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Clinical History

• 60 year old female with a previous history of squamous cell and basal cell carcinomas of the face
• Presented with a 0.8 cm well demarcated white lesion on the posterior fourchette
• The lesion had been increasing in size over the past 3 months
The lesion showed marked acanthosis with both a flat and papillomatous architecture
The papillary areas show prominent keratosis and parakeratosis
There is marked parakeratosis but the granular layer is not prominent. There is no nuclear atypia in the upper layers of the epithelium.
The dermal papillae are elongated and contain abundant foamy cells.
Histologic Features

- Fairly uniform acanthosis with papillomatosis, hyperkeratosis and parakeratosis
- No significant nuclear atypia
- Dermal papillae are expanded by foam cells
- No significant inflammation
- HPV ISH negative (DAKO…)}
Diagnosis

Verruciform Xanthoma of the Vulva
Verruciform Xanthoma

- Uncommon lesion with distinct histologic features
- Most commonly found in the oral cavity
- Less than 10 cases reported in the vulva
- Associations: Japanese males, underlying skin conditions, CHILD syndrome
Verruciform Xanthoma

Gross appearance

- Clinical appearance is not diagnostic
- Usually single papillary or sessile warty growth
- Sharply delineated with raised edges
Verruciform Xanthoma

Microscopic appearance

- Uniformly hyperplastic epithelium lacking nuclear atypia
- Hyperkeratosis and parakeratosis but the granular layer is not prominent
- Foamy macrophages expand the dermal papillae
Verruciform Xanthoma

Additional studies

• Foam cells are positive with PAS and diastase resistant

• Foam cells are positive for CD68(KP1) and negative for cytokeratins and S100 consistent with a macrophage origin

• EM has demonstrated fat droplets within these cells
Differential Diagnosis

- Condyloma acuminatum
  - Koilocytosis, parakeratosis, nuclear atypia confined to upper 1/3
Vulvar Condyloma

- Nearly all contain HPV 6/11
- 20-50% may have co-infection with other HPV types including oncogenic
- Immuno – 50% positive for HPV capsid antigen
- In Situ Hyb – other vulvar lesions can be positive
Prophylactic efficacy analysis

- Women were enrolled regardless of baseline HPV status, but were counted only in the analysis of the type(s) for which they were naïve at enrollment and through 1 month Postdose 3.

- For example, women infected with HPV Type 16 at baseline were not included in the efficacy analysis for HPV 16, but were counted in the efficacy analyses for the other 3 types.

- Women received all 3 doses within 1 year of enrollment.

- Women had no major deviations from the study protocol.
Differential Diagnosis

- SK, SH, papilloma
Differential Diagnosis

- VIN, SCC, Verrucous ca
Verruciform Xanthoma

Pathogenesis

• Frequently occur in areas prone to trauma / irritation
• Cases outside the oral cavity are often associated with an underlying inflammatory process
• Is VX an unusual reactive morphology rather than a true entity?
• What comes first – the epithelial changes or the foam cells?
Verruciform Xanthoma

Hu J et al, APMIS, 2005
- found that Matrix Degrading Metallo-proteinases 2 & 9 are strongly expressed in both the epithelium and foam cells
- degradation of the basement membrane leads to keratinocyte breakdown and foamy macrophage production
Verruciform Xanthoma

Mehra S et al, Arch Dermatol, 2005
- CHILD syndrome – ipsilateral anomalies and scaling dermatoses
- 3B hydroxysteroid dehydrogenase is inactivated through mutation
- Novel mutation in 3BHSD a/w VX

? VX arises due to excess formation of lipid droplets
Verruciform Xanthoma

Association with HPV
- Most cases to date including vulvar have not been shown to contain HPV DNA
- Khaskely, Am J Derm, 2000 reported one case of VX from the scrotum of a 67 male containing HPV 6 DNA
- Relationship still unclear
Verruciform Xanthoma

Treatment

• Local surgical excision is usually diagnostic and curative
• Reich, Int J GYN Path, 2004 has reported one case of vulvar VX that recurred after 8 years
Summary

- Verruciform xanthoma is an unusual but distinctive lesion that can occur on the vulva
- Uniform epithelial hyperplasia, hyper/parakeratosis and dermal foam cells
- Likely a reactive process 2° to keratinocyte damage
- Main importance of recognizing VX may be the distinction from HPV related lesions
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