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We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.
Palmoplantar Keratoderma and Leukokeratosis anogenitalis: The Second Case of a New Disease

Abstract
An increasing number of syndromes with palmoplantar keratoderma (PPK) with associated diseases are being identified, representing a wide spectrum of distinct entities. At present only one case report has described the combination of marked anogenital leukokeratosis with diffuse PPK evolving in a collodion baby. We report a patient with a diffuse, nonprogressive PPK in combination with an intermittently pruritic, slowly progressive anogenital leukokeratosis. Hyperkeratosis of the perineal area was most pronounced and extended to the distal portion of the anal mucosa. The opalescent lesion was also visualized at the margin of the major labia. Vulvar structures were not otherwise involved or dystrophic. There were no signs or symptoms of ectodermal dysplasia. Specifically, the nails were normal and showed no signs of pachyonychia congenita. Other differential diagnoses included dykeratosis congenita and white sponge nevus, which may be associated with anogenital leukokeratosis, but a keratoderma is not associated with these entities. Keratin immunocytochemistry showed marked expression of suprabasal K17 and absence of K6 and K16. Further examination of the initial case described by Litin and Ruffi demonstrated the same expression pattern and supports the contention that these two cases represent the same entity.

Discussion
PPK refers to a heterogeneous group of skin diseases characterized by marked keratotic lesions involving the palms and soles [2, 3]. There is a large and increasing number of PPK with associated diseases [4], but only one case report has identified the association of PPK with leukokeratosis anogenitalis [1].

Differential diagnosis in the present case includes white sponge nevus, which is characterized by spongy lesions mostly of the oral mucosa. Rarely, external mucosa may be affected [5], and one case has been reported with white sponge nevus exclusively affecting the genital mucosa [6]. Histopathological findings in white sponge nevus are not spe-
Fig. 1. Diffuse PPK with an ill-defined border.
Fig. 2. Marked anal leukokeratosis.
Fig. 3. Whitish opalescence extending to the labium majus.
Fig. 4. Hyperorthokeratosis without epidermolytic changes. Hematoxylin-eosin. x32.
Fig. 5. a Marked expression of suprabasal K17 in the present case. b Identical expression pattern of K17 in the initial case [1].

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cific and resemble the features of our case. However, PPK has never been observed in conjunction with white sponge nevus. More recently, molecular genetic investigations have revealed underlying mutations of K13 and K4 in white sponge nevus [7, 8]. Some forms of acquired genital hyperkeratosis have been reported [9, 10], but they showed epidermolytic histopathology in men and were not associated with PPK. Leukokeratosis of the mucous membranes can be found in dyskeratosis congenital [11], but other characteristic clinical features such as nail dystrophy, reticulate pigmentation and progressive bone marrow aplasia were absent in this case. Anal or oral hyperkeratosis may occur in pachyonychia congenita. This entity is characterized by overcurved and thickened nails, PPK, hyperkeratosis of knees and elbows and tiny cutaneous horns over different skin areas. Although pachyonychia congenita genotype 2 has been associated with mutations of K17 [12] and nail involvement may be of late onset [13], this syndrome is not likely to account for the pathologic findings in our case.

Keratin staining was performed to further delineate the epidermal pathology in this case and to determine possible similarities with the case of Itin and Rufli [1]. Interestingly, both cases exhibited expression of K17, which is not expressed in normal stratified human epidermis. It is expressed, however, in hyperplastic epidermis and is found in association with several hyperproliferative epithelial diseases, including squamous and basal cell carcinoma, psoriasis and viral warts [14, 15]. Since K6/16 was absent, the epidermal pathology in this case cannot be simply explained by hyperproliferation. We believe that this reported case, even in the absence of lamellar desquamation after birth, represents the same syndrome as that published by Itin and Rufli [1].

Identification of further cases and additional investigation, including sequencing of the K17 gene, will be needed to clarify the pathogenesis and exact nosologic classification of this syndrome.

References