

Pruritic Linear Papules on a 75-Year-Old Woman: A Case of Localized Darier-White Disease

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GOAL

To describe the presentation, etiology, and treatment of Darier-White disease (DWD)

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Identify the differences between generalized and localized DWD.
2. Recognize the histology of DWD.
3. Discuss treatment of DWD.

CME Test on page 224.

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Darier-White disease (DWD), commonly called Darier disease or keratosis follicularis, is a

genodermatosis seen in clinical practice. It exists more commonly in the generalized form but can present as a localized condition. Localized DWD is a rare entity characterized by epidermal changes that are like those seen in the generalized form but that are confined to a small area of skin. This entity is postulated to result from a postzygotic mutation and has the potential to be transmitted to offspring, which may result in the severe generalized form. We report a case of localized DWD diagnosed after biopsy of a recalcitrant linear dermatitis and discuss the salient features of this condition.

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The localized form of Darier-White disease (DWD) is an uncommon entity. Sometimes referred to as linear, zosteriform, segmental, or unilateral, it is characterized by abnormal keratinization of a localized area of epidermis. This entity is postulated to result from a postzygotic mutation and has the potential to be transmitted to kin, resulting in the generalized form. We report a case of this localized DWD and discuss its clinical aspects, differential diagnosis, histopathologic findings, modes of transmission, and treatment.

Case Report

A 75-year-old white woman presented with a linear grouping of papules on the right inferior medial thigh during a routine skin cancer screening. The patient stated that these papules had developed approximately 2 to 3 years earlier, and she associated them with intermittent intense pruritus. Furthermore, she denied a family history or personal history of any significant skin disease.

Numerous discrete 1- to 2-mm flesh-colored to brown papules were seen arranged linearly on the right aspect of the inferior medial thigh (Figure 1). There was no involvement of the oral cavity or nails.

The patient was initially prescribed triamcinolone ointment twice a day for what was thought to be a nonspecific dermatitis. After approximately 1.5 months of unsuccessful treatment, clobetasol ointment was applied to the lesions twice a day. One month of this treatment was also unsuccessful, therefore a punch biopsy of a lesion was performed (Figures 2 and 3).

Results of the biopsy were positive for acantholytic dyskeratosis, which is consistent with a diagnosis of linear DWD. Acantholytic dyskeratosis is characterized by suprabasal clefting, acantholytic keratinocytes in the cleft spaces, and dyskeratotic cells in the spinous layer (corps ronds) and stratum corneum (grains). Tazarotene gel was applied at bedtime for 3 to 5 minutes (short-contact therapy). After approximately 3 months of treatment, the patient discontinued the medication because of local irritation, though she reported a decrease in pruritus. On reexamination, the papules were still present but had decreased in thickness. No new lesions were noted.

Comment

DWD, or keratosis follicularis, was first described in 1889.^{1,2} This condition is characterized by abnormal keratinization of the epidermis, nails, and mucous membranes. Inherited as an autosomal dominant condition presenting in the first or second decade, it is characterized by eruptions of



Figure 1. Flesh-colored to brown verrucous papules in linear grouping on the right inferior medial thigh.

multiple yellow, brown, or flesh-colored pruritic papules. These are often found in a seborrheic distribution. These lesions may coalesce and become hypertrophic disfiguring growths. Often they are secondarily infected and malodorous. The nails may exhibit red and white linear streaks along the vertical axis, distal V-shaped notching, and subungual keratotic debris. Less commonly, mucosal membranes, including the oral cavity, can be affected. Small papules form a cobblestone appearance on these surfaces.³

Kreibich⁴ first described a localized variant of DWD in 1906. The localized variant is also referred to as zosteriform, linear, unilateral, or segmental DWD.⁵ Some also have proposed the term *acantholytic epidermal nevus* to describe this localized variant.^{6,7} Unlike generalized DWD, the localized variant involves a solitary area of the skin with lesions following Blaschko lines.^{5,6,8,9} Familial associations and nail or mucous membrane involvement are less common. The skin outside the lesion is completely normal.⁵ The generalized form of DWD is rare; in Scandinavian countries, the prevalence is 1 in 100,000.¹⁰ The linear variant, however, is even more uncommon; the English literature includes approximately 40 case reports.⁹ There is no sex predilection in linear DWD, and the mean age of onset is in the third or fourth decade (mean age, 27 years).⁹ This age of onset is later than that of the generalized form.³ As with the generalized form, patients with linear disease

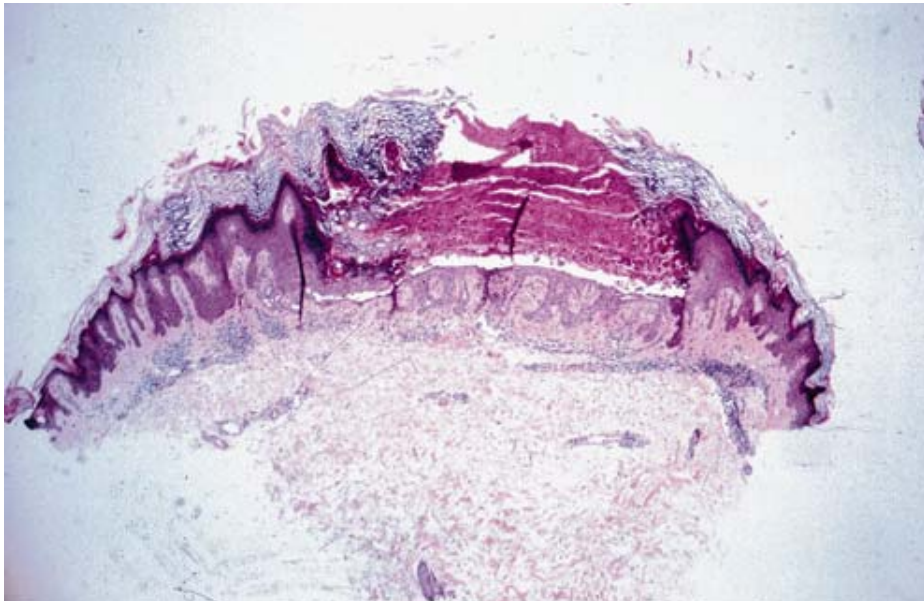


Figure 2. A lesion with signs of acantholysis and dyskeratosis (H&E, original magnification $\times 20$).

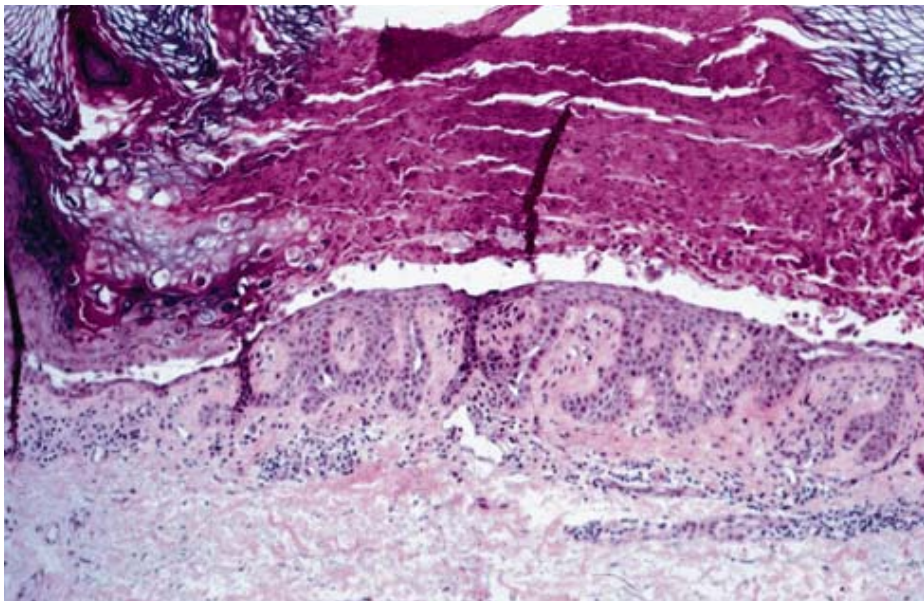


Figure 3. Characteristic lesion with signs of acantholysis and dyskeratosis (H&E, original magnification $\times 40$).

often report that their dermatitis appeared after significant sun exposure and worsens with heat, perspiration, mechanical trauma, and exposure to UVB light.⁹

The differential diagnosis of generalized DWD includes Grover disease (transient acantholytic dermatosis), seborrheic dermatitis, atopic dermatitis, benign familial pemphigus, and epidermal nevi. The diagnosis of linear DWD can generally be made conclusively by histologic examination. Management and treatment involve removal of exacerbating factors; wearing of cool clothing; and

use of sunscreen, topical steroids, oral and/or topical retinoids, oral antibiotics, and urea or lactic acid emollients.⁸

DWD is the result of a mutation of the *ATP2A2* (chromosome 12q23-24) gene, which encodes a sarcoplasmic or endoplasmic reticulum calcium-ATPase (adenosine triphosphatase). This abnormality may interfere with normal cell growth and differentiation.¹¹ In the type 1 segmental manifestation of DWD, a postzygotic somatic mutation is thought to create this variant. Thus, the heterozygous state causes the segmental findings,

whereas the skin surrounding the affected areas is completely normal.⁶ It is further hypothesized that, if the genetic mosaicism involves the gonads, transmitting the mutation to offspring may be possible. This may potentially result in generalized DWD.⁶ Although there is no clear evidence that the linear form of DWD is a precursor to the generalized form, the potential for transmission to offspring exists, and the patient should be appropriately counseled.

Given the limited severity of the localized variant of DWD, treatment predominantly involves topical therapy. A mild or moderately potent topical steroid may be of benefit, but the effects generally are disappointing.⁸ Topical retinoids have reduced hyperkeratosis within several months. Often these are used in combination with a topical corticosteroid to decrease the associated irritation.¹² Tazarotene gel is the newest retinoid used for the treatment of DWD. Several authors have found that treatment with tazarotene gel is superior to treatment with other topical therapies. Slight irritation, which is often noted, can be reduced by decreasing the concentration of applied medication.^{13,14} Bacterial colonization can be reduced with the application of antiseptics. Moisturizers (particularly those containing urea or lactic acid), sun protection, and cool cotton clothing also may help to reduce irritation.⁸

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