruciform Xanthoma, Periodic Acid Schiff (PAS) and IHC staining was performed. PAS staining was found to be negative. The immunohistochemical staining for CD68 was positive for the foamy macrophages. All the foam cells were strongly stained with anti-macrophage antibodies (Figures 5 and 6). Surgical excision was done under local anesthesia. Postoperative check-up showed no sign of recurrence.



Fig 1: Whitish pink exophytic growth on right labial mucosa of lower lip



Fig 2: Grossing of the specimen showing prominent crypts resembling pebbly surfaces (Stereomicroscope)

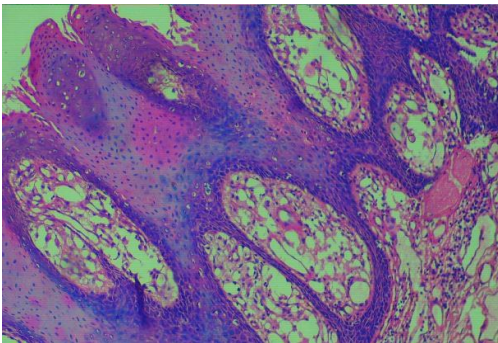


Fig 3: Photomicrograph showing papillary projections within epithelial rete ridges with connective tissue papillae having numerous xanthomacells (H&E Stain, 10X)

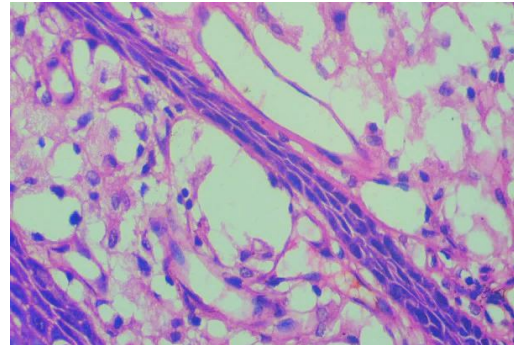


Fig 4: Photomicrograph showing presence of xanthomacells (H&E stain, 40X)

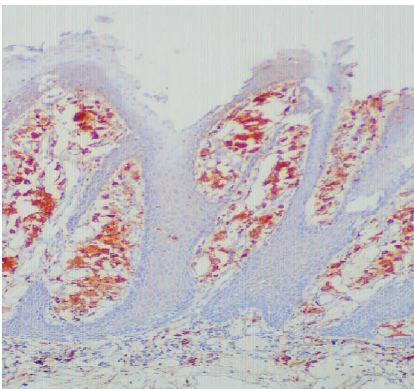


Fig 5: Photomicrograph showing foam cells with strong immunoreactivity to antibody CD68 (IHC stain, 10X)

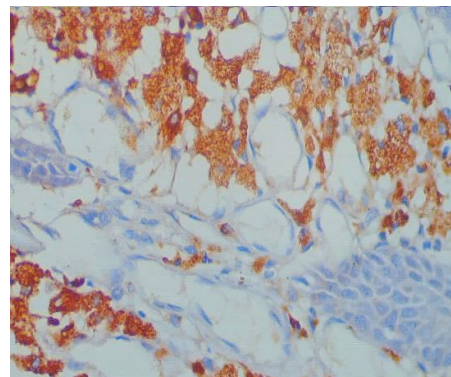


Fig 6: Photomicrograph showing foamy histiocytes with strong cytoplasmic CD68 immunostaining (IHC)

DISCUSSION:

VX is a benign epithelial lesion that irrespective of intra or extraoral development can simulate benign and malignant lesions causing diagnostic dilemmas. Extraoral verruciform xanthoma was first described on vulva by Santa Cruz and Martin⁶. The most common intraoral sites of its occurrence are gingiva, alveolar mucosa and hard palate². The etiology still remains obscure. It can be because of the damage to the squamous cells due to trauma, local irritation or infection, which can cause epithelial entrapment and increased epithelial turnover leading to the disease. The epithelial degeneration leads to an inflammatory response and releases lipid material from the degenerated cells⁴. The damaged and degenerating keratinocytes that moved downwards into the papillary dermis and submucosal region are engulfed by dendritic cells, which develop into foam cells¹.

Because of its clinical and histopathological resemblance to human papilloma virus-induced lesions, verruciform xanthoma was believed to be caused by HPV. However, no evidence was found for the presence of HPV in these lesions⁷. Cobb et al. (1976) supported the theory that VX is inflammatory in origin, generally occurs on the masticatory mucosa while some authors interpreted that it is an immune-mediated process⁸. Verruciform Xanthoma is associated with conditions such as pemphigus vulgaris, lichen planus, discoid lupus erythematosus, warty dyskeratoma, epidermal nevus/ Congenital hemidysplasia with ichthyosiform erythroderma and limb defects syndrome, dystrophic epidermolysis bullosa and seborrheic keratosis⁹.

Clinically, the lesions of VX presented a papillary aspect, pink to white color, normally ranging between 0.2 to 2 cm. Neville et al. (1980) described that VX may differ from "white and verruciform" to "red and ulcerated"¹⁰. It may be sessile or pedunculated and can resemble leukoplakia or squamous papilloma. Most commonly occurs in 4th–6th decade of life with equal distribution between both genders. However, V. Raphael et al. (2012) has reported that there is a slight male predilection for Verruciform Xanthoma^{3,4,11}. Intraorally, the lesion is usually present on alveolar ridge, gingiva, followed by buccal mucosa, palate, floor of the mouth and lip^{9,12}. In our case, whitish pink, exophytic lesion, measuring 1 x 1 cm approx. in size, was found over lower right labial mucosa which was asymptomatic and soft inconsistency.

Histologically, VX shows three patterns: verrucous or warty (most common), papillary or cauliflower (least common), and flat or slightly raised¹³. The papillary pattern exhibits a finger-like exophytic epithelial proliferation covering thin cores of connective tissue, whereas in the flat pattern, the lesion demonstrates "endophytic" (below the surface) growth. In the flat pattern, abundant foam cell accumulation can be observed in the lamina propria, thus leading to the rete ridge elongation and thinning of the covered oral epithelium through compression¹⁴. Sometimes, there is parakeratosis of the hyperplastic epithelium. The rete pegs are thin, elongated and uniform.

The connective tissue papillae between the rete pegs are characterized by massive accumulation of large swollen foam cells known as xanthoma cells, which are restricted to the extension of the rete pegs. The cytoplasm of the foam cells contains tiny PAS-positive granules. The nuclei are small, round and eccentrically placed¹⁵. Still, controversy over the exact origin of these cells exists. They are suggested to be a lineage of monocytes/macrophages¹⁴. The lipid found in the xanthoma cells resembles the same as seen in other inflammatory reactions⁹. In our case, parakeratinized stratified squamous epithelium showed varying degrees of exophytic proliferation with thin rete ridges and entrapped connective tissue core. Mild dysplastic features such as nuclear hyperchromatism and increased nuclear cytoplasmic ratio were evident. Adjacent papillary connective tissue showed presence of large foam cells. Also, mild degree of chronic inflammatory cell infiltrate and vascularity was evident throughout connective tissue. CD68 is a cytoplasmic marker confirming the possible role of macrophages in the formation of foam cells⁹. In our case, the foam cells showed strong CD68 immunoreactivity. The treatment of choice is complete surgical excision which is very effective without signs of recurrence¹⁶.

CONCLUSION:

Verruciform Xanthoma is a rare muco-cutaneous lesion because of multifactorial chronic reactive process. Its clinical appearance is not pathognomonic. Histopathological examination and IHC marker CD68 are the paramount for accurate diagnosis. The clinicians should be aware that clinically, verruciform xanthoma may mimic malignancy. Hence, it should be considered in the differential diagnosis of commonly occurring verruciform-papillary lesions in the oral

cavity.

REFERENCES:

- 1) Shafer WG. Verruciform xanthoma. *Oral Surg Oral Med Oral Pathol.* 1971;31(6):784–9.
- 2) Sah K, Kale AD, Hallikerimath S. Verruciform xanthoma: Report of two cases and review on pathogenesis. *Journal of Oral and Maxillofacial Pathology.* 2008 Jan 1;12(1):41.
- 3) S Belknap AN, Islam MN, Bhattacharyya I, Cohen DM, Fitzpatrick SG. Oral verruciform xanthoma: a series of 212 cases and review of the literature. *Head and neck pathology.* 2020 Sep;14(3):742-8.
- 4) B. Sivapathsundharam, Shafer's Textbook of Oral Pathology, 9th edition, 2020
- 5) Rawat G, Aiyer HM. Verruciform Xanthoma of the Tongue: Case Report and Review of Literature. *J Exp Pathol.* 2021;2(2):63-66
- 6) Santa Cruz DJ, Martin SA. Verruciform xanthoma of the vulva: Report of two cases. *Am J Clin Pathol*1979; 71:224-8.
- 7) 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.
- 8) Cobb CM, Holt R, Denys FR. Ultrastructural features of the verruciform xanthoma. *J Oral Pathol*1976; 5:42-51.
- 9) S. S. Farahani, N. S. Treister, Z. Khan, and S.-B. Woo, "Oral verruciform xanthoma associated with chronic graft-versushost disease: a report of five cases and a review of the literature," *Head and Neck Pathology*, vol. 5, no. 2, pp. 193–198, 2011.
- 10) Neville BW, Weathers DR. Verruciform xanthoma. *Oral Surg Oral Med Oral Pathol.* 1980;49(5):429-34.
- 11) V. Raphael, H. Das, R. Sarma, and B. Shunyu, "Oral verruciform xanthoma: a case report," *International Journal of Oral and Maxillofacial Pathology*, vol. 3, no. 2, pp. 65–67, 2012.
- 12) De França GM, Galvão HC, de Oliveira PT, Felipe J, da Silva WR, Medeiros CK. Verruciform xanthoma associated with lichen planus. *Autopsy and Case Reports*, 2022;12:1-7.
- 13) Bhalerao S, Bhat P, Chhabra R, Tamgadge A. Verruciform xanthoma of buccal mucosa: A case report with review of literature. *Contemp Clin Dent* 2012; 3:257-9.
- 14) Vasileios I. Theofilou, Alexandra Sklavounou, Prokopios P. Argyris, EvanthiaChrysomali, "Oral Verruciform Xanthoma within Lichen Planus: A Case Report and Literature Review", *Case Reports in Dentistry*, vol. 2018, Article ID 1615086, 5 pages, 2018
- 15) A. K. Pouloupoulos, A. Epivatianos, T. Zaraboukas, and D. Antoniadis, "Verruciform xanthoma coexisting with oral discoid lupus erythematosus," *British Journal of Oral and Maxillofacial Surgery*, vol. 45, no. 2, pp. 159–160, 2007
- 16) De Aragão Almeida A, de Souza Arantes C, Parizi JL, Nai GA. Oral cavity verruciform xanthoma—the importance of total excision—report of two cases. *Research, Society and Development.* 2022 Jan 14;11(1)