An Atlas of Nail Disorders, Part 11

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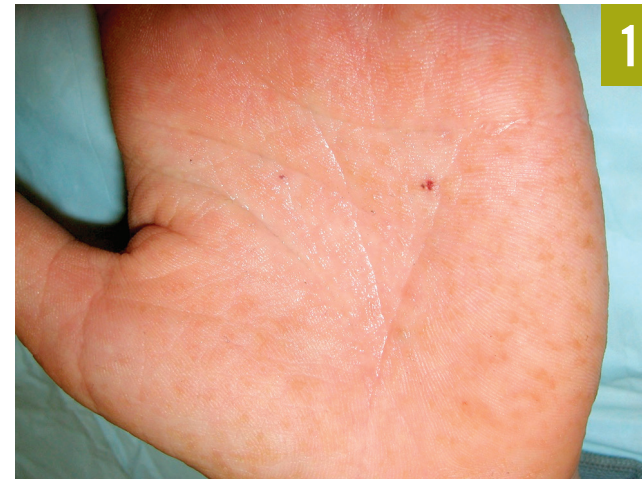
EDITOR'S NOTE: This article is part 11 of a 15-part series of Photo Essays describing and differentiating conditions affecting the nails. Parts 12 through 15 will be published in upcoming issues of *Consultant*. To access previously published articles in the series, visit the *Consultant* archive at www.Consultant360.com and click the "Journals" tab.

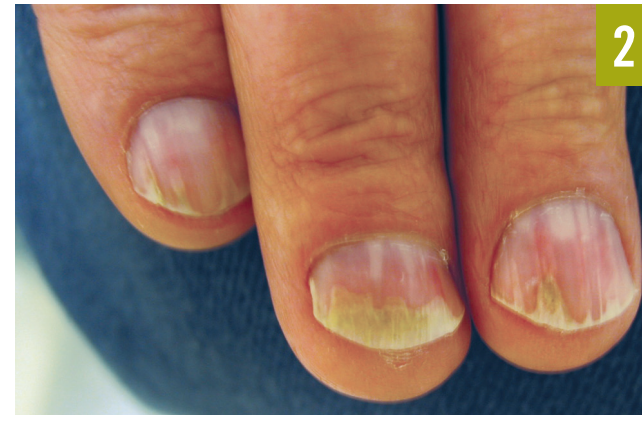
Nail Changes in Darier Disease

Darier disease, also known as keratosis follicularis, is a rare genodermatosis characterized clinically by keratotic papules and plaques in seborrheic areas and characterized histologically by acantholysis, dyskeratosis, and hyperkeratosis.[1,2] The disease is inherited as an autosomal dominant trait with high penetrance and variable expressivity.[3,4] The disease is caused by mutations in *ATP2A2* (ATPase, Ca^{2+} transporting 2) gene that encodes a sarcoplasmic/endoplasmic reticulum Ca^{2+} adenosine triphosphatase isoform 2 protein (SERCA2).[1,3,4] Sporadic mutations are common.[5] The sex ratio is approximately equal.[5,6] Typically, patients present at between 6 and 20 years of age, with onset peaking around puberty.[5,7]

Skin changes are characterized by greasy, discrete, flat-topped, hyperkeratotic papules that occur in seborrheic areas such as the trunk, lateral sides of the neck, scalp, limbs, and forehead.[2,4,5] The distribution is often symmetric. Lesions are itchy, skin-colored, yellow-brown, brown, or red-brown, and feel like coarse sandpaper.[2,8,9] They may coalesce to form large, crusted papillomatous or verrucous plaques/masses.[4,5,10] Lesions may have a foul odor if there is secondary infection or colonization.[2] In



On the palms and soles, Darier disease lesions often appear as hyperkeratotic papules, centrally depressed pits, and, less frequently, hemorrhagic macules.



Nail changes in Darier disease may include white and red longitudinal bands, onychorrhexis, onycholysis, brittle nails, splinter hemorrhages, longitudinal ridges of nails, wedge-shaped subungual hyperkeratosis, and V-shaped nicking/notching at the distal end of the nail plate.

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intertriginous areas, lesions may present as large, malodorous, fleshy, warty, vegetative, exuberant growths, sometimes with painful fissures.[4,6,7] On the palms and soles, lesions often appear as hyperkeratotic papules, centrally depressed pits, and, less frequently, hemorrhagic macules (**Figure 1**).[1,4,9,11,12] Flat verrucous papules known as acrokeratosis verruciformis may be seen on the dorsa of hands and feet.[2,9,13] In severe cases, palmoplantar hyperkeratosis may occur.[4] Other cutaneous features include café au lait spots and leukodermic macules.[11,14,15]

More than 95% of persons with Darier disease have nail changes that may include white and red longitudinal bands (longitudinal erythronychia), onychorrhexis, onycholysis, brittle nails, splinter hemorrhages, longitudinal ridges of nails, wedge-shaped subungual hyperkeratosis, and V-shaped nicking/notching at the distal end of the nail plate (**Figure 2**).[2,3,6,8,10-13] These changes may precede other signs of the disease.[2,12] While red longitudinal stripes are characteristic of Darier disease, the combined "sandwich" of white and red longitudinal bands resembling candy canes, often with a notch or onycholysis at the free margin of the nail, is pathognomonic.[1,4,7,8] Fingernails are affected more than toenails.[3]

Papules with a central depression, fissures, and ulcers may develop on the palate, buccal mucosa, or tongue.[2] The oral mucosa may assume a cobblestone appearance.[8,11] Intermittent parotid gland swelling is an infrequent but notable feature.[7,12] Affected patients often have dry eye syndrome with and more often without Sjögren syndrome, keratotic plaques on the eyelid, corneal opacities, and focal keratinization in the limbal conjunctiva.[16] ■

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Nail Changes in Dystrophic Epidermolysis Bullosa

Epidermolysis bullosa (EB) is a clinically and genetically heterogeneous group of rare inherited connective tissue disorders characterized by markedly mechanical fragility of epithelial tissue with blisters and erosions in skin and mucosal membranes in response to rubbing or frictional trauma.[1] A positive family history is supportive.

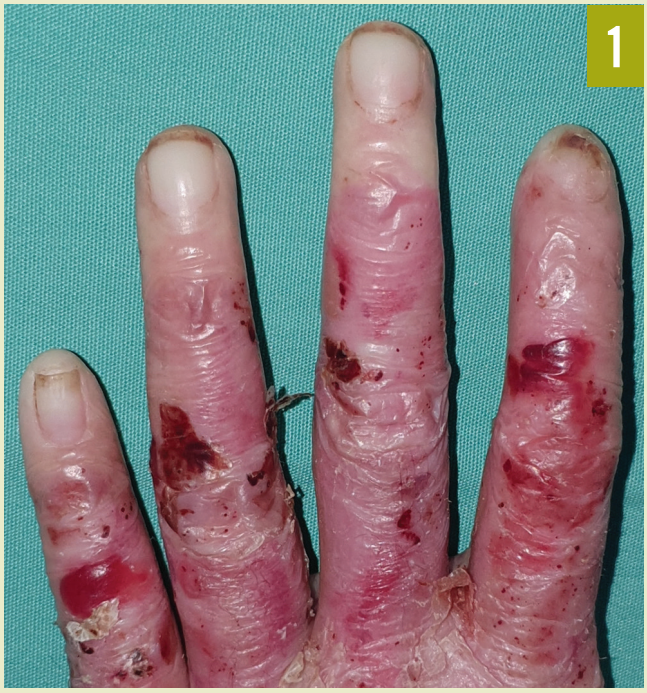
Based on the precise location at which skin cleavage or blistering occurs, EB is classified into 4 major categories: EB simplex (intraepidermal skin cleavage), junctional EB (skin cleavage within the lamina lucida or central basement membrane zone), dystrophic EB (cleavage below the lamina lucida), and Kindler syndrome (cleavage at multiple levels: intraepidermal, intra–lumina lucida, and sub–lumina lucida).[2] By far, EB simplex is the most common, accounting for approximately 80% of cases. On the other hand, nail changes are most common in dystrophic EB.[3]

Dystrophic EB is caused by mutations in the *COL7A1* gene, which encodes the α1 chain of type VII collagen, the major component of the anchoring fibrils.[3-5] The disorder is inherited as either an autosomal dominant or autosomal recessive trait.[3,6]

Dystrophic EB is characterized by skin fragility, mucocutaneous blistering in response to minor trauma with subsequent scarring, milia formation, and nail dystrophy (**Figure 1**).[2,6,7] Nail changes include periungual granulomatous tissue, nail erosions, onychogryphosis, and anonychia due to scarring and atrophy of the nail matrix and nail bed (**Figures 2 and 3**).[2]

In the severe form of autosomal recessive dystrophic EB, blisters are present at birth or shortly thereafter.[3,8] The blisters can affect the whole body.[3] Other clinical manifestations include aplasia cutis congenita, chronic nonhealing wounds, intractable skin ulcers, scarring, contractures, pseudosyndactyly of fingers, nail dystrophy, ankyloglossia, microstomia, corneal erosions/scarring, esophageal erosions/strictures, deformed and carious teeth, urethral erosions/strictures, anal erosions, and malnutrition.[3,8-10]

In the localized and generalized form of autosomal recessive dystrophic EB, the clinical manifestations are milder.[3] The blistering is often localized to the hands, elbow, knees, and feet



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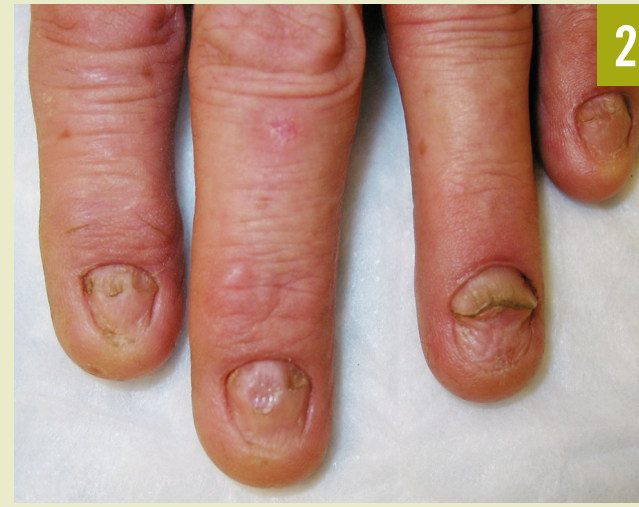
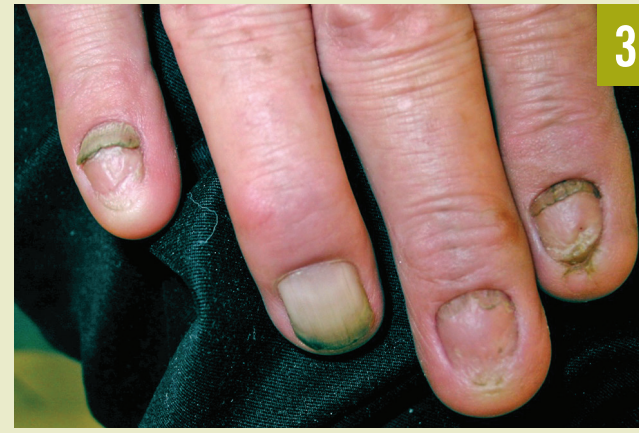
but can be more widespread to involve the trunk, but without the mutilating scarring seen in the severe form of autosomal recessive dystrophic EB.[3] Nail dystrophy is often present.[3,8]

In autosomal dominant dystrophic EB, the clinical manifestations are mild, and blistering is often limited to the hands, elbows, and knees.[3] On the other hand, nail dystrophy is common, and anonychia may occur (**Figures 2 and 3**).[3] In fact, onychodystrophy is the most important clue to the diagnosis of autosomal dominant dystrophic EB, especially in adults, because most patients have only limited scars that become less obvious with age.[2,3,11] ■



Nail changes in dystrophic EB include periungual granulomatous tissue, nail erosions, onychogryphosis, and anonychia due to scarring and atrophy of the nail matrix and nail bed.



In autosomal dominant dystrophic EB, nail dystrophy is common, and anonychia may occur.

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