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A case of segmental form of type 1 mosaic Darier's disease

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Abstract

Darier's disease is a rare genetic disorder with autosomal dominant inheritance. It is characterized by hyperkeratotic papules in seborrheic areas. Associated abnormalities include nail abnormalities and changes in the mucous membranes. Exacerbation of the disease occurs with exposure to high temperatures, sun, and sweating, resulting in a worsening clinical picture in summer months. The unilateral zosteriform pattern is a rare variant that is clinically manifested by a unilateral outbreak of erythematous keratotic papules without any other associated symptoms. Here we present a 52-year-old male with a zosteriform pattern of Darier's disease. We also discuss the most important clinical and pathohistological characteristics of the disease and various treatment options.

Keywords: zosteriform Darier's disease, acantholytic dermatosis, regression, partial abrasion, CO_2 laser

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Introduction

Hereditary acantholytic dermatosis, or Darier's disease, is an autosomal dominant genodermatosis characterized by scaly papules and plaques in seborrheic regions of the skin, and changes to the nails and mucous membranes. The prevalence of Darier's disease ranges from 1 in 30,000 to 100,000 individuals. The disease affects both men and women with equal frequency (1).

Darier's disease is caused by a mutation in a gene encoding the enzyme ATPase A2A, which is important for the functioning of the calcium pump. Improper functioning of the pump results in compromised intercellular adhesion and consequent acantholysis.

Skin changes usually occur during adolescence. In most cases, the clinical picture is generalized and symmetrical, and less than 10% of all cases present with various localized lesions. The unilateral zosteriform pattern of Darier's disease is a rare variant that is clinically manifested by a unilateral outbreak of erythematous keratotic papules without any other associated symptoms (2).

Here we present a case of a unilateral zosteriform pattern of Darier's disease with lesions localized on the lower right abdominal region with histopathological confirmation.

Case report

A 52-year-old male patient presented with multiple brown warty papules localized on the lower right abdominal region (Fig. 1). The lesions first appeared 2 years earlier. Deterioration of the clinical picture occurred during the summer months as a result of increased exposure to sunlight and higher environmental temperatures. During the other seasons, the lesions partly regressed; however, thus far they have never disappeared completely. Over time, the number of lesions increased and they spread to the right lumbar region. No one in the patient's family has had any similar condition in the past.

On local cutaneous examination, multiple brownish hyperkeratotic papules were seen on the lower right abdominal region in a linear distribution. The lesions extended into the right lumbar region. Examination of the nails and mucous membranes did not reveal any significant changes or deviations. Laboratory parameters were not significantly elevated, and all other routine examinations were within normal ranges.

Given that the clinical picture was not very clear, we initially decided to treat the skin lesions with medium-potency corticosteroids. The patient was scheduled for follow-up in 2 months. However, the condition had not improved by then, and so we decided to perform a biopsy and histopathological examination of the tissue.

A shaving biopsy of the lesion on the lower right abdomen was performed and the sample was sent for histopathological examination, which revealed suprabasal acantholysis as the leading histological change, hyperkeratosis, acantholytic keratinocytes, and dyskeratotic cells referred as round bodies or granules, which are typical in Darier's disease.

Based on the histopathological findings, the skin lesions in our patient could be attributed to three possible diagnoses: transient acantholytic dermatosis (a.k.a. Grover's disease), acantholytic acanthoma, or Darier's disease. Based on the correlation between clinical presentation and histopathological examination, the patient was diagnosed with a zosteriform pattern of Darier's disease.

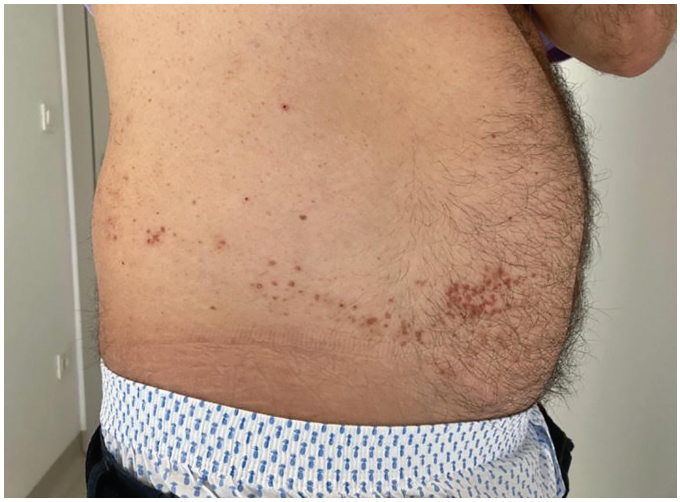

Figure 1 | Presence of warty papules over the lower right abdominal region.

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After unsuccessful local use of corticosteroid cream, a test ablation with a carbon dioxide laser was performed on a palm-sized area of the skin covered with lesions. In our case, the skin lesions regressed completely 2 months after partial abrasion with a carbon dioxide laser. Interestingly, regression occurred almost entirely in the whole area and not only in the treated area. Local cutaneous examination showed slight hyperpigmentation; otherwise, there were no hyperkeratotic papules characteristic of Darier's disease. The patient was monitored with regular checkups at the outpatient dermatology clinic for another year, and during this time, no recurrence was observed (Fig. 2).

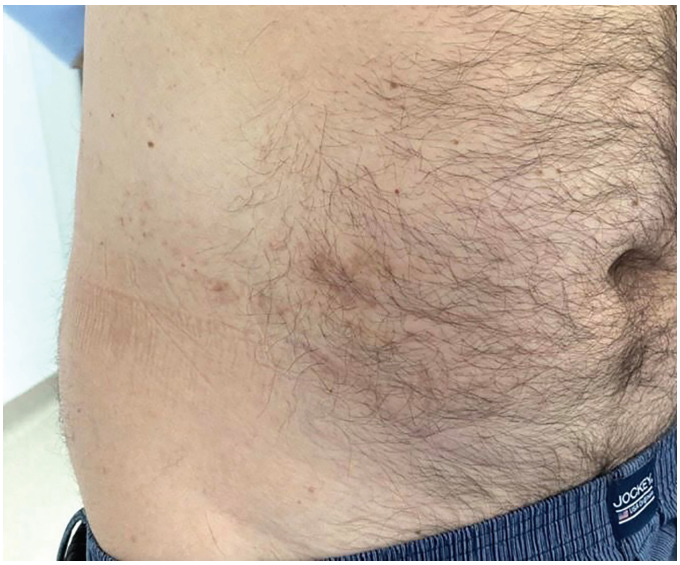

Figure 2 | Hyperpigmentation without characteristic keratotic papules 4 months after partial abrasion with a carbon dioxide laser.

Discussion

Darier's disease is a genodermatosis that was first described in 1889 by Darier and White. The prevalence of the disease ranges from 1:30,000 to 1:100,000 and the disease affects men and women with equal frequency. Inheritance of the defective ATP2A2 gene is autosomal dominant. The ATP2A2 gene carries information for the SERCA enzyme or pump, which is required for calcium transfer in the cell. Calcium deficiency leads to incorrect expression of P-cadherin in desmosomes, resulting in cell contacts not functioning properly.

Skin changes usually occur in adolescence, with a peak incidence at puberty. The clinical picture usually includes oily, scaly papules on the seborrheic areas of the face, scalp, neck, back, central part of the thorax, and skin folds (axillary, inguinal, and intergluteal). Papules may coalesce into plaques. Nail involvement and changes to the mucous membranes, palms, and soles can be observed (3).

Although skin involvement is symmetrical in most patients, various segmental forms are observed in about 10%. In the case of unilateral presentation of Darier's disease, it is thought to be a postzygotic somatic mutation in the ATP2A2 gene, leading to genetic mosaicism and unilateral skin involvement along Blaschko's lines (4, 5). Usually, such changes first appear in the 3rd or 4th decade of life, and patients have a negative family history. Other characteristic changes in the context of Darier's disease (involvement of nails and mucous membranes) are usually absent. Triggers for the change include exposure to the sun, heat, sweating, friction, or infection (6).

In our case, the lesions first appeared on the skin of our patient at age 50. Thus, the condition can be considered type 1 mosaic Darier's disease. The patient presented with characteristic skin lesions in a seborrheic pattern. Further examination of the nails and mucous membranes showed no other abnormalities, and no other family member has had any similar condition in the past. The patient's condition worsened during the summer and slightly improved during other seasons.

Diagnosis is based on the presence of typical skin lesions and skin biopsy. Histological examination is crucial for definitive confirmation of the diagnosis. The histological picture of Darier's disease is the same in the extended and segmental form and shows dyskeratotic cells and follicular hyperkeratosis in the upper layers of the epidermis. Two types of dyskeratotic cells are observed: large, round, acantholytic keratinocytes with dark nuclei surrounded by a light pink ring of condensed keratin in the spinous layer, and flattened cells with a very small remnant of a dark nucleus usually located in the stratum corneum. Two other options—Grover disease (Fig. 3) and acantholytic acanthoma—could easily be excluded on clinical grounds.

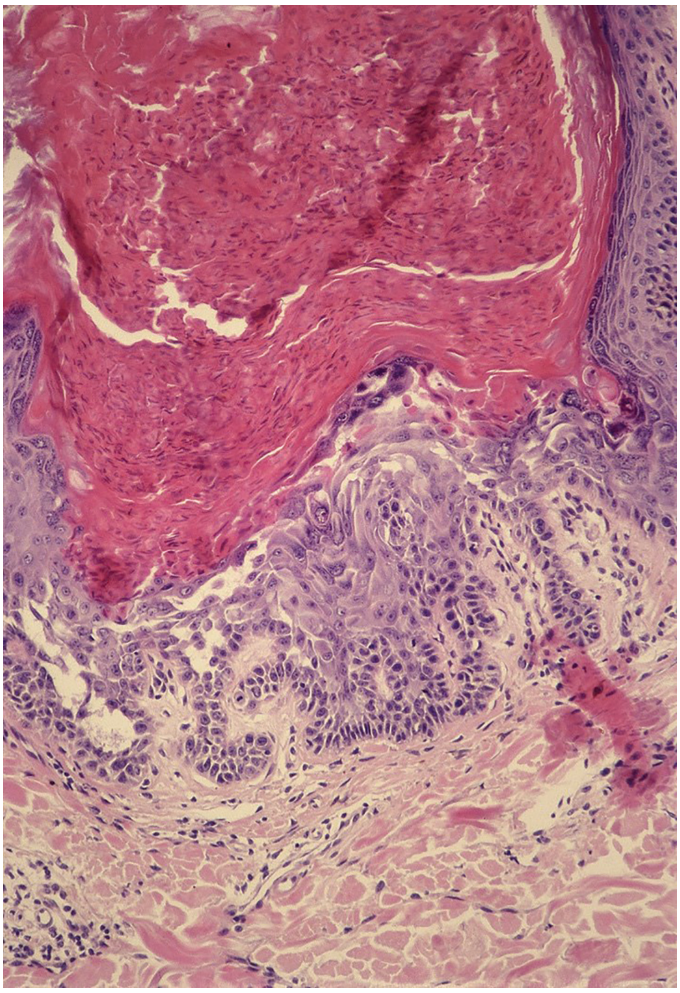

Figure 3 | Transient acantholytic dermatosis / Grover's disease.

Although systemic retinoids are the basis of treatment for the disseminated form of Darier's disease, they are less frequently needed in the segmental form. Because the disease is usually mild, the use of medium-potent corticosteroids and behavioral measures are usually sufficient to treat the localized form of Darier's disease. These include avoidance of triggers, regular use of emollients, wearing cotton clothing, and use of sunscreen creams when exposed to the sun (8). For persistent problems, topical reti-

noids, keratolytic preparations (with salicylic or lactic acid), calcineurin inhibitors, 5-fluorouracil, or vitamin D3 analogues can be used (9–11). Antiseptic soaps and topical antibiotic ointments help prevent secondary infections (7). In lesions resistant to other treatments, excision (after which recurrence may otherwise occur), the use of electrosurgery, dermabrasion, laser ablation, photodynamic therapy, or, in the case of excessive sweating, application of botulinum toxin may be considered (12, 13).

In our patient, regression occurred after partial abrasion with a carbon dioxide laser. Interestingly, there was a regression of skin lesions in the entire area and not only in the treated area.

Conclusions

The segmental form of Darier's disease, known as the zosteriform or linear form, is a rare inherited autosomal dominant disorder. Histological examination is indispensable to confirm the diagnosis, but the final diagnosis is always based on a correlation between the clinical presentation and histopathological findings. Late age of presentation is a rule. Grover's disease and acantholytic acanthoma should be considered as differential diagnoses.

Behavioral measures and moderate topical corticosteroids are usually sufficient to treat the symptoms of the localized form of Darier's disease. Other treatment options for this type of the disease include topical retinoids and keratolytic agents. In lesions resistant to other treatments, laser abrasion with a carbon dioxide laser can be a promising method.

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