Our Dermatology Online

Case Report

Disseminated form of Darier's disease

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ABSTRACT

Darier's disease is a rare genetic skin disorder with two types: type 1, which is unilateral, and type 2, which is bilateral and more common. This article presents the case of a sixty-year-old patient with disseminated Darier's disease successfully treated with acitretin. The patient was diagnosed through clinical examination and a biopsy, which showed typical features such as acantholysis and dyskeratotic keratinocytes. The disease usually begins in childhood due to a mutation in the ATP2A2 gene. It manifests as keratotic lesions on seborrheic areas (chest, neck, trunk, face) that may be itchy and uncomfortable, with possible nail and oral mucosa changes. Darier's disease is chronic and recurrent, and treatment aims to alleviate symptoms and improve quality of life. Understanding its clinical and genetic aspects is crucial for effective management.

Key words: Darier's disease, Genodermatosis, Type 2 Darier's disease, Acitretin

INTRODUCTION

Darier's disease is a rare autosomal dominant genodermatosis. It is associated with a mutation in the ATP2A2 gene resulting in the dysfunction of endoplasmic reticulum calcium ion-dependent ATP-ase, an enzyme responsible for the formation of intercellular bonds and cell adhesion. There are two types of the disease: unilateral and disseminated. The disseminated form is more common. It is characterized by the occurrence of keratotic papules located mainly in the seborrheic areas of the skin involving the truck, scalp, face, and lateral aspects of the neck. Additionally, the clinical picture may include changes in the nail plates and mucous membranes. Histopathological examination shows acantholysis and dyskeratosis. In the treatment of Darier's disease, general therapies and local preparations are used.

CASE REPORT

A sixty-year-old patient came to the Dermatology Department of the Provincial Hospital in Elbląg for the diagnosis and treatment of skin lesions located mainly on the trunk. They were accompanied by slight itching. The patient associated the appearance of skin lesions with exposure to UV radiation and sweating. The family history of dermatological diseases was positive: the patient's brothers were diagnosed with Darier's disease.

During the physical examination, the patient reported additional problems, namely arterial hypertension, chronic kidney disease, osteoarthritis of the spine, a stroke of the brain stem with paralysis of the facial nerve on the right side, and implantation of a DDD stimulator in the past. The patient also reported hypersensitivity to non-steroidal anti-inflammatory drugs. The patient had chronically been taking torasemide, nebivolol, carbamazepine, amlodipine with indapamide, and perindopril.

A physical examination revealed red to brown keratotic papules located on the trunk, with a tendency to merge in the right mammary and deltoid areas and in the presternal area (Figs. 1a – 1d), and longitudinal red and white lines as well as notching of the free edge of the nail plate in the left hand (Fig. 2).

The videodermatoscopic image of the skin lesions revealed a central, yellowish-brown polygonal area surrounded by a white halo (Fig. 3a). Within the

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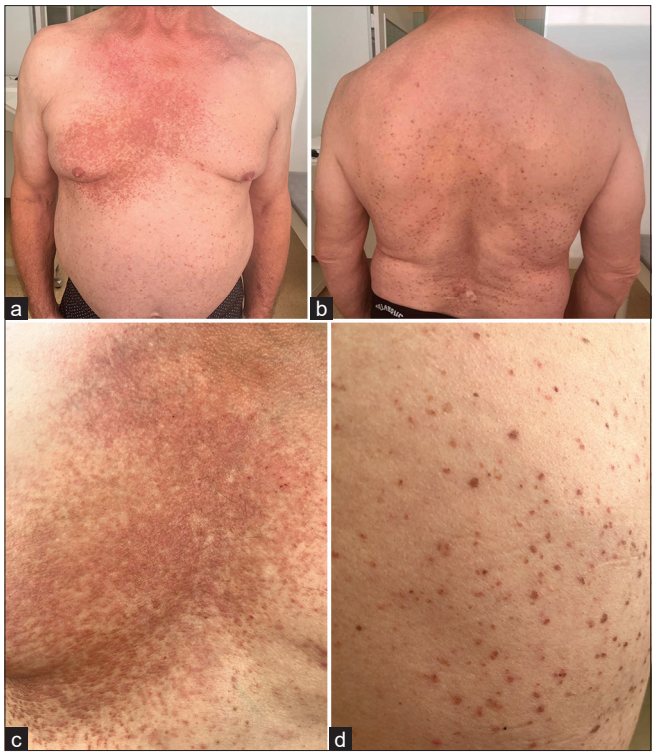

Figure 1: (a-d) Truncal involvement with a predilection for seborrheic areas. The Keratotic papule may vary from red to brown in color and may become confluent.

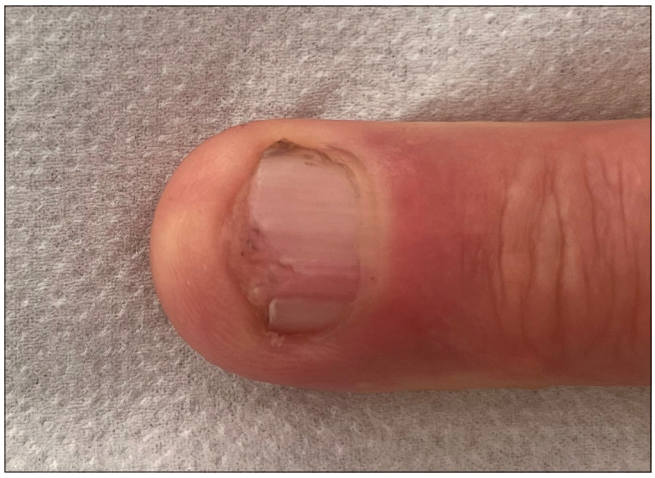

Figure 2: Longitudinal red and white lines as well as notching of the free edge of the nail plate in the left hand.

nail plate, red and white longitudinal stripes with a V-shaped indentation of its free edge were revealed (Fig. 3b).

Laboratory blood tests showed increased levels of total cholesterol, LDL cholesterol, triglycerides, creatinine, urea, and glucose. During hospitalization, a biopsy was taken from the affected skin. A histopathological examination described hyperkeratosis, grains, and *corps ronds* in addition to acantholysis, leading to suprabasilar clefting.

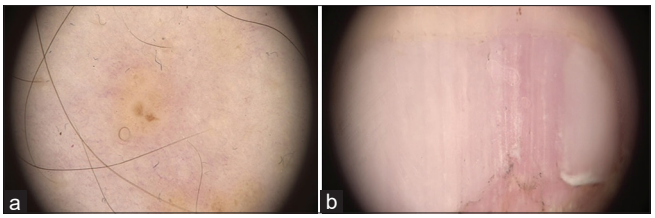

Figure 3a: a) Videodermatoscopic image of the skin lesion on the trunk. b) Videodermatoscopic image of the altered left hand's fingernail plate.

Based on the clinical, videodermatoscopic and histopathological findings, the patient was diagnosed with Darier's disease. During the stay at the Dermatology Department, general treatment with acitretin (20 mg daily) and a local glucocorticosteroid, exfoliation, and moisturizing treatment were administered, resulting in a reduction of skin lesions. Moreover, due to lipid disorders, lipid-lowering treatment was initiated. The patient was discharged home with a recommendation for further care at the Hospital Dermatology Clinic.

DISCUSSION

Darier's disease (DD) or Darier–White disease, also known as keratosis follicularis, is a rare genodermatosis inherited as autosomal dominant (AD), yet not always familial. Approx. 47% of patients do not have a reported family history of the condition [1].

The present patient had a known family history: two of his brothers were diagnosed. Therefore, patients should be provided with genetic counseling that includes information about the likelihood of genetic transmission to their children. DD occurs with the frequency of 1 in 30000–100000 population and has an equal sex and ethnic distribution [2,3]. The onset typically occurs during childhood or adolescence [4]. Approx. 70% of patients experience the disease onset between the ages of 6 and 20 [5].

It was described for the first time in 1889 by Jean Darier and James Clark White [6].

The defect that occurs in this disease is a heterozygous mutation in the ATP2A2 gene, which encodes type 2 of sarcoendoplasmic reticulum Ca2+pump(SERCA2), which transfers calcium ions from the cytosol into the sarcoplasmic or endoplasmic reticulum, facilitating the hydrolysis of adenosine triphosphate (ATP) in conjunction with calcium transport.

ATP2A2 may be expressed in the skin and the brain. Therefore, in some cases, DD presents with neuropsychiatric manifestations [7]. A biopsy of the impacted region is essential for confirming the diagnosis. The characteristic histological features in DD include acantholysis above the basal layer and dyskeratotic keratinocytes referred to as *corps ronds*, and parakeratotic cells, referred to as *corps grains*, are distinctive histological markers of the condition [6,8].

DD belongs to the group of dyskeratotic acantholytic dermatoses, which also includes Hailey–Hailey disease, warty dyskeratoma, and acantholytic dyskeratotic acanthoma. These conditions share common features such as acantholysis and dyskeratosis, which are consequences of abnormal keratinization [9].

Immunofluorescence of a skin biopsy may distinguish between various acantholytic disorders [10]. Patients commonly present with keratotic lesions in seborrheic areas of the upper body, which includes the chest, neck, trunk, and face, which may appear as vesicles or pustules and are frequently associated with itching and discomfort. Furthermore, specific changes may be observed in the nails and oral mucosa [10,11].

Mucous membrane involvement is observed in 15% of patients [12].

The patognomic symptoms of this disease are typical nail changes: V-shaped nick at the free margin of the nail, red and white longitudinal bands, and longitudinal nail ridges [10].

DD follows a chronic course marked by recurrent episodes. The factors that may make the condition worse include lithium carbonate, exposure to UV light, perspiration, heat, and infections [10].

Several other clinical variations have been documented, such as unilateral, linear, segmental, and zosteriform DD [13].

CONCLUSION

The main aim of treating DD is to alleviate symptoms and enhance the patient's quality of life. Systemic retinoids, including isotretinoin and acitretin, which are viewed as providing symptomatic relief rather than being curative, are the initial treatment of choice for all patients and demonstrate efficacy in 90% of cases [14,15]. Numerous dermatological side effects associated with systemic retinoids have been documented, with common occurrences such as dry lips and cheilitis [16].

The duration of treatment should be adjusted based on the patient's clinical response. Recognizing the clinical features and genetic basis of Darier's disease is crucial for precise diagnosis and effective management of affected individuals. With appropriate care, patients with this condition may live rewarding lives.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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