

Case 19

A 40 year-old Thai woman from Surat Thani

Chief complaint: Multiple pruritic rashes for 30 years



(Fig. 19.1)



(Fig. 19.2)

Present illness: 30 years ago, she gradually developed multiple pruritic brownish papules on face, retroauricular area, neck, chest and extremities. The lesions worsened by sunlight, heat and sweating. She had only minimal improvement after treating with topical steroids.

Past history: None

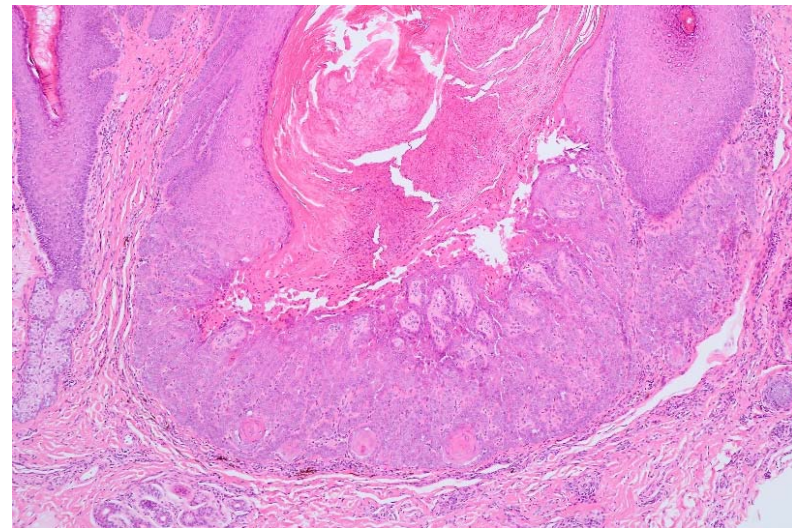
Family history: No family history of similar cutaneous lesions

Physical examination: Unremarkable

Dermatological examination: (Fig. 19.1, 19.2)

- Multiple pruritic brownish hyperkeratotic papules on face, retroauricular area, neck, chest and extremities
- Multiple, ill-defined, painless whitish papules with cobblestone appearance on hard palate
- Palmar pits on both palms and soles
- Multiple discrete minute hypopigmented macules
- Alternating longitudinal erythroleukonychia with V-shape notches

Histopathology: (S17-04271, right ear) (Fig.19.3)



(Fig. 19.3)

- Multifoci of focal acantholytic dyskeratosis in association with invagination of the acanthotic epidermis

Diagnosis: Darier disease

Treatment:

- Acitretin 10 mg/day
- 20% urea cream apply on thick lesions twice a day
- Cream base apply face twice a day
- Sun protection

Presenter: Saneerat Porntharukcharoen, MD

Consultant: Vipawee Ounsakul, MD

Discussion:

Darier disease, also known as Darier-White disease, keratosis follicularis, and dyskeratosis follicularis, is an uncommon autosomal dominant disorder, first reported by Darier and White in 1889.^{1,2} The occurrence of sporadic cases is reported approximately 40-50%.² Mutations in the *ATP2A2* gene, which encodes a sarco/endoplasmic reticulum Ca²⁺ ATPase (SERCA2), cause abnormal intracellular Ca²⁺ signaling resulting in both acantholysis and induction of apoptosis in Darier disease.^{1,2} The prevalence is reported from 1/30,000 to 1/100,000.² Men and women are equally affected.^{1,2} The disease begins between the ages of 6 and 20 years, with a peak onset during puberty.³

Darier disease is characterized by multiple firm, greasy yellowish-brownish hyperkeratotic papules coalescing into plaques or papillomatous masses distributing in seborrheic areas of the trunk, face and scalp.³ The lesions in particular papules developing at sites

of friction such as groin and axillae, are often associated with itching and malodor. It is worsened by sunlight, mechanical trauma, heat, humidity, infection and menstrual period.^{1,2} Mucosal involvement presents with white umbilicate or cobblestone papules.⁵ Oral, esophageal, cervical and rectal mucosa may be affected.^{1,5} Oral lesions are most commonly located on the palate, followed by the gingiva, buccal mucosa, tongue and the base of the mouth.^{4,5} Nail abnormalities are characterized by red and white longitudinal bands and distal V-shaped notches of the nail plate.^{1,2} Other associated findings include palmoplantar pits, guttate leukoderma, skin-colored, flat-topped papules in the dorsum of hands and feet.^{1,2,3,4} Additionally, psychiatric symptoms including depression, suicidal attempts and bipolar disorder were reported to be associated with Darier disease.⁶

Histologically, the section shows suprabasillary clefts with acantholysis and dyskeratosis.^{1,7} Acantholysis is caused by loss of intercellular adhesion.¹ Dyskeratosis is due to apoptosis of keratinocytes.¹ These dyskeratotic cells are described as "corps ronds" in malpighian layer and "grains" in stratum corneum.^{1,7}

Treatment of Darier disease is challenging and difficult. It is required only if there are troublesome symptoms. Mild disease can be managed by emollient, sun protection and avoiding of heat and sweating.^{1,8} Numerous treatments including topical corticosteroids, topical retinoids, topical 5-fluorouracil, diclofenac sodium 3% gel, doxycycline and laser therapy have been reported with limited success.^{1,9-13} Systemic retinoids such as acitretin, isotretinoin and alitretinoin are the most effective treatment for Darier disease, but their use are limited by their side effects, the need for regular monitoring and cost.^{1,14,15}

References:

1. Engin B, Kutlubay Z, Erkan E, Tüzün Y. Darier disease: A fold (intertriginous)dermatosis. *Clin Dermatol*. 2015;33:448-51.
2. Takagi A, Kamijo M, Ikeda S. Darier disease. *J Dermatol*. 2016;43:275-9.
3. Zeglaoui F, Zaraa I, Fazaa B, Houimli S, El Fekih N, Ezzine N et al. Dyskeratosis follicularis disease: case reports and review of the literature. *J Eur Acad Dermatol Venereol*. 2005;19:114-7.
4. Goh BK, Ang P, Goh CL. Darier's disease in Singapore. *Br J Dermatol*. 2005;152:284-8.
5. Bernabé DG, Kawata LT, Beneti IM, Crivelini MM, Biasoli ER. Multiple white papules in the palate: oral manifestation of Darier's disease. *Clin Exp Dermatol*. 2009;34:e270-1.
6. Yang JJ, Lopes RS, Pereira MC, Tebcherani AJ, Pires MC. Severe Darier's disease in a psychiatric patient. *An Bras Dermatol*. 2015;66-8.
7. Kassar S, Tounsi-Kettiti H, Charfeddine C, Zribi H, Bchetnia M, Jerbi E et al. Histological characterization of Darier's disease in Tunisian families. *J Eur Acad Dermatol Venereol*. 2009;23(10):1178-83.
8. Heo EP, Park SH, Yoon TJ, Kim TH. Induction of Darier's disease by repeated irradiation by ultraviolet B; protection by sunscreen and topical ascorbic acid. *J Dermatol*. 2002;29:455-8.
9. English JC 3rd, Browne J, Halbach DP. Effective treatment of localized Darier's disease with adapalene 0.1% gel. *Cutis*. 1999;63:227-30.
10. Le Bidre E, Delage M, Celerier P, De Muret A, Lorette G. Efficacy and risks of topical 5-fluorouracil in Darier's disease. *Ann Dermatol Venereol*. 2010;137:455-9.
11. Millán-Parrilla F, Rodrigo-Nicolás B, Molés-Poveda P, Armengot-Carbó M, Quecedo-Estébanez E, Gimeno-Carpio E. Improvement of Darier disease with diclofenac sodium 3% gel. *J Am Acad Dermatol*. 2014;70:e89-90.
12. Sfecci A, Orion C, Darrieux L, Tisseau L, Safa G. Extensive Darier Disease Successfully Treated with Doxycycline Monotherapy. *Case Rep Dermatol*. 2015;7:311-5.
13. Brown VL, Kelly SE, Burge SM, Walker NP. Extensive recalcitrant Darier disease successfully treated with laser ablation. *Br J Dermatol*. 2010;162:227-9.
14. Anuset D, Goutorbe C, Bernard P, Reguiat Z. Efficacy of oral alitretinoin for the treatment of Darier disease: a case report. *J Am Acad Dermatol*. 2014;71:e46-8.
15. Zamiri M, Munro CS. Successful treatment with oral alitretinoin in women of childbearing potential with Darier's disease. *Br J Dermatol*. 2013;169:709-10.