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Case report

Penile multifocal mucocutaneous verruciform xanthoma clinically mimicking squamous cell carcinoma: A case report and a brief literature review

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Abstract

Verruciform xanthoma is a rare benign condition of unknown aetiology that occurs mainly in the oral mucosa but occasionally involves the anogenital region and skin. These lesions, particularly when multiple, may clinically mimic malignant tumours and pose a diagnostic challenge. The characteristic histological feature is the presence of histiocytic infiltrates in the papillary dermis. We report a case of multifocal mucocutaneous verruciform xanthoma of the penis in a 75-year-old man, which clinically mimicked a squamous cell carcinoma. We highlight the importance of being aware of this benign condition and discuss the morphology, aetiopathogenesis and treatment options.

Key words: verruciform xanthoma, foamy histiocytes

Introduction

Verruciform xanthoma (VX) is an uncommon benign disorder first reported by Shafer in the oral cavity in 1971 (1). Verrucous epithelial proliferation and accumulation of foamy histiocytes within the dermal papillae are the hallmark of this lesion. It shows a marked predilection for the oral mucosa. Extraoral lesions are much rarer and have been reported mostly in the genital skin, including the penis, scrotum and vulva (1,2,3). A single case of VX has been reported on the nasal mucosa (4). However, cutaneous forms of VX have been reported in the extremities, axilla and breast.

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Case report

A 75-year-old man presented with a rapidly growing penile lesion of 3-months duration associated with mild itchiness (Figure 1).

On examination, the prepuce was unretractable and studded with multiple soft pinkish-red nodules of varying sizes, ranging from 0.5 mm to 15 mm in diameters. The outer skin of the prepuce showed a whitish ill-

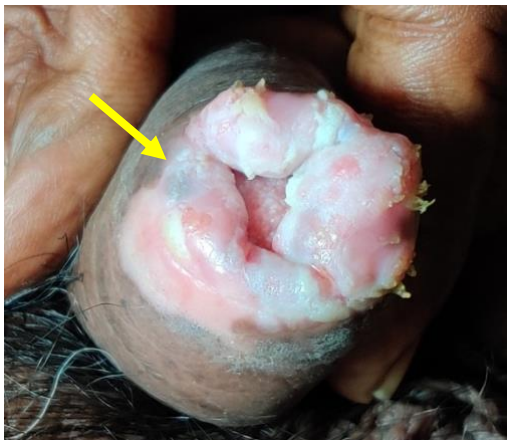

Figure 1: Multiple soft pinkish red nodules in the prepuce (before circumcision).

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defined patch suggestive of lichen sclerosus. The glans penis had a circumscribed pinkish-red warty plaque with yellowish borders measuring 20 mm in diameter, and this lesion extended towards the urethral meatus. Another small yellowish papule was present along the corona of the glans penis. There was no ulceration or regional lymphadenopathy. His blood tests, including the lipid profile, were within the normal range.

A clinical diagnosis of squamous cell carcinoma (SCC) was made, and an incision biopsy was obtained from one of the foreskin lesions to confirm the diagnosis. Microscopically, the biopsy showed regular epidermal hyperplasia, papillomatosis, hyperkeratosis and focal parakeratosis. Scattered foam cells were also noted in the papillary dermis with chronic inflammatory cells within the upper dermis. There was no cellular atypia or evidence of malignancy.

Subsequently, an excisional biopsy of a single lesion was performed, which showed similar histological features; parakeratosis extending along the rete-ridges, neutrophil exocytosis within the parakeratotic layer and characteristically, more prominent aggregates of foamy histiocytes within the papillary dermis (Figures 2 & 3).

Foamy cells contained periodic acid-Schiff (PAS) positive, diastase resistant cytoplasmic granules. The positive staining with the immunohistochemical stain CD68 and negative staining with AE1/AE3 confirmed the histiocytic nature of the foamy cells and facilitated the diagnosis of VX, excluding the possibility of carcinoma including a clear cell carcinoma (Figure 3).

As the next step, circumcision was performed, and the features confirmed the presence of multifocal VX. The adjacent tissue showed evidence of lichen sclerosus. The involvement of both skin and mucous membranes of the penis was compatible with the diagnosis of multifocal mucocutaneous VX. A few lesions remained in the glans penis following circumcision (Figure 4).

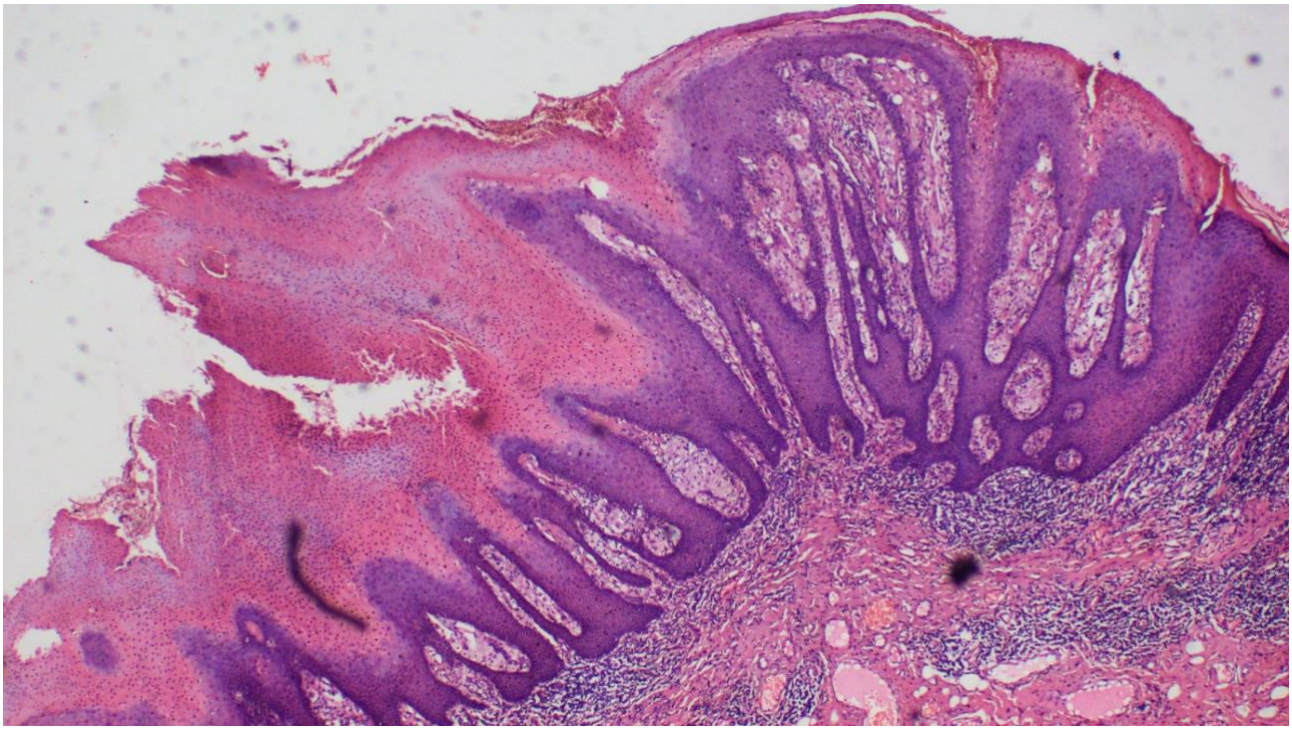

Figure 2: Epidermal hyperplasia, hyperkeratosis and parakeratosis extending along the rete ridges and aggregates of foamy histiocytes within the papillary dermis. (H & E x40)

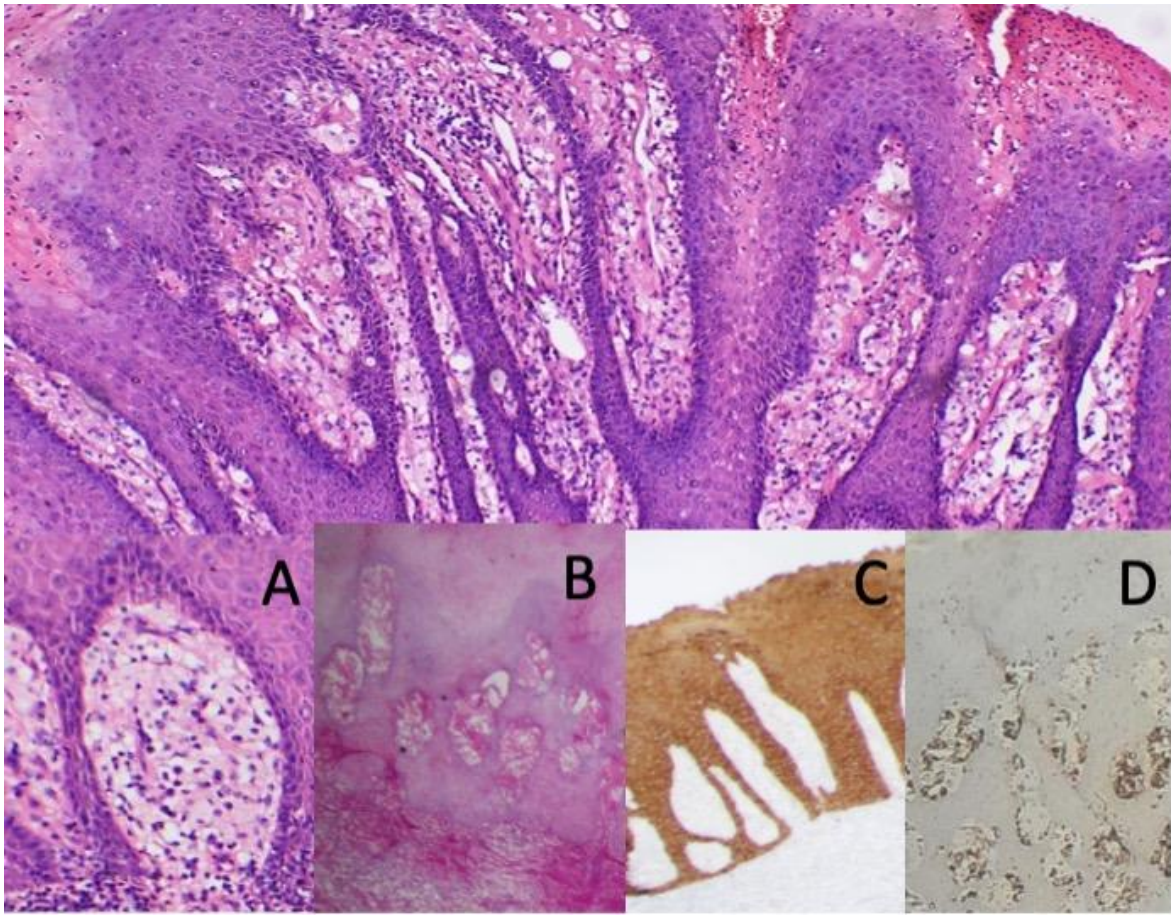

Figure 3: A Collections of foamy histiocytes within the papillary dermis and neutrophil exocytosis within the parakeratotic layer (H & E x400) **B** PAS-D **C** AE1/AE3 (IHC) **D** CD68 (IHC)

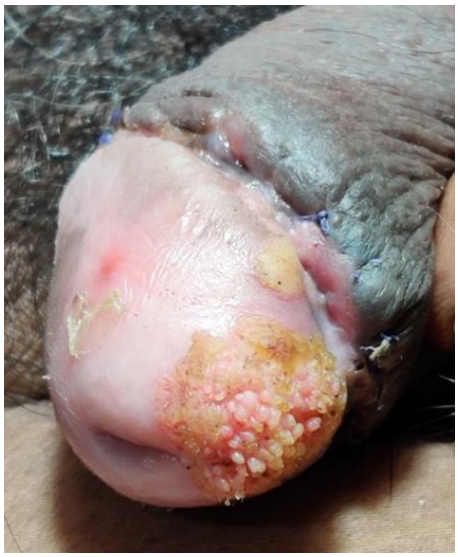

Figure 4: Lesions remaining in the glans after circumcision

Discussion

VX is an asymptomatic yellowish red to grey colour warty, papule, plaque or polypoid lesion. The size of the lesion ranges from 2 mm to 20 mm in diameter. Oral lesions are much common in middle-aged men and extra-oral lesions show a greater predilection for middle-aged to elderly men. However, according to a study carried out by Tamiolakis et al, VX could occur in a wide age range from 2.5 to 89 years (5). VX may clinically mimic many benign and malignant lesions, including viral warts, condyloma acuminatum and verrucous or conventional squamous cell carcinoma (3,6,7).

VX is usually solitary but very rarely multifocal (8,9). All the multifocal lesions that have been reported to date were in the upper aero-digestive tract. In 2014, Tang et al. have

reported an unusual case of disseminated VX with oral, cutaneous and genital involvement, without an obvious underlying cause (10). Further, Tamiolakis et al. have reported that multifocality as a rare finding, and they have also reported a single case of disseminated VX (5).

VX is usually sporadic (8). Recent studies have speculated that VX may show an association with chronic inflammatory conditions, systemic and metabolic disorders and benign and malignant neoplasms including lymphoedema, graft versus host disease, discoid lupus erythematosus, systemic lipid storage disease, lichen planus, lichen sclerosus, epidermal nevi, CHILD (congenital hemidysplasia, ichthyosiform erythroderma and limb defect syndrome) and in-situ or invasive SCC (7,8,10). Our patient showed an association of VX with lichen sclerosus.

The aetiopathogenesis of VX is yet to be determined, although many studies have claimed that this is probably a reactive process following epithelial damage. As this lesion shows an architectural resemblance to verrucous mucocutaneous lesions, human papilloma virus (HPV) has been suggested as a causative agent of VX. However, many studies have failed to detect HPV in VX lesions. Mohsin et al. proposed that damaged keratinocytes attract neutrophils and stimulate rapid epidermal growth (4). Zegarelli et al. claimed that VX may result from releasing of lipids from degenerating keratinocytes following local damage due to irritation or trauma (11). The released lipids are then engulfed by dermal macrophages, forming foam cells. This concept is strongly supported by a study carried out by by Tamiolakis et al. (5). Therefore, it has been speculated that VX may be a unique reaction pattern to local irritation leading to recruitment and persistent accumulation of foamy histiocytes in the dermal papillae. However, some authors have proposed different etiological mechanisms such as local immunological reactions and autoimmune processes (3,5). Overall, there is insufficient evidence for a definite pathogenetic mechanism of VX.

VX is an exophytic lesion showing marked hyperkeratosis, parakeratosis and acanthosis of epidermis with uniformly elongated rete-ridges and papillomatosis with flattened bases. Characteristically parakeratosis blends with the keratinocytes of deep rete-pegs. The presence of an intense neutrophilic infiltrate predominantly within the parakeratotic layer is another consistent feature of this condition (1). However, the diagnostic feature of this lesion is the aggregates of foamy histiocytes within the dermal papillae, characteristically limited to the papillary dermis. The base of the lesion shows a plasma cell infiltrate of varying intensity. Most importantly, this lesion shows no cellular atypia.

Surgical excision is the treatment of choice for VX while electrocautery CO2 laser, cryotherapy and radiotherapy are other options (12,13). Imiquimod, an immune response modifier, usually used to treat genital warts, superficial basal cell carcinomas, and actinic keratosis, has also been shown to be effective in some cases. Our patient was started on cryotherapy, which is being continued every three weeks. He has shown gradual, but slow improvement during the four months of treatment.

Conclusion

This is an extremely rare case of multifocal mucocutaneous VX of the penis clinically mimicking SCC. To the best of our knowledge, this is the first case of verruciform xanthoma reported in Sri Lanka. Awareness VX and its diagnostic features help to prevent unnecessary surgical interventions. Furthermore, considering the association of VX with malignant tumours, follow up is mandatory for early detection of such complications.

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