

## Classic Darier's Disease in Family Presentation: 2 Case Reports

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### ABSTRACT

*The Darier disease is a rare genodermatosis, of dominate autosome heritage with variable penetration. That's why, cold present cases of variable phenotypes, also in patients with high degree of kinship. It was related two cases of Darier disease in a family (mother and daughter) with different phenotypic patterns. **Case 1:** female, 17 years old, student, relate the hyperkeratotic papules appearance of brownish color initially in anterior trunk that evolutes to neck and abdomen there is 5 years. Without lesions on face or scalp. **Case 2:** 48 years old, female, farmer, until the 19 years with appearance of brownish papules and plaques, hyperkeratotic initially in face that with the years pass evolutes to scalp, dorsum and inferior members. The phenotype of the disease could variate on generations and also inside of one same generation. In those cases, is perceptible the phenotype variety: in case 1, there is more commitment of trunk and neck, without commitment facial, scalp and member; the case 2 (mother) presents high commitment facial, scalp and inferior members.*

### Keywords

Darier disease, Phenotype, Treatment, Evolution.

### Introduction

Darier disease (DD) or Darier-White disease, also known as keratosis follicularis, is an autosomal dominantly inherited genodermatosis characterized by greasy hyperkeratotic papules in seborrheic regions, nail abnormalities and mucous membrane changes, of autosomal dominant inheritance with variable penetrance [1,2]. The disease remains uncertain, but it was suggested that it is caused by ATP2A2 gene mutations that codified a reticulum endoplasmic Calcium pump. The abnormal function of sarcoplasmic reticulum isoform 2b leads to the abnormal signalization of calcium intracellular [3]. The result is the loss of the suprabasal cellular adhesion (acantholysis) and the induction of apoptosis (dyskeratosis).

The prevalence is almost 1/50000, and it appears regularly in the beginning of puberty or adult life. It affects both the genders. Clinically, the distinctive lesion is characterized by hyperkeratotic papules that coalesce into plaques and occur primarily not only

in seborrheic but also in intertriginous areas. Coalescence of the papules produces irregular warty plaques or papillomatous masses, which, in the flexures, become hypertrophic and malodorous with painful fissures. Associated abnormalities include nail abnormalities characterized by nail fragility, red and white longitudinal stripes and V-shaped notches at the free margin of the nails. Secondary infection is common. Sun, heat and sweating exacerbate the disease. DD never remits, but oral retinoids may reduce hyperkeratosis. DD has also been associated with an increased prevalence of a variety of neuropsychiatric conditions. This work presents two cases of DD in a family (mother and daughter) with different phenotype patterns.

### Case 1

Female patient, 17 years old, single, student, reports the appearance of hyperkeratotic papules of brownish color initially on the anterior trunk that evolved to the neck region and abdomen there was 5 years. Refers to slight itch and worsens of the picture with solar, warm or sweat explosion. Never realized specific treatment for each lesion. Claim that in the family, mother and two maternal aunts present similar cases. In the physical exam,

they verified (Figures 1 and 2) several brownish perifollicular and hyperkeratotic papules in cervical region, anterior and posterior chest, inframammary region and abdomen. Without lesions in the face and scalp. Presence of alternated erythematous longitudinal lines with white lines that extend from base to free edge on fingernails bilaterally (Figures 3 and 4).



Figure 1 and 2



Figure 3 and 4

Realized histopathologic exam that revealed epidermis with compact hyperkeratosis with formation of grains and granulosus layer with round bodies (Figure 5). It is still observed suprabasal acantholytic cleft (Figure 6). Papillary dermis and superficial reticular with mild lymphocytic infiltrate. The histological picture confirms the clinical hypothesis of Darier Disease.

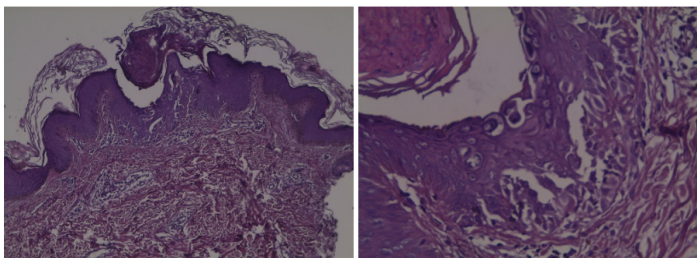


Figure 5 and 6

Evolution and treatment: Beginning the treatment with topical Trethionone 0.05% and orientations of to use cotton clothes, solar protector and avoid solar exposition. The patient returned to the clinic two months after beginning the treatment with partial improvement of the symptoms. At this moment was chosen to initiate oral Isotretinoin 20 mg/day, after realization of laboratorial exams including the beta HCG.

## Case 2:

Patient 48 years, female, farmer, relate that until the 19 years realize the appearance of brownish papules and plaques, hyperkeratosis initially on face that with years past evolutes to scalp, back, superior members, abdomen and inferior members. She relates the worst of the lesions with sweating and solar exposition. She says that searched several physicians, although the clinic diagnosis was confirmed 10 years after the beginning of the symptoms. She used Isotretinoin 20 mg/day and posteriorly 40 mg/day, without satisfactory answer. There are 3 years since Acitretin in the dose of 25 mg/day with an unsatisfactory answer yet (Figures 7 and 8).



Figure 6 and 7

## Discussion

The Darier disease is a disturbance of keratinization hereditary autosomal dominant. Has complete penetrance, although presents variable expression. The phenotype of the disease could variate into the generations and also inside of one same generation, not possibly make previsions respect to the gravity of commitment in offspring of an affected person. In the presented cases, is perceptible this phenotype variety, while in case 1, there is major commitment of chest and neck, without commitment of face, scalp and members; the case 2 (mother) presents intense facial, scalp and inferiors' members bilaterally commitment.

These dermatoses tend to appear during the two first decades of life that corroborate the study's cases, in which the disease signals and symptoms appeared into 13 and 19 years of age. The lesions are constituted by brownish papules, rough, and could be recovered by lipidic crust. The disease has predilection by body seborrheic areas: scalp, front, nasolabial sulcus, ears, dorsum and pre-external region. The ungues alterations in Darier Disease are characteristic,

could have tuning and fragility of the ungual lamina, red and/or white longitudinal lines that pass by until nail base to the free edge. When these red and white lines alternate, made an image in sandwich that is considered an aspect pathognomonic of the disease. The principals' histopathologic findings are acantholysis by loss of cellular adhesion and keratinocytes dyskeratotic (round bodies) in the prickly/ grainy layer and "grains" in horny platform. Because it will be a rare genetic character disease it is important to recognize it so that there is not a mistaken diagnosis, avoid interventions, costly and not resolute.

To date, there is no cure for Darier's disease. Treatment goals include alleviating symptoms (such as irritation, itching, and foul odor), preventing or treating infectious complications, and improving aesthetics [4].

Patients with DD should prioritize the use of light cotton clothing, the routine use of sunscreens, more frequently in the summer period, as well as avoiding hot environments, in order to minimize sweating. Topical treatments mainly include corticosteroids and retinoids. Low to medium potency topical corticosteroids are chosen to reduce the most inflammatory lesions. As for topical retinoids, Tretinoin 0.1% and Adapalene 0.1% are used in patients with mild or localized disease to reduce hyperkeratosis and flatten popular lesions. There are isolated reports of response to topical treatment with Fluorouracil, Tacrolimus, Pimecrolimus and 3% Sodium Diclofenac gel [7]. Oral retinoids, including Acitretin and Isotretinoin, decrease hyperkeratosis, smooth papules, reduce odor, and produce significant clinical improvement in most patients with severe or generalized DD. Acitretin and Isotretinoin are generally administered in doses of up to 0.5 and 1 mg/kg/day, respectively.

In cases 1 and 2, due to the large extent of cutaneous involvement

and refractoriness to topical treatment (Case 1), treatment with systemic retinoids was chosen, in addition to guidelines to avoid excessive sweating, regular use of sunscreen and use of emollients potent. As it is a rare disease of a genetic nature, it is important to know how to recognize it so that there is a correct diagnosis, as well as the necessary guidelines and therapeutic measures. It is also valid the genetic orientation for the carriers of such disease.

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