CASE REPORT

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DARIER'S DISEASE: A CASE REPORT AND REVIEW OF LITERATURE

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Abstract. Introduction: *Darier's disease is an autosomal dominant disorder caused by mutations in the ATP2A2 gene, and clinically presented with hyperkeratotic papules and plaques in a seborrheic region.* ***Clinical Case Description:*** *We observed a 48-year-old male patient who presented with persistent pruritic skin lesions on the trunk and extremities. Physical examination revealed erythematous and hyperkeratotic papules and follicular keratosis. The diagnosis of Darier's disease was based on the clinical presentation and confirmed with histological examination. Treatment with low-dose methylprednisolone resulted in significant improvement.* ***Discussion and Conclusions:*** *The case highlights the importance of considering Darier's disease in patients with persistent pruritic skin lesions and emphasizes the need for accurate diagnosis and adequate treatment.*

Key words: *Darier's disease, clinical features, diagnosis, treatment*

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INTRODUCTION

Darier's disease (DD), also known as keratosis follicularis, was described by Darier and White in 1889 [1]. It is autosomal dominant disorder caused by mutation in the ATP2A2 gene on chromosome 12q23-q24.1, which codes a calcium pump channel of the endoplasmic reticulum [2]. Typical onset of DD occurs during adolescence with hyperkeratotic papules and plaques in a seborrheic area such as chest, back, forehead, scalp margins, and ears. In addition to the cutaneous manifestations, Darier's disease is characterized by palmoplantar pits and acral keratosis [3].

Nail involvement is also common and is characterized by alternating white and red longitudinal streaks, commonly referred to as candy-cane nails, as well as V-shaped notches at the free edge of the nail. Oral involvement may present as cobble-stoning of the oral mucosa, gingival hypertrophy, and sialadenitis [4].

We present a clinical case of DD, presented with pruritic skin lesions on various body parts, which persisted despite prior treatment for seborrheic dermatitis and discuss its clinical features, diagnosis and treatment.

CLINICAL CASE DESCRIPTION

A 48-year-old male patient presented with pruritic skin lesions on the trunk, upper, and lower extremities. The aggravation of lesions occurred three months prior, and despite receiving prolonged treatment for

seborrheic dermatitis the patient experienced minimal improvement.

Clinical examination revealed multiple erythematous papules with crust on the trunk (Fig. 1A). Hyperkeratotic papules are disseminated in seborrheic areas, such as the anterior chest (Fig. 1B) and back. The papules at flexural sites had a tendency to coalesce, forming large, often exophytic plaques. Additional characteristic features included flat papules affecting the dorsal surfaces of the hands and feet. In addition to cutaneous involvement, the patient exhibited nail abnormalities, including longitudinal lines and ridging and V-shaped notches at the free edge (Fig. 2). The prominent feature of the patient's condition was consistent with a diagnosis of Darier's disease.

The histology of skin reveals acantholysis, dyskeratosis and hyperkeratosis in epidermis. Dyskeratosis refers to eosinophilic structures termed "corps rounds" that are characteristic of Darier's disease (Fig. 3).

Treatment for this patient commenced with methylprednisolone 40 mg/24 h, resulting in a significant improvement in the patient's condition.

This case study underscores the importance of considering Darier's disease in patients presenting with persistent pruritic skin lesions. Accurate diagnosis and timely administration of appropriate treatment, such as systemic corticosteroids, are essential for achieving positive clinical outcomes.

DISCUSSION

Darier's disease belongs to the group of acantholytic dyskeratoses. As autosomal dominant disorder DD has chronic course with relapses and remissions.

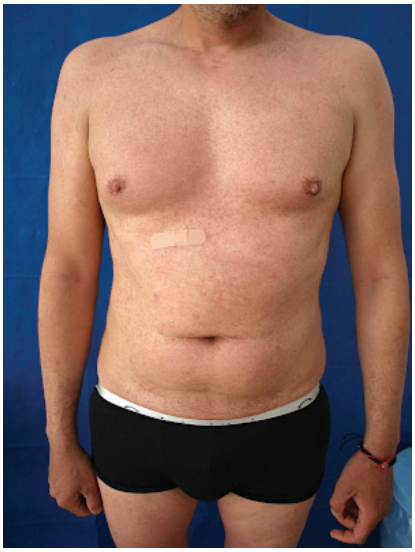

Fig. 1 A. Multiple erythematous and hyperkeratotic papules with crusts on chest, abdomen, and upper limbs

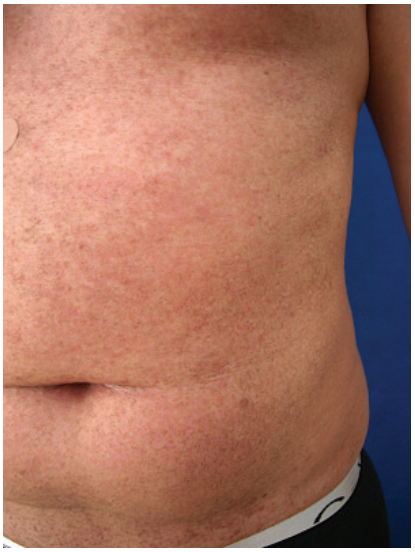

Fig. 1 B. Hyperkeratotic papules on chest and abdomen at higher magnification

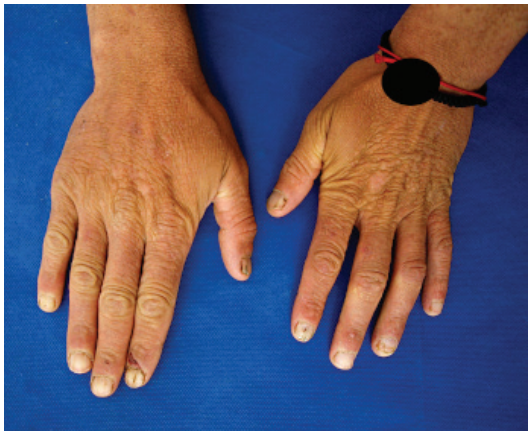

Fig. 2. Cobblestone papules on hands and fingers, longitudinal bands and ridging and V-shaped notches of nails

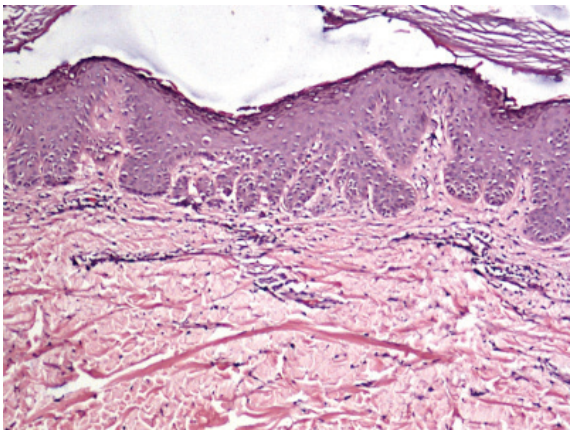

Fig. 3. The histology of lesional skin shows acantholysis, dyskeratosis with "corps rounds" and hyperkeratosis in epidermis (H&E 100x)

Pruritus is the most commonly reported complaint among patients [5]. Pain may also be present, although some individuals may not experience any symptoms. Patients also complain of an unpleasant odor, particularly in areas of skin folds where secondary infections are more likely to occur [5]. Environmental factors such as heat, sweating, sunlight, and stress can exacerbate the lesions. In women of childbearing age, there may be a premenstrual exacerbation of the disease.

Clinical forms of Darier disease include disseminated or localized variants with hypertrophic, bullous, dyspigmented and linear arranged lesions [6-8]. Keratotic papules or plaques are distributed in a unilateral, linear, zosteriform, or localized pattern and may follow Blaschko's lines [7, 8].

Palmar pits and punctate hyperkeratotic papules on both the dorsal and palmar aspects of the hands, described as acrokeratosis verruciformis of Hopf are regarded as genetic evidence of unitary origin with allelic similarities [9]. Nail involvement manifests as longitudinal bands and ridging, V-shaped notches at the free margin, and subungual hyperkeratotic debris [10].

Oral involvement may present with a granular or cobblestone papules affecting the palate, tongue, buccal mucosa, gums, epiglottis, and pharyngeal walls and in some cases mimic leucoplakia [11].

Diagnosis of DD is supported by characteristic histology. Epidermal changes include: acantholysis and suprabasal clef formation, dyskeratosis with the presence "corps rounds" and enlarged pale keratinocytes in the granular layer. Hyperkeratosis and parakeratosis are commonly present. It is important to differentiate DD from other acantholytic dyskeratoses, such as Hailey–Hailey disease and Grover disease [12]. Ultrastructural studies demonstrate separation of keratin filaments from the desmosome complex, so the keratinocytes not only lose their ability to adhere, but also have increased proliferation leading to abnormal keratinization [13, 14].

Darier's disease is generally not accompanied by concurrent medical conditions; however, certain families have exhibited an increased prevalence of neuropsychiatric disorders, including bipolar affective disorder, mental retardation, schizophrenia, and epilepsy [15]. Additionally, a slowly progressive encephalopathy has been reported (16).

Patient management involves providing appropriate advice, such as maintaining a cool environment and wearing cotton clothing. Photoprotection with high sun protection factor (SPF) sunscreens is recommended for photosensitive patients during the summer [17]. Mild cases typically require the use of emollients, sunscreens, and protection from excessive heat. In moderate to severe cases, various treatment options have been tried with varying degrees of success. Oral retinoids, such as acitretin, isotretinoin and alitretinoin, have shown promising results [19-21]. Antibiotics are commonly used as adjuvants to treat superimposed cutaneous infections; however, in two patients treated with doxycycline was reported complete disease remission [22].

Topical retinoids like tretinoin and isotretinoin have demonstrated different therapeutic responses, but their effectiveness is limited due to potential irritation [18]. However, topical adapalene [23] and tazarotene [24] have shown improvement in localized DD. To maintain remission, it is important for patients to avoid triggers such as UV light exposure, mechanical trauma, and certain medications [25].

Laser treatments have emerged as a promising modality. Fractional CO_2 laser vaporization has been effective in removing persistent and symptomatic plaques, particularly when targeting the follicular infundibulum [26]. A newer approach using erbium YAG laser, which minimizes thermal injury through vaporization, has also shown success [27].

With the knowledge that gene mutation is the underlying cause of Darier's disease, future treatment options may become more effective. Efforts in this direction hold the potential for more successful therapies in the future.

CONCLUSIONS

In conclusion, DD should be considered in patients with persistent pruritic hyperkeratotic lesions, aggravating in summer and after sun exposure. Accurate diagnosis and timely treatment are crucial for positive clinical outcomes. Continued research and increased awareness of this condition are vital for facilitating early recognition and effective management of Darier's disease.

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