GENETICS AND GENODERMATOSES

A RARE CASE OF FAMILIAR PALMOPLANTAR KERATODERMA AND ITS DIFFERENTIAL DIAGNOSIS

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Background: Palmoplantar keratodermas (PPKs) are a group of disorders that are diagnostically and therapeutically problematic in dermatogenetics1-3. Punctate PPKs are characterized by circumscribed hyperkeratotic lesions on palms and soles with considerable heterogeneity. In 18 families with autosomal dominant punctate PPK (OMIM #148600), we report heterozygous loss-of-function mutations in AAGAB, encoding alpha- and gamma-adaptin binding protein p34, at a previously linked locus on 15q22. p34, a cytosolic protein with a Rab-like GTPase domain, was shown to bind both clathrin adaptor protein complexes, indicative of a role in membrane traffic. Ultrastucturally, lesional epidermis showed abnormalities in intracellular vesicle biology. Immunohistochemistry showed hyperproliferation within the punctate lesions. Knockdown of p34 in keratinocytes led to increased cell division, which was linked to greatly increased epidermal growth factor receptor (EGFR) protein expression and tyrosine phosphorylation. We hypothesize that p34 deficiency may impair endocytic recycling of growth factor receptors such as EGFR, leading to increased signaling and proliferation.
Palmoplantar keratoderma describes a group of heterogeneous skin disorders, characterized by thickening (hyperkeratosis) of the palm and sole epidermis. Palmoplantar keratoderma can be either acquired during the lifetime or inherited. The disorder have been classified according to the pattern of lesions (diffuse, focal, punctate, striate), as well as histopathologic changes. Hereditary forms of palmoplantar keratoderma may also be associated with other ectodermal defects or extracutaneous manifestations. Hailey–Hailey disease, or familial benign chronic pemphigus, is a rare autosomal dominant acantholytic disorder, most commonly presents in young adulthood. It is characterized by outbreaks of erosions and flaccid blisters usually in the intertriginous regions.

Observation: The authors present a case of a 63-year-old male patient with a positive family- and personal history for palmoplantar keratoderma. He has been hospitalized several times for palmoplantar keratoderma, at his last hospitalization his plantar keratoderma caused inability of walk. Besides his palmoplantar keratoderma, especially in the intertrigionous areas, erosive, blistering, verrucous, cracked, erythematous plaques

were observed. His sister is suffering from same symptom. Based on positive family history and histopatholocial findings, an associated Hailey-Hailey was confirmed.

Key message: Familiar palmoplantar keratoderma and Hailey–Hailey disease are both very rare disorders, the association of this two condition is even rarer.