CLINICAL VIGNETTE

A Case of Unilateral Blaschkoid Darier's Disease

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Case Synopsis

A 35-year-old woman with unilateral left-sided Darier's disease in a blaschkoid distribution presents to dermatology clinic with complaints of recurring disease flare-ups several times per month. She was initially diagnosed at age 12 with biopsy confirmation at a dermatology clinic in Oregon. She otherwise has no significant past medical or family history. She also reports moderate-to-severe pruritus associated with her skin lesions, especially with exposure to heat. She was previously treated with topical tretinoin 0.05% and Tazorac 0.05% creams. She reported improvement in the appearance of the face and chest lesions with tretinoin 0.05% cream, and left thigh lesions with tazorotene 0.05% cream. Her daughter, age 15, is beginning to exhibit similar skin lesions.

On physical exam, there are multiple skin-colored and erythematous, often grouped, hyperkeratotic papules in a blaschkoid distribution on her left lateral neck and chest (Figures 1 and 2). More prominent hyperkeratotic erythematous papules coalescing into plaques were noted on her left buttock and left posterior thigh (Figure 3). There was mild V-shaped notching of distal nail plates on multiple fingernails.

Discussion

Darier's disease is an uncommon, autosomal dominant genodermatosis with an estimated prevalence of around 1/50,00-100,000.[1] This disease classically manifests within the first two decades of life with peak incidence during puberty.[1] Men and women are equally affected. Classic Darier's disease is clinically characterized by bilateral, symmetrically distributed, red-brown hyperkeratotic papules that may coalesce into warty plaques, usually found in seborrheic regions of the skin but also found in intertriginous areas.[2] These lesions may be malodorous and may have a greasy appearance. Pruritus is commonly observed, and symptoms are exacerbated with exposure to heat, sunlight, and perspiration.[2] Nail changes associated with Darier's disease include red and white longitudinal streaking and V-shaped notching at the distal free margin of the nails.[2] White papules of the oral mucosa (cobblestoning) and pitting (punctuate keratosis) on the palms and soles may also be observed.[2] Darier's disease is caused by mutations in the critical region within 12q23-24.1, which encodes ATP2A2, the gene for the sarcoendoplasmic reticulum calcium ATPase type 2 (SERCA2).[2] It is thought that mutations in this protein lead to abnormalities in keratinocyte adhesion and keratinization.[2]

In about 10% of Darier's disease cases, clinical manifestations are unilateral and typically spread along lines of Blaschko (Figure 4).[3] Two clinical variants have been described: type 1 is more common and follows a unilateral spread along Blaschko's lines, while type 2 is characterized by generalized, symmetrical skin involvement with a superimposed and increasingly severe unilateral streaks following Blaschko's lines.[4] Type 1 is felt to represent mosaicism due to post-zygotic somatic mutations representing localized areas of loss of heterozygosity. Type 2 is thought to represent heterozygous germline mutation with superimposed post-zygotic mutations in the wild-type allele.[4]

Pathological confirmation is needed for diagnosis. On histology, Darier's disease shows areas of acantholysis, characterized by intraepidermal suprabasal clefts and dyskeratosis in the form of eosinophillic "corps rods" and "grains" in the epidermis and stratum corneum (Figure 5).[4]

In addition to skin, nail, and mucosal changes, Darier's disease has been associated with neuropsychiatric abnormalities such as epilepsy, mood disorders, and intellectual difficulties.[5] It has been thought that mutations in the ATP2A2 gene increase the susceptibility to these disorders.[5] However, it is unclear whether this is directly related to the ATP2A2 gene or due to genetic linkage with a nearby locus that co-occurs more frequently in these patients.

For patients with mild or localized disease, avoidance of triggers, use of sunscreen and emollients, and topical retinoids are generally sufficient. For more severe cases, oral retinoids are most effective. Relapses, however, are common after cessation of retinoid therapy.[1,2]

Images

Figure 1: Left lateral neck.

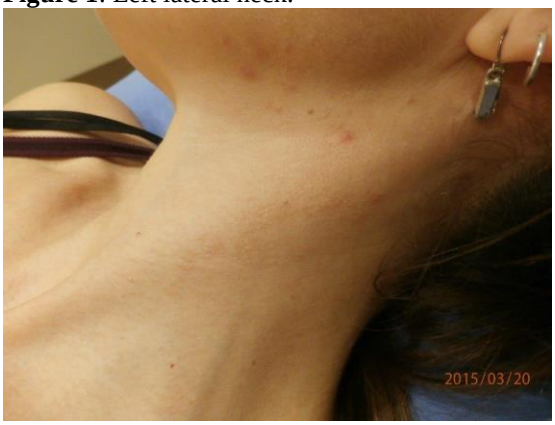


Figure 2: Chest

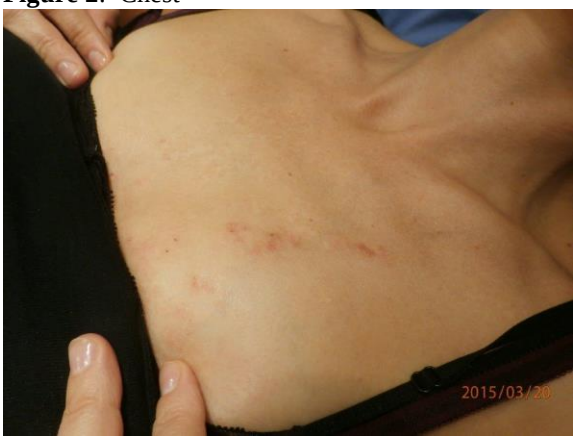


Figure 3: Left posterior thigh

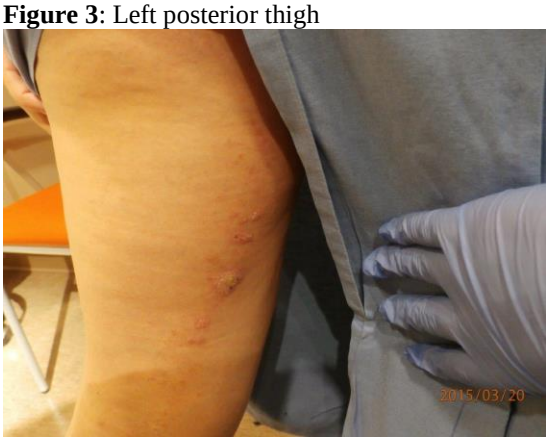


Figure 4: Blaschko Lines. Image reproduced with kind permission from Sun et. al.[3]

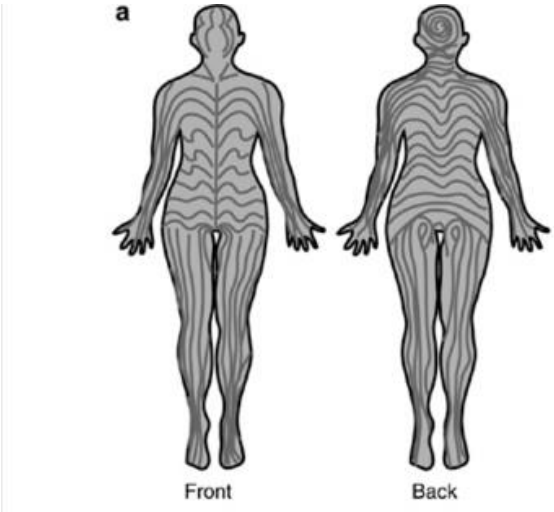
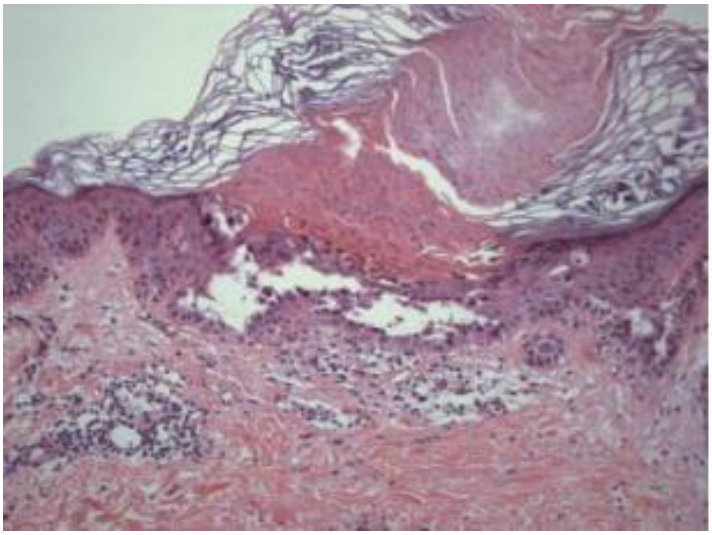


Figure 5: Biopsy revealing suprabasilar acantholysis with corp rods and grains. Image reproduced with kind permission from Sanderson et. al.[4]



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