

Clustered Vesicles in a Blaschkoid Pattern

What's the diagnosis?



A 42-year-old woman presented with an intermittent nontender and minimally pruritic rash localized to the left side of the trunk of 20 years' duration. Four to 6 times per year blisters would develop and then resolve after 1 to 2 weeks with mildly pruritic brown patches. These patches would resolve within approximately 4 weeks. Most notably, the condition was exacerbated by sunlight and heat, though stress sometimes led to an outbreak of vesicles. The patient reported that the eruption, which she was told was recurrent shingles, would improve with oral valacyclovir 1 g twice daily and did not improve with topical steroid usage. She never had antecedent or concurrent fevers, shortness of breath, arthralgia, or cold sores. There was no family history of any blistering skin conditions such as epidermolysis bullosa, pemphigus, Darier disease, or bullous pemphigoid. Her partner also did not have a history of similar rashes, and the patient denied any history of travel outside of England and the southwestern United States. Initial physical examination revealed clustered vesicles surrounded by brown-pink patches in a blaschkoid pattern spanning from the anterior to posterior aspects of the left flank. Notably, the patient had no oral lesions and no changes of the hair or nails.

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The authors report no conflict of interest.

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The Diagnosis: Linear Vesiculobullous Keratosis Follicularis (Darier Disease)

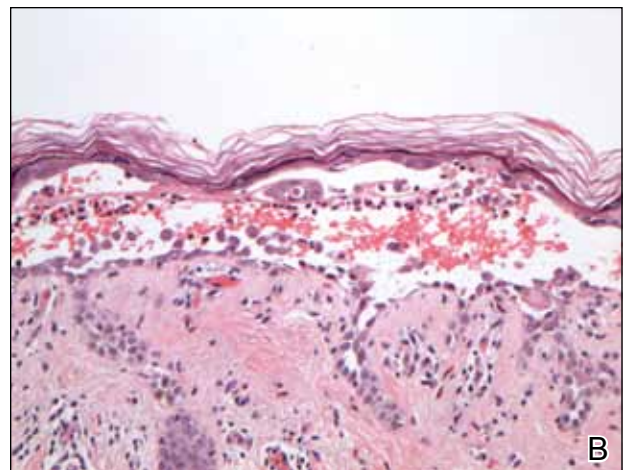
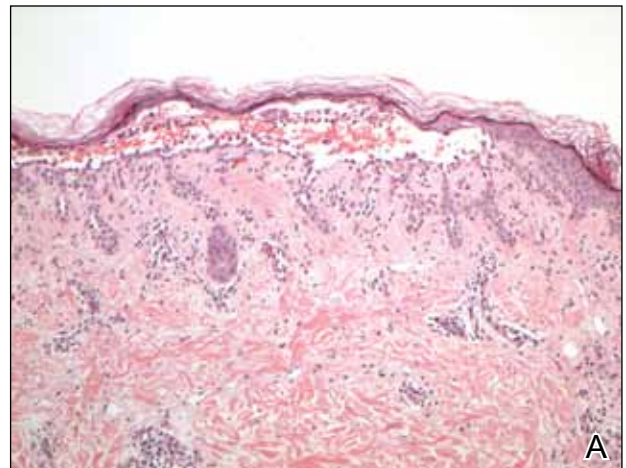
Darier disease (DD), or keratosis follicularis, is typically an autosomal-dominant disorder that is characterized by greasy hyperkeratotic papules that coalesce into warty plaques with a predilection for seborrheic areas. The lesions usually are pruritic; malodorous; and may be exacerbated by sunlight, heat, or sweating. Darier disease may be accompanied by oral mucosal involvement including fine white papules on the palate.¹ The condition also can be accompanied by hand and nail involvement (95% of cases) including palmar pitting, punctate keratoses, hemorrhagic macules, palmoplantar keratoderma, and acrokeratosis verruciformis–like lesions on the dorsal aspects of the hands and feet. Nail changes predominately occur on the fingers, manifesting as longitudinal splitting, subungual hyperkeratosis, or characteristic white and red longitudinal bands with V-shaped nicks at the free margin of the nail. In linear DD, hand and nail involvement is rare and, when present, ipsilateral to the primary lesions.^{1,2}

The clinical variants of DD are classified by lesion morphology or distribution, or both. Morphological variants include vesiculobullous, cornified, erosive, acral hemorrhagic, and guttate leukodermic macular.^{1,2} The clinical features of chronic relapsing vesicular lesions and histologic findings described in this case are consistent with vesiculobullous DD, though genetic testing was not performed.^{3,4} As in our case, some patients lack a family history and the disease is thought to be the result of genetic mosaicism or somatic postzygotic mutations that affect a limited number of cells. These mosaic variants are named by their cutaneous distribution (ie, linear, segmental, unilateral, localized) and tend to course along the Blaschko lines, most commonly on the trunk. Studies have shown various types of mutations specific to the *ATP2A2* gene in the affected tissue but not in the unaffected skin.⁵ This gene encodes for sarcoplasmic/endoplasmic reticulum ATPase SERCA2, which is responsible for intracellular calcium signaling. These mosaic forms of DD are unlikely to be inherited by offspring, in contrast to patients with mosaic epidermal nevi with epidermolytic hyperkeratosis who have a high likelihood of having children with generalized epidermolytic hyperkeratosis.⁶

Darier disease is a chronic incurable disease. Topical corticosteroid, retinoid, 5-fluorouracil, keratolytics, and laser ablation or excision are used in mild and limited disease with mixed outcomes.⁷ Oral retinoids are effective in severe or systemic cases of DD by

inhibiting hyperkeratosis.⁸ Individuals with DD are predisposed to infection, warranting regular surveillance and use of antimicrobials and bleach baths. In addition to prophylaxis for bacterial superinfection, patients also are predisposed to getting disseminated herpes simplex virus in the form of eczema herpeticum.

In our patient, the diagnosis was confirmed by performing a punch biopsy from one of the vesicular lesions. Histopathologic examination revealed suprabasal acantholytic dyskeratosis with



Histopathology revealed suprabasal acantholysis forming an intraepidermal cleft with superficial perivascular inflammation (A)(H&E, original magnification $\times 100$) and acantholysis with dyskeratotic keratinocytes floating within the intraepidermal cleft (B)(H&E, original magnification $\times 200$).

superficial perivascular and interstitial inflammation with eosinophils (Figure). Immunohistochemical staining showed no evidence of varicella-zoster virus or herpes simplex virus type 1 or type 2.

Our patient was prescribed tretinoin cream 0.1% daily and was advised to use sun protection and stop valacyclovir. At follow-up she noted decreased frequency of outbreaks after starting the tretinoin cream and the patient has now been free of any outbreaks for 8 months.

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