Verruciform Xanthoma: A Case Report with Immunohistochemical Finding

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Authors’ contributions

This work is the result of collaborative work of all the authors. Author UH carried out all the pertaining investigations, drafted the manuscript. Author VGD carried out literature search and author HSS prepared the manuscript. All the authors approved the final manuscript.

ABSTRACT

Verruciform xanthoma is a rare clinicopathologic entity which occurs primarily in the oral mucosa. It is difficult to make a diagnosis of verruciform xanthoma based on the clinical findings alone. But the microscopic findings of the characteristic foam cells in the papillary portion of the connective tissue aids in its definitive diagnosis. The origin of the foam cells were thought to be epithelial/dermal dendritic cells (langerhans cells)/neural. But with the advent of immunohistochemistry, it has been established that the foam cells are of monocyte-macrophage lineage because of the strong positivity of these cells to CD-68 antibody. Although no specific etiologic agent or the exact mechanism of its etiopathogenesis is known, a local inflammation or trauma to various triggering factors along non-specific pathways has been suggested. Verruciform xanthoma is known to occur along with other epithelial lesions such as lichen planus, pemphigus etc, but no case has been reported to occur in the same area as the pre-existing site of oral submucous fibrosis in the same patient. This article presents a case of verruciform xanthoma on the left buccal mucosa of a male patient who had history of oral submucous fibrosis in the same area, along with the immunohistochemical findings.
Keywords: Verruciform xanthoma; CD68 antibody; oral submucous fibrosis; foam cells.

1. INTRODUCTION

Verruciform xanthoma is a benign papillary or cauliflower-like lesion that primarily affects the oral mucosa and was first described by Shafer in 1971 [1]. It was Santa Cruz and Martin, who first described two extraoral lesions in the vulva [2]. Clinically, they are asymptomatic, slow growing, sessile or pedunculated lesions with a papillary, granular or verrucous surface. They rarely exceed 1 cm in diameter and are normal, red or yellowish in color [2]. Because of this appearance and the rarity of these lesions, they are often diagnosed clinically as papilloma, verruca, verrucous carcinoma or squamous cell carcinoma. But the histopathological finding of foam/xanthoma cells in the connective tissue papillae between the epithelial rete pegs gives a confirmatory diagnosis [3].

Different views exist on the origin of the foam cells. But with the advent of immunohistochemistry, the positive staining of foam cells to CD68, it is definitely known to be of monocyte-macrophage lineage [4,5,6,7]. Chronic inflammation due to local trauma or inflammation seems to trigger the development of this lesion through various non-specific pathways [7].

2. CASE REPORT

A 39 year old male patient complained of growth on the left side of the cheek since one year. Patient had a past positive history of oral submucous fibrosis (OSMF) which was treated conservatively by intralesional steroid injection in the same area. There was no evidence of any growth in that region during the treatment procedure. Presently patient showed mouth opening of 4 cm. On examination, sessile, pink, papillary growth was noted on left buccal mucosa. It was soft, painless and about 1x1.5 cm in size. The provisional clinical diagnosis of papilloma was given. The excised specimen was sent for histopathological evaluation (Fig. 1).

The H & E stained section showed papillary epithelial surface covered by thick parakeratin layer. The rete ridges were elongated almost to a uniform length (Fig. 2). Numerous large macrophages with foamy cytoplasm (xanthoma cells/foam cells) typically confined to the connective tissue papillae were seen (Fig. 3). The underlying connective tissue stroma showed a few inflammatory cells and no evidence of xanthoma cells. Based on these findings a diagnosis of verruciform xanthoma was given.

Immunohistochemically, the foam cells in the lesion were positive for CD68 reinforcing the origin of foam cells to be of monocyte macrophage lineage (Fig. 4).

Fig. 1. Papillary growth on the left buccal mucosa

Fig. 2. Photomicrograph showing granular cells between the epithelial rete ridges [Haematoxylin & Eosin Staining, Magnification X100]

Fig. 3. Photomicrograph showing granular cells between the epithelial rete ridges [Haematoxylin & Eosin Staining, Magnification X400]

Fig. 4. Photomicrograph showing CD68 positive granular cells [IHC Staining, Magnification X 100]
3. DISCUSSION

Verruciform xanthoma is a relatively uncommon hyperplastic condition of the epithelium affecting primarily the oral mucosa [3]. The extra oral occurrence has been reported mainly involving the anogenital mucosa and skin. Gingiva, alveolar mucosa and hard palate are the most common intraoral sites of its occurrence [2]. It usually presents as a solitary, sessile or pedunculated lesion with rough or pebbly surface. It is generally asymptomatic and is about 2 mm to 1.5 cm in size with a normal or pale, white/red in color. It is reported to occur in adults between 40-70 years [3]. The review by Philipsen et al. [2] has suggested that oral verruciform xanthomas are common in males below the age of 50 years and a reverse trend was noted in females showing slight predilection below the age of 50 years and a reverse trend. Verruciform xanthoma occurs as an isolated solitary lesion in most cases. But multiple lesions and its association with other diseases such as snuff dipper’s keratosis, oral pemphigus vulgaris, carcinoma-in-situ, lichen sclerosus, solar keratoses, dyscoid lupus erythematosus, epithelial nevus, CHILD syndrome [8], regressive dystrophic epidermolysis bullosa [9], seborrhic keratosis [10] and psoriasis [6] have been reported.

It has also been reported in an immunocompromised patients, [11] in patients with hyper cholestrolemia and hepatitis C virus carriers. Concomitantly verruciform xanthoma has been reported with other oral mucosal diseases such as lichen planus, leukoplakia and amyloidosis [7]. Only one report of its association with systemic lipid storage disease has been reported [8]. Hence, it does not seem to be related to any lipid metabolism abnormality. In the present case, a papillary sessile growth on the left buccal mucosa measuring about 1cm was noted in a 39 year old male patient. Although gingiva, alveolar mucosa and hard palate are the most common intra oral sites, our case presented with lesion on the left buccal mucosa. Further, a growth was seen on previously diagnosed and treated area of oral submucous fibrosis. This occurrence of verruciform xanthoma to the best of our knowledge is the first reported case in the same site as that of previous occurrence of OSMF.

The characteristic histopathological findings help in arriving at a conclusive diagnosis. Microscopically, a hyperplastic, parakeratinised squamous epithelium lining the papillary projections with elongated rete ridges of relatively uniform depth, the parakeratin filling the clefts or crypts between the epithelium projections will be seen. The hallmark of this lesion is the presence of numerous large macrophages with foamy cytoplasm typically confined to the connective tissue papillae, which extend high into epithelium, close to the surface known as xanthoma cells [3]. Other important features are the exocytosis of neutrophils in the parakeratin layer of epithelia and a mixed chronic inflammatory cell infiltrations in the submucosa [12]. In our case, the clinical diagnosis of papilloma was ruled out and the diagnosis of verruciform xanthoma was given after histopathological examination.

Local trauma, inflammation [7] and conditions other than epithelial trauma, which affect the turnover of epithelium such as verruciform xanthoma within carcinoma in situ, candidial infection, a local immunological disorder [4] and also a viral etiology [6], have been considered as the different possible etiologic agents in verruciform xanthoma. The ultrastructural and in-situ hybridization findings in verruciform xanthoma, disclosed negativity for the HPV in these lesions. Hence the viral etiology has not gained much impetus [6]. In few cutaneous verruciform xanthoma mutation of 3β- hydroxysteroid dehydrogenase was noted, suggesting a genetic etiology [9]. In the present case, local trauma and inflammation seem to be the most probable initiating factor in the etiopathogenesis of the lesion.

The origin of foam cells had been an area of debate and was thought to be of epithelial/nerveal/dermal-dendritic in nature [6]. The immunohistochemical studies have ruled out the above possibilities. Numerous independent findings of CD68 positivity in the cytoplasm of foam cells has suggested the origin to be of monocyte-macrophage lineage [4,5,6,7]. We also recorded CD68 positivity in the present case, supporting the findings of other authors. In general, the treatment option for verruciform xanthoma is local surgical excision and its recurrence is rare [1].

4. CONCLUSION

We come across papillary, sessile or pedunculated growths on the oral mucosa quite commonly and diagnose them clinically either as papilloma or verruca or verrucous carcinoma. Verruciform xanthoma, although rare, also presents a similar clinical picture and hence has
to be considered in the clinical differential diagnosis. The histopathological features of epithelial hyperplasia and presence of foam cells in the connective tissue papillae between the epithelial ridges and not in the deeper stroma is diagnostic of this lesion. Though it has now been definitely established that the foam cells are of monocyte-macrophage origin, the exact mechanism of its etiopathogenesis remains unclear. It is thought to be a reactive process with multifactorial triggering factors with unique and non specific pathways.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

ACKNOWLEDGEMENTS

We sincerely acknowledge Dr. Laxman Kannan, Pathologist, Kannan Diagnostics, Mysuru, and Dr. Anita Nithin, Vikram Perfect, Mysuru for their contribution and support.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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http://sciencedomain.org/review-history/11168