

Importance of dermoscopy in assisting the non-invasive diagnosis of Darier's disease

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Abstract We herein present a case of patient affected with Darier's disease along with dermoscopic findings to raise awareness of importance of dermoscopy in non-invasive diagnosis of this disease. It allows specialists to differentiate the condition from other disorders with similar clinical and histopathological pictures, such as Grover's disease, Hailey-Hailey disease and seborrheic dermatitis.

Key words

Darier's disease, dermoscopy, hyperkeratosis, pseudocomedones, acantholysis.

Introduction

Darier's disease (DD) is a rare genodermatosis characterized by an autosomal dominant inheritance. Although the exact mechanism of disease still remains under investigation, it has been established that a mutation in ATP2A2 is the main cause of this disorder.¹ This gene encodes for Ca²⁺-ATPase isoform 2 (SERCA2),² the calcium pump highly expressed in keratinocytes. Its abnormal functioning leads to impaired flow of calcium ions into the endoplasmic reticulum causing acantholysis and hyperkeratinization of epidermis¹ the main hallmarks of disorder.³ Darier's disease is predominantly manifested by hyperkeratotic papules, occasionally accompanied by pruritus and malodor.⁴ The most commonly affected sites include seborrheic areas such as head, neck, central chest and back. Punctuate pits on the palms and soles as well as acrokeratosis verruciformis on the dorsum of hands and feet might also be observed.⁴ Additionally, disease

might manifest itself in white papules in cobblestone pattern on oral, anal and vulvar mucous membranes and also in nail dystrophy.^{4,5} Non-dermal manifestations, such as neuropsychiatric features, including major depression, bipolar disorder, learning difficulties might accompany Darier's disease.⁶⁻⁹ Moreover, medicaments used in the treatment of epilepsy and bipolar disorder show calcium channel activity.¹⁰ Symptoms occur mainly from late childhood to early adulthood. However, they often vary widely between individuals, even family members.¹¹ Mostly, patients experience flare-up and remission cycles as they are prone to exacerbating environmental factors, such as: humidity, sunlight and heat.⁴ Bacterial and *Herpes simplex* infections may also cause a condition's relapse. Kaposi-Juliusberg syndrome is often observed as a complication.⁶ The diagnosis of disease is usually based on specific clinical symptoms and histopathological examination. Darier's disease as a congenital condition is untreatable, however, we can affect severity of disorder and frequency of remissions. Emollients, UV protection and exacerbating factors elimination are crucial among patients with mild symptoms. Localized lesions might be treated with topical and gel retinoids.⁶ Oral

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retinoids and cyclosporine are widely used among individuals experiencing more severe course of disease.⁶ Moreover, an important aspect of therapy is working against bacterial, fungal and viral infections. Although Darier disease is a chronic and unremitting condition, most patients live a relatively normal life. To raise awareness of dermoscopy in non-invasive diagnosis of Darier's disease, we herein report a 20-year-old affected patient along with dermoscopic, onychoscopic and histopathological findings.

Case report

A 20-year-old male patient presented to the Department of Dermatology with chief complaint of keratotic lesions and itching exacerbation for the past months. On eliciting medical history, the patient had been diagnosed with Darier's disease 5 years ago. 30mg/day of systemic acitretin was used as a first line treatment, later substituted with 20mg/day of oral isotretinoin due to intensified hair loss and dryness of the skin. The patient reported a consistent adherence to his prescribed dermatologic regimen. Patient's family members

including grandfather, mother and siblings were also diagnosed with DD. On admission, hyperkeratotic papules were localized mainly on face, upper chest, both sides of neck and forearms. Physical examination of fingernails revealed fragility, splitting, thinning of distal parts and subungual hyperkeratotic fragments. The results of laboratory tests were found to be within normal ranges.

Dermoscopic appearance

Dermoscopy of the skin lesions performed with DermLite DL4 revealed centrally localized polygonal, star-like, roundish, yellow-brown colored areas, surrounded by a whitish halo, overlying a pink homogeneous structureless background along with dotted or linear vessels (**Figure 3,4**).

Onychoscopic appearance

White and red longitudinal lines resembling "candy canes" as well as V-shaped nicking of distal, fragile nail edges were displayed in onychoscopy (**Figure 5,6**).



Figure 1 Multiple nodules with pus discharging sinuses present over upper left chest and left shoulder region



Figure 2 Hyperkeratotic papules located on neck with accompanying skin xerosis



Figure 3 Whitish scale covering polygonal yellowish structure.



Figure 4 Multiple polygonal, yellowish-brownish areas surrounded by a whitish halo, overlying a pinkish homogenous background along with dotted and linear vessels.

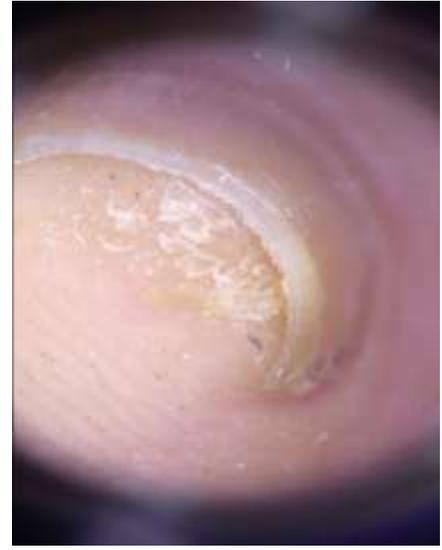


Figure 5 Fingernails. Subungual hyperkeratotic fragments.



Figure 6 Fingernails. Red and white longitudinal lines known as "candy canes" along with V-shaped notch on the distal nail edge.

Histopathological examination

Histopathological examination showed acantholysis forming a suprabasal cleft, parakeratosis and dyskeratosis with peculiar

grains and corps ronds which were consistent with Darier's disease diagnosis.

After flare-up, the patient was hospitalized and treated with topical chloramphenicol. He was finally discharged with 10 mg/day of isotretinoin and 20mg/g of topical sulfathiazole. A month after treatment, at follow-up, the patient showed a major improvement.

Discussion

Dermoscopy is increasingly being appreciated as a non-invasive, inexpensive and widely accessible tool which allows for a quick and accurate diagnosis of skin conditions. It also plays a tremendous role in distinguishing within a large group of dermatoses with similar clinical presentation, providing supplementary information concerning their submacroscopic aspects. Many clinical disorders hardly differentiable with an unaided eye, can be identified with the use of trichoscopy, onychoscopy and dermoscopy. While analyzing

their findings, our attention should be focused on vessel patterns, colors, scaling arrangements and any other specific characteristics. However, we should keep in mind that dermoscopic image is only an additional information and should always be interpreted within patient's medical history and physical examination.¹² Darier's disease, also known as Darier-White disease, frequently presents a diagnostic challenge. Although the definitive diagnosis is based on histopathological examination, dermoscopy, reflectance confocal microscopy and onychoscopy might be very helpful for assisting its non-invasive identification.¹³ First dermoscopic description of Darier's disease was presented in Vasquez-Lopez F.¹⁴ study on 5 patients in 2004 and described dilated openings with raised/flat borders and central yellowish hyperkeratotic plugs known as "giant pseudocomedones". The crucial aspect of dermoscopic examination of patients with Darier's disease is a differentiation between other conditions characterized by acantholysis and dyskeratosis.¹² They include mainly Grover's disease and Braf-Inhibitor-Induced Acantholytic Dyskeratosis.¹² Despite the fact that the findings in dermoscopic examinations frequently overlap,¹⁵ the most characteristic pathological changes in Darier's disease include the polygonal, star-like, roundish, brownish-yellowish areas surrounded by whitish halo and linear or dotted vessels.^{12,16} Specific dermoscopic findings correspond with histopathological examination. The central polygonal, brownish areas with surrounding whitish halo correlate with acantholysis and hyperkeratosis,¹⁶ whilst the homogenous areas and specific pattern of vessels reflect the inflammatory process.¹⁶ Apart from typical acantholytic and dyskeratotic diseases, dermoscopy allows us also to distinguish Darier's disease from other skin conditions with similar clinical presentation, especially acne vulgaris characterized by erythematous area with

pustules and comedones,¹⁵ seborrheic dermatitis presenting with yellowish scaled area and dotted vessels,¹⁷ acanthosis nigricans displayed as lesions more abundant in pigment,¹⁷ confluent reticulate papillomatosis represented as brownish, flat and poorly outlined borders, accompanied by light scales,¹⁷ lichen planus showing Wickham striae, round or linear, reticular white patterns,¹⁶ pityriasis rubra pilaris identified by areas of yellowish morphology surrounded by mixed pattern of vessels,¹⁵ pityriasis lichenoides chronica appearing as homogenous, yellowish areas and vessels with or without dotted pattern¹⁵ and infectious folliculitis characterized by inflammatory pustules.¹⁵ However, we should also consider less common conditions, such as Hailey Hailey disease showing multiple pinkish-whitish areas along with white colored regions arranged in a cloudy pattern¹⁸ or Dowling Deigo disease displaying irregular reddish-brownish background with hypopigmented cyst in the center.¹⁸

Conclusion

Dermoscopy is helpful in differential diagnosis.

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