

## Palmar Pit-Like Lesions as a Rare Presentation in Epidermodysplasia Verruciformis: Case Report

Epidermodysplasia verruciformis (EV) is a rare inherited syndrome characterized by early onset of numerous plane, vulgaris and versicolor-like warts especially on the face, neck, trunk and extremities with lifelong course and occasional cutaneous squamous cell carcinomas (SCCs) (1,2).

Palmar pit-like lesions have been reported in one case of EV from United Arab Emirates (3) and our cases share the same features including their histologic findings, supporting the probable relationship between the pit-like lesions and at least some EV human papilloma virus (HPV) types.

Here we report on a 17-year-old girl with EV, presenting with palmar pit-like lesions in addition to otherwise typical clinical presentation.

A 17-year-old girl with 11-year history of refractory eruption as shiny pink to skin colored plane papules on her hands, face and chin and perioral areas was referred to the skin clinic in our hospital. Clinical examination revealed hypopigmented maculae and patches on her neck, forearms, several verruca vulgaris on extremities and multiple asymptomatic well-defined pin-point to 2-3 mm pink to brown pit-like lesions on her palms (Fig. 1). She was otherwise healthy. Two biopsy specimens were obtained from her body and palmar lesions for histologic examination.

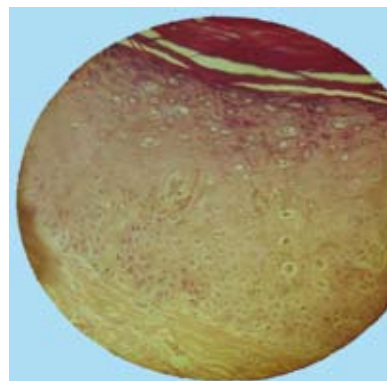
Histologic analysis showed hyperkeratosis, acanthosis with prominent vacuolar changes, especially in the granular layer of the epidermis, and scattered large atypical nuclei, compatible with HPV infection (Fig. 2).

All family members were examined to detect the possible evidence of EV in her relatives. Her parents had no symptoms, but three siblings had evidence of EV with the same palmar pit-like lesions and warts on other body parts (Fig. 3). These features were consistent with EV.

Epidermodysplasia verruciformis was first described in 1922 (4). It is a very rare, chronic, mostly autosomal recessive syndrome characterized by early onset of widespread persistent warts (plane, vulgaris, versicolor-like) on the face, neck, trunk, hands and feet, with lifelong course and susceptibility to cutaneous SCC (1,2). The 5, 8 and 47 EV HPV types are found in more than 90% of EV skin cancers (5-7).



**Figure 1.** Several pin-points to 2-3 mm brownish pit-like lesions on the palms of the patient.



**Figure 2.** Histology of the pit-like lesion shows hyperkeratosis, acanthosis with prominent vacuolar degeneration in granular layer and scattered large atypical nuclei (H&E, X40).

Histopathology of benign lesions shows hyperkeratosis, acanthosis and presence of large clear cells with vacuolated nuclei and cytoplasm with prominent granules of keratohyalin in the upper layers of the epithelium, while immunohistochemical examination reveals HPV antigens in the cell nuclei of the epithelium (1,8).

The exact pathogenesis of EV is unknown, but it is thought to be a species specific defect of cell-me-



**Figure 3.** Pit-like lesions on the palms of two sisters (the patient and her sister) with diffuse warts on the face, neck and hands.

diated immunity against a group of phylogenetically related HPVs referred to as EV types, such as HPV 5, 8, 9, 12, 14, 15, 17, 19-25 and 36-8 (1). On the other hand, it has been shown that cutaneous tumors in transplant recipients receiving immunosuppressants, as well as healthy skin samples and plucked hairs of immunocompetent patients often contain multiple HPV types with a high frequency of those associated with EV (5). Recently, mutations in two genes, TMC6 (EVER1) and TMC8 (EVER2) in EV1 locus of chromosomes 17Q and 2P, have been identified as the cause of EV in many but not all cases. These genes encode transmembrane proteins with unknown function localized to the endoplasmic reticulum (9).

Immunohistochemical technique can be used to detect the capsid proteins (such as L1, L2 antigens) which are common in most HPVs, in clinical materials including formalin-fixed tissue, but immunohistochemistry is neither sensitive enough nor routinely performed (5). Also, HPV typing may be helpful in confirming the diagnosis of EV and will reveal whether or not the patient is infected with a type that is associated with cutaneous malignancy (1,5).

To our knowledge, there is only one report of palmar pit-like lesions in EV, but our cases are the first familial ones with this unique feature in the world with positive histologic findings suggesting a probable direct relationship between the palmar pit-like lesions with at least some of the EV HPV types that should be considered as a unique feature of the syndrome and confirmed with newer, more sensitive techniques.

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