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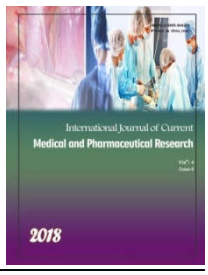

DARIER DISEASE: A RARE CASE REPORT OF COMEDONAL VARIANT

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ABSTRACT

Darier disease, also known as keratosis follicularis is a rare autosomal dominant genodermatosis, commonly presents with follicular and extrafollicular greasy hyperkeratotic papules and plaques, arising primarily in seborrheic areas. However, other uncommon clinical presentations have been reported. This paper reports a rare presentation of Darier's disease, which mainly showed comedonal papules. The patient is a 35 year-old male presented with 8 months history of mildly itchy slowly progressive generalized skin lesions. His past medical history, drug history and review of systems were all unremarkable. His parents are non-consanguineous and no similar case in the family. Skin examination revealed multiple tiny non-scaly brownish papules (comedonal like) scattered on his scalp, neck, upper extremities, abdominal wall, chest wall and back. His nails showed Longitudinal red and white streaks as well as notching of the free edge of the nail plate. Hairs, and mucus membranes were all normal. Skin biopsy showed Hyperkeratosis, acanthosis, epidermal acantholysis and suprabasal clefting. Based on the clinical and the histopathologic features, the diagnosis of Darier Disease was made.

INTRODUCTION

Darier disease is an autosomal dominant genodermatosis with complete penetrance and variable expressivity. Men and women are equally affected.[1] It commonly begins between the ages of 6 and 20 years. Although, the disease initially described as follicular dyskeratosis, the papules are not limited to a perifollicular location. Darier disease, commonly presents with follicular and extrafollicular greasy keratotic red to brown papules and plaques, arising primarily in seborrheic areas involving the scalp; especially its margins; face, trunk, and lateral aspects of the neck. However, in addition to this classical presentation, there are other uncommon clinical variants listed in table 1.[2] The disease has characteristic mucous membrane and nails findings. Histologically, it showed Hyperkeratosis, acanthosis, epidermal acantholysis with suprabasal clefting, and dyskratotic acantholysis with corps and ronds appearance.[3]

Case report

A 35-year- old male presented with 8 months history of slightly itchy slowly progressive generalized skin lesions. Past medical history, drug history and review of systems were all unremarkable. His parents are non-consanguineous and no similar case in the family. Skin examination revealed Skin examination revealed multiple tiny non-scaly brownish papules (comedonal like) scattered on his scalp, neck, upper extremities, abdominal wall, chest wall and back (figure 1). His nails showed Longitudinal red and white streaks as well as notching of the free edge of the nail plate (figure 2).

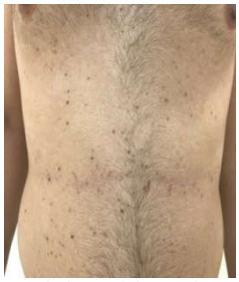

Figure 1 Multiple tiny non scaly brownish papules (comedones- like) scattered on the abdomen

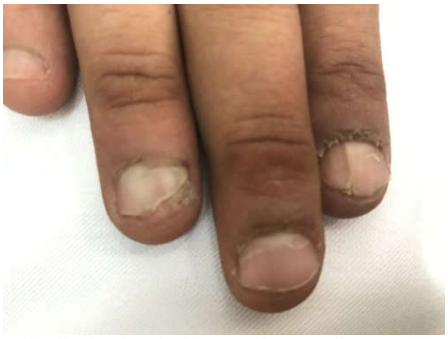

Figure 2 Longitudinal red and white streaks as well as notching of the free edge of the nail plate

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Hairs, and mucus membranes were all normal. Skin biopsy showed Hyperkeratosis, acanthosis, epidermal acantholysis and suprabasal clefting (figure 3).

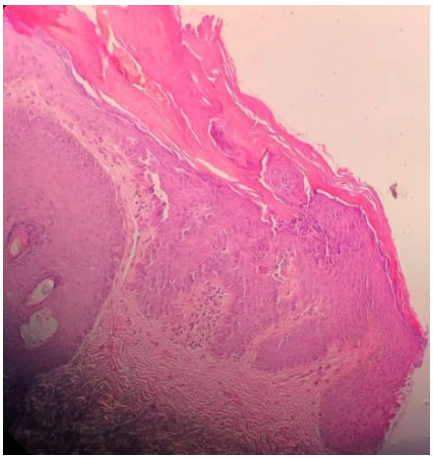

Figure 3 histopathology of the skin lesions showing hyperkeratosis, acanthosis, intra-epidermal acantholysis with suprabasal clefting

Based on the above clinicopathological features, a diagnosis of Darier Disease was made. The patient was reassured about his condition. He was offered a genetic counseling. A topical 0.05% tretinoin cream was prescribed and to be followed regularly in dermatology clinic.

Table 1

Variants of Darier Disease
Guttate hypopigmentation
Hyperpigmented flat-topped papules and macules (freckle-like)
Acral hemorrhagic lesions
Vesiculobullous lesions
Comedones, facial cysts, acne conglobata
Keratoderma
Localized e.g intertriginous areas, acral sites, or the scalp
Segmental
Periocular nodulocystic lesions
Alopecia, cutis verticis gyrata

DISCUSSION

Darier disease was first described by Jean Darier and James C White in 1889. [4,5] It is an autosomal dominant genodermatosis with complete penetrance and variable expressivity. Mutations in the *ATP2A2* gene which encodes an endoplasmic reticulum (ER) Ca^{2+} ATPase pump, SERCA2,[6] Insufficient function of the 2b isoform of the sarco/endoplasmic reticulum Ca^{2+} ATPase (SERCA2b) leads to abnormal intracellular Ca^{2+} signaling. This results a loss of suprabasilar cell adhesion (acantholysis) and an induction of apoptosis (dyskeratosis). Lithium carbonate has also been reported to induce Darier's disease in some individual. [7]

The peak onset of the disease is during puberty (ages 11–15 years). In our patient the disease has later onset where it started during the 4th decade of life. The primary lesions are keratotic, sometimes crusted, red to brown papules, which develop in a "seborrheic" distribution involving the face, trunk, scalp (especially its margins), and lateral aspects of the neck. Small (2–3 mm) hypomelanotic macules may be admixed with the keratotic papules are the predominant feature. However, our patient has the comedonal variant of the disease showing widespread tiny brownish nonscaly comedone- like papules scattered on his scalp, neck, trunk and upper extremities. The exacerbating or the triggering factors of the disease include, the summer, sweating, heat, and occlusion. The odor of the disease is distressing, which can lead to social isolation. The skin lesions in Darier disease are prone to secondary infections, a feature which was not seen in our patient. The reason behind the frequent secondary infections is due to evidence for an impaired local immune response in Darier disease. Characteristic nails findings which was present in our patient include longitudinal red and/or white lines, longitudinal ridging and fissuring, wedge-shaped subungual hyperkeratosis, and V-shaped notches. Oral mucosa changes include painless whitish papules or rugose plaques are noted in 15–50% of patients with Darier disease. The hard palate is the most common site of involvement, followed by the gingiva, buccal mucosa, and tongue. Corneal opacities or ulcers, salivary gland obstruction, laryngeal involvement, salivary glands involvement and neuropsychiatric disorders have all been reported to be associated with Darier disease. None has been present in our patient. Darier disease follows a chronic course with fluctuations in disease severity.

The main differential diagnosis in our case was acne. However, the widespread involvement of scalp and upper extremities, the characteristic histopathology ruled out acne.

Different modalities of therapy have been presented in the literature, such as topical retinoids, topical steroids and the liberal use of emollients. Isotretinoin, acitretin, and alitretinoin are effective treatments.[8] Surgical treatment may be an effective alternative for focal recalcitrant lesions. Dermabrasion, excision followed by split-thickness grafting, and laser therapy can be helpful. [9,10] Antibiotics and antifungal agents can be used to reduce malodor secondary to infections.

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