Case 29

Multiple brown papules on the face and flexures

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Patient: A 12-year-old Thai girl from Bangkok

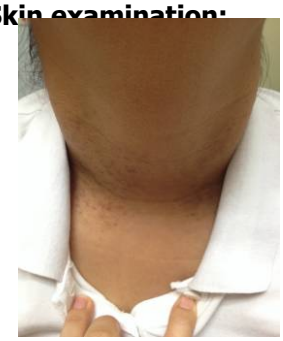
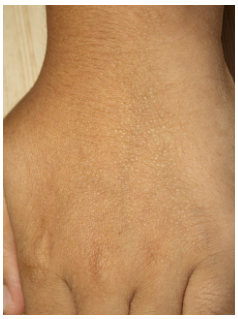
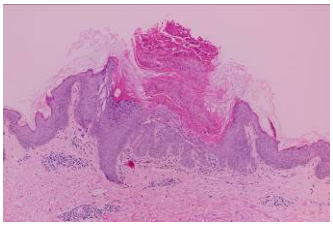
Chief complaint: Rash on the face and flexural areas for 3 years

Present illness: The patient presented with a 3-year history of multiple asymptomatic brownish papules on the face, neck, both axillae and groin. The rash got worse and became redness with heat, sunlight and sweating. Her mother took her to the private hospital and skin biopsy was done. She was treated with topical steroids but slightly improved.

Past history:
- Normal growth and development
- Complete immunization

Family history: No other family members showing similar skin lesions

Skin examination:

Skin
- Multiple brownish hyperkeratotic papules on the neck, both axillae and groin
- Multiple skin-colored, flat top papules on both dorsum of hands and palms

Nails:
- Alternate white and red longitudinal bands
- V-shaped nick at nail edges

Oral mucosa: No lesions

Histopathology: **(**S14-17067A and B; neck and scalp)
There is epidermal hyperplasia with focal acantholytic dyskeratosis.

Diagnosis: Darier disease

Treatment:

- Patient education about the natural history
- Advice to avoid the precipitating factors
- Isotretinoin 10 mg/d
- 0.025% Topical vitamin A apply once at bedtime
- 10% Urea cream apply twice daily

Discussion:

Darier disease is an uncommon autosomal dominant skin disease caused by a mutation in the ATP2A2 gene. This mutation leads to the malfunction of a SARCO/ENDOPLASMIC reticulum calcium ATPase and is believe to be responsible for the loss of epidermal cells and abnormal keratinization.[1] Two heterogenous mutation in Axon 12 of ATP2A2 gene in two different families in Darier disease were reported.[2]

Clinical features are usually in form of greasy, crusted, keratotic, yellow-brown papules found particularly on flexure and seborrheic areas of the body, palmo-plantar pit and papules of hands and feet. It maybe also affected in mucous membranes and nails. Oral and esophageal involvement have been described.[3,4] A case of basal cell carcinoma developing in a patient with type 2 segmental Darier disease as been reported, however, malignant transformation is rare.[5] In patient with pigmented skin might develop depigmented macules or guttate leucoderma.[6]

Darier disease can be exacerbated by the stress condition, radiation, mechanical trauma and infection. The abundant reports on Darier disease in patients were skin types I-IV, skin type V is scarce.[7] The skin types of the patients hold the key of the severity of disease. Skin type V-VI provide protection of UVB radiation, likely result in less UVB induced exacerbation of disease. Moreover, patient with darker skin types are high risk of developing vitamin D3 deficiency and disrupted calcium physiology.[8] A number of clinical studies have also described the co-occurrence of neurologic and psychiatric symptoms with Darier disease including mental retardation, epilepsy, a slowly progressive encephalopathy and mood disorder.[9]

Histologically, the lesions present suprabasal cleft in the epithelium with acantholytic and dyskeratotic cells.

Treatment of Darier disease is often difficult and unsatisfactory because of its chronicity and many exacerbating factors. Topical treatments include corticosteroid, retinoid, keratolytic agents, antiseptics and emollient. Due to UVB radiation is known to stimulate the cyclo-oxygenase-2 pathway within keratinocyte. There are 2 case report of Darier disease that responded to 3% topical diclofenac sodium gel.[11] This increase the production of prostaglandin E2 and reduces the expression of ATP2A2 and its protein product SERCA2.[10] We proposed a new therapeutic approach using COX inhibitor such as diclofenac.[11]

Furthermore therapeutic options are laser therapy, dermabrasion and antibiotics. Systemic therapy with vitamin A derivatives such as acitretin and isotretinoin is the treatment of choices.[12] There is evidence that Alitreinoin might be a well-tolerated alternative for the systemic treatment of the patient with retinoid responsive skin disease, among them in Darier disease, as suggested by a recent case report. Alitretinoin has a more favorable safety profile than other vitamin A derivatives especially as regards mucocutaneous side effects, sever itch and superinfection.[13]

In addition, unlike acitretin, contraception for women of childbearing age

needs to be extended for only one more month after the end of treatment with Alitretinoin because of its shorter biological half-life.[13]

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