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Case Report

Clinical diagnostic dilemma: Oral verruciform xanthoma

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ABSTRACT

Verruciform xanthoma is a specific but not so common, papillary growth typically occurring on the oral mucosa of middle-aged persons. It is a unique entity and has found to be incident in 0.025-0.05% of all cases reported as per the literature study. One such case of 75 days duration was successfully managed with complete local surgical excision. The surgical site was monitored for one year postoperatively with no signs of recurrence or other postoperative complications. Clinical perspective, histopathological highlights and differential interpretation is discussed in this article with an in-depth review of the literature. It is important to consider this rare entity in the differential diagnosis of lesions involving oral mucosa as its clinical and histological features overlap with several other lesions.

1. Introduction

Verruciform xanthoma is a non-malignant, solitary lesion the etiology of which is not known.[1] It is distinguished by verrucous configuration, surface epithelium parakeratosis, and appearance of foam cells in connective tissue papillae.[1] Age of affected individuals is about 45 years and there are no reports of any sex or race predilection.[2]

The lesions typically do not show any symptoms and could measure from two millimeters to about two centimeters in size.[2] Among the reported cases, oral cavity was affected predominantly; reason remains obscure.[3] In spite of verruciform xanthoma being a papillary lesion, human papillomavirus does not participate in its pathogenesis.[4]

2. Case Description

A 42-year-old male from Belagavi reported to us with chief complaint of a white patch on the lower lip since the past 75 days. White plaque was noted over lower lip near the vestibule measuring one centimeter in diameter, irregular in shape (Figures 1 and 2). The lesion was found to be soft (velvety surface), non-tender, immobile and no lymphadenopathy was present on palpation. The lesion was raised, verrucous, white.

2.1. Histopathological examination: (Figures 3, 4, 5 and 6)

The hematoxylin and eosin (H&E) stained sections showed hyperkeratotic epithelium proliferating in a papillary, finger-like projections with evenly elongated rete pegs. Parakeratin plugging was noted on papillary surface as well as in the crypts between finger-like projections.

The underlying connective tissue papillae which were of varying sizes extended towards the surface. Innumerable

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Fig. 1: Photograph showing irregularly shaped white patch on lower lip near the vestibule

Fig. 2: Photograph of the same patient showing irregularly shaped white patch on lower lip near the vestibule

large lipid-filled macrophages with round eccentric nuclei and foamy cytoplasm were visible on the papillary region of lamina propria. The loose to dense underlying connective tissue contained fibroblasts, blood vessels lined by epithelium, RBCs and inflammatory cell infiltrate. No traces of abnormal changes or malignancy were noticed. The foam cells were spotted to be confined to the margins of papillae thereby affirming the diagnosis of verruciform xanthoma.

On powerful staining of foam cells with anti-macrophage antibodies, CD68 turned out positive. The macrophages may be partly accountable for foam cell formation. This hypothesis is backed by CD68 cell marker.

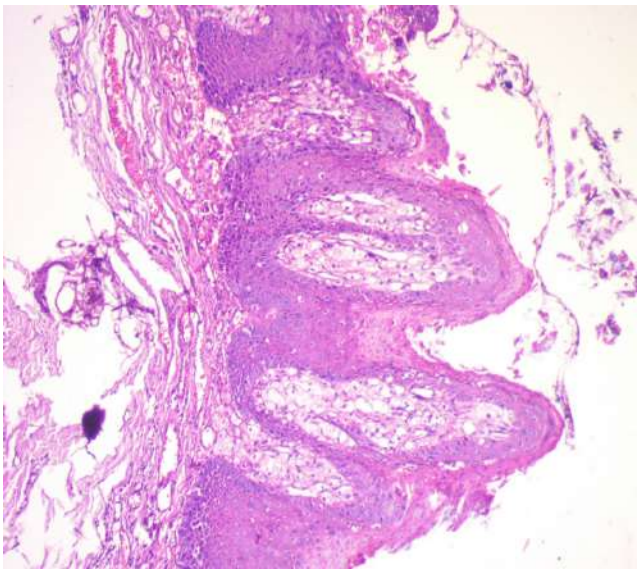

Fig. 3: Exophytic papillomatous epithelial hyperplasia with parakeratosis and elongated rete pegs (H&E stain 10x)

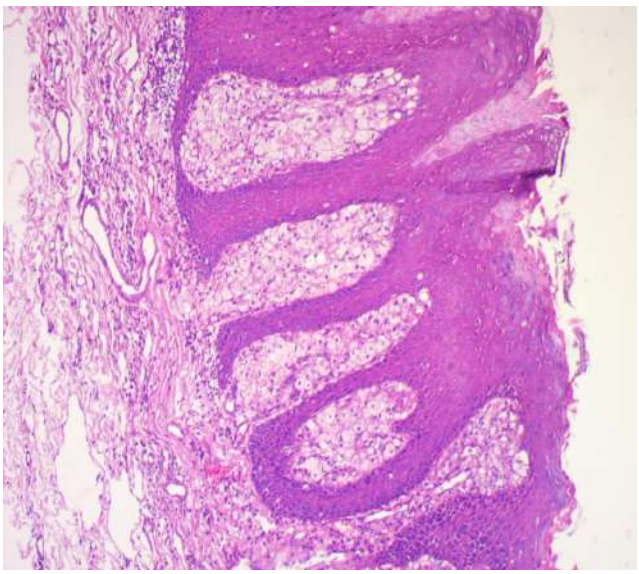

Fig. 4: Evenly elongated rete pegs & large quantity of foam cells limited to connective tissue papillae (H&E stain 10x)

The lesion was surgically excised under local anesthesia.

3. Discussion

Verruciform xanthoma is unique and as of now does not display similarity with any other conditions, and the patient was free from any known medical condition. The patient had history of smoking and chewing tobacco for six years and has stopped the habit since two years, although no strong

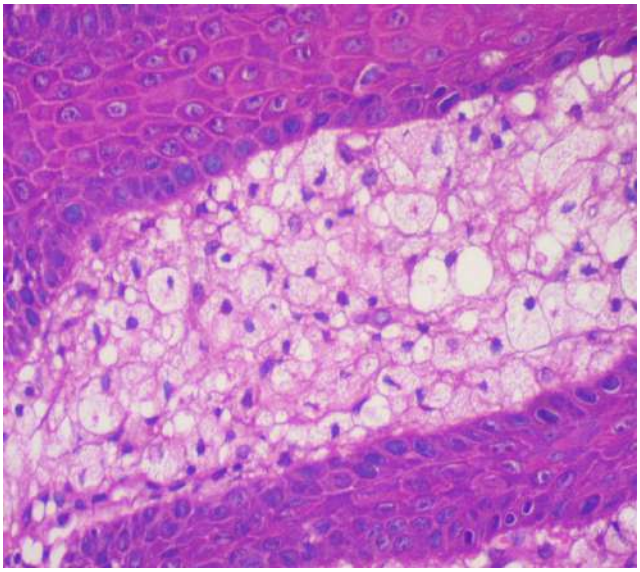

Fig. 5: Appearance of lipid-laden foamy macrophages in the connective tissue papillae (H&E stain 40x)

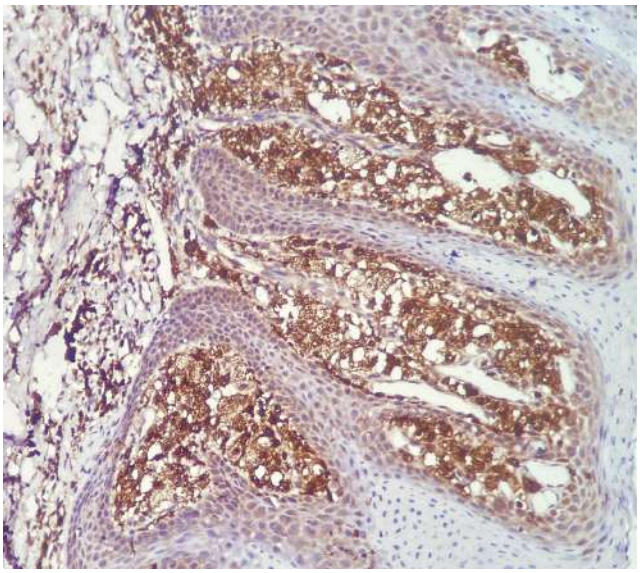

Fig. 6: Elongated connective tissue papillae stuffed with foam cells with strong cytoplasmic CD68 positive immunostaining (IHC stain 10x)

association have been established between the habit and the entity. A duration of 75 days after noticing the lesion was reported by the patient.

The lesion represents an unusual immune reaction to localized epithelial injury.[5] This concept is backed by cases that have been found to develop in association with disturbed epithelium (e.g. lupus erythematosus, epidermolysis bullosa, lichen planus, pemphigus vulgaris, warty dyskeratoma).[5] The lesion becomes apparent as a well-demarcated, soft, painless, stalkless, marginally lifted mass with a white, ruddy or yellowish papillary or rough surface.[6] Research insinuates that verruciform xanthoma with oral submucous fibrosis possesses a tendency of malignant transformation.[6] This does not make verruciform xanthoma potentially malignant; it implies that verruciform xanthoma can occur following degenerative changes in dysplastic lesions.

Structurally, xanthoma cells are nothing but fat-laden macrophages and histiocytes.[7] It has been proposed by many studies that lesions occur due to local inflammation through gradual disintegration of epithelial cells and subsequent release of lipid content which is collected by macrophages.[7] There is a possibility that foam cells in chronic inflammatory reactions also contains the same fatty material.[7]

Foam cells in verruciform xanthoma eventually replace connective tissue components within the papillae. Epithelial cells are affected by these foam cells in terms of nutrition and metabolism, thereby leading to parakeratosis.[7] Nowparast et al suggested that the verrucous and papillary architecture may be due to the presence of foam cells, which may induce formation of parakeratotic cells from epithelium between connective tissue papillae, causing their premature exfoliation and crypt formation.[7]

It was proposed by Zegarelli regarding the pathogenesis of lipid-laden macrophages in the connective tissue papillae that degeneration of keratinocytes takes place following damage to keratinocytes which is caused by an inciting agent.[8] This in turn draws connective tissue dendrocytes which engulfs the debris.[8] The dendrocytes also ingest lipids from the degenerating keratinocytes thus giving rise to foam cells. According to another postulation regarding the pathogenesis of verruciform xanthoma, cytokines chemotactic for neutrophils are released as a result of damage to keratinocytes.[9] This event is accompanied by fast growth of the epithelium to produce verruciform structure and parakeratosis.[9] The affected keratinocytes migrate downwards into the papillary connective tissue and submucosal region and are engulfed by dendritic cells giving rise to foam cells.[9] The monocyte-macrophage lineage can be imagined looking at the extreme positivity of foam cells to CD68 antibodies.[10] Moreover, these foam cells were found to belong to chronic inflammatory phenotypes rather than acute inflammatory phenotypes.[11]

Number of studies have been performed till date; but pathogenesis is still elusive today and needs clarification.[12]

Verruciform xanthoma presents histopathologically as a verrucous, acanthotic surface epithelial tissue with overlaying parakeratin.[2] CD68, vimentin and factor XIII will show positive stains. S100, keratin will show negative or weak stains.

Differential diagnosis includes squamous papilloma and verrucous carcinoma. Squamous papilloma shows presence of koilocytes in upper epidermis, lack of foamy

macrophages. Verrucous carcinoma exhibits fungus-like lobules of mature squamous epithelium containing large rete pegs, minimal to no structural abnormality in cells, lack of foamy macrophages.

Looking at the clinical presentation, one can misdiagnose verruciform xanthoma as verrucous carcinoma, papillomas, leukoplakia and may even associate it with squamous cell carcinoma. This mandates the increased importance of histopathological study as the treatment plan of verruciform xanthoma is much less aggressive in comparison to its clinical replicas such as verrucous carcinoma, often treated by wide local excision of the lesion, marginal mandibulectomy or ipsilateral selective neck dissection depending on the nodal involvement, size and invasiveness of the lesion.

Resistance was shown to cryosurgery.[13] When managed by local surgical excision, recurrence is scarce and no malignant metamorphosis has been detailed. Nonetheless, two instances have been detailed in the literature where it occurred in conjunction with squamous cell carcinoma or carcinoma in situ.[14,15] Studies reveal excellent prognosis of verruciform xanthoma when treated with complete surgical excision.[14]

4. Source of Funding

None.

5. Conflict of Interest

None.

Acknowledgments

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