Enfermedad de Darier con afectación esofágica, un caso clínico

Darier disease with esophageal involvement, a case report

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ABSTRACT

Darier's disease (DD) is an autosomal dominant dermatosis caused by a mutation in the ATP2A2 gene at 12q23-24, characterized histologically by acantholysis and dyskeratosis. It is a rare disease, distinguished by the presence of red-brown keratotic papules, typically distributed follicularly, palm-plantar, on nails, and less frequently in the oral mucosa.

We report the case of a 70-year-old woman with a medical history of neuropsychiatric disorders, chronic kidney disease (CKD), anemia of CKD, diabetes mellitus type 2, and hypertensive heart disease. Upon admission, she presented with widespread hyperkeratotic skin lesions and erythronychia. A skin biopsy confirmed the diagnosis of DD. An upper gastrointestinal endoscopy revealed extensive esophagitis, histologically suggestive of an association with DD.

Some extracutaneous manifestations have been described, mostly neuropsychiatric disorders, with only a few cases of esophageal mucous membrane involvement. This appears to be due to the pleiotropic effect of mutations in ATP2A2 in other cells.

Keywords: Darier's disease, acantholysis, dyskeratosis, esophageal involvement.

RESUMEN

La enfermedad de Darier (ED) es una dermatosis autosómica dominante causada por la mutación del gen ATP2A2 en 12q23-24, caracterizada histológicamente por acantólisis y disqueratosis. Es una enfermedad rara, caracterizada por la presencia de pápulas queratósicas marrón rojizo de distribución folicular, palmo-plantar, ungueal y menos frecuentemente en la mucosa oral.

Presentamos el caso de una mujer de 70 años con antecedentes de trastornos neuropsiquiátricos, enfermedad renal crónica, anemia de CKD, diabetes mellitus tipo 2 y cardiopatía hipertensiva. A su ingreso presentó lesiones cutáneas hiperqueratósicas diseminadas y eritroniquia. La biopsia cutánea confirmó el diagnóstico de ED. La endoscopia digestiva alta reveló una esofagitis extensa, histológicamente a favor de una asociación con ED.

Se han descrito algunas manifestaciones extracutáneas en la ED, la mayoría trastornos neuropsiquiátricos, y en pocos casos se ha reportado afectación de la mucosa esofágica. Esto parece ser debido al efecto pleiotrópico de las mutaciones en ATP2A2 en otras células.

Palabras clave: Enfermedad de Darier, acantólisis, disqueratosis, afectación esofágica.

INTRODUCTION

Darier's disease (DD) is an autosomal dominant dermatosis caused by a mutation in the ATP2A2 gene at 12q23-24, characterized histologically by acantholysis and dyskeratosis. It is a rare disease, distinguished by the presence of red-brown keratotic papules, typically distributed follicularly, palm-plantar, on nails, and less frequently in the oral mucosa.

CASE REPORT

A 70-year-old Portuguese woman with a significant medical history of neuropsychiatric disorders (schizophrenia and bipolar disorder), chronic kidney disease (CKD) stage 3b, anemia of CKD, diabetes mellitus type 2, arterial hypertension, hypertensive heart disease, and a family history of skin disorders since childhood. Since DD is an autosomal dominant genetic disease, we investigated the family history and found that the patient's father, aunt, both daughters, and a grandson had similar skin lesions. Extracutaneous manifestations were unknown in these family members.

She was admitted to our hospital's emergency department following a lumbar trauma after a fall. After clinical evaluation and laboratory workup, she was transferred to the Internal Medicine department with the following diagnoses: iron deficiency anemia, acute on chronic renal disease, hyperkalemia, acute on chronic heart failure, and exacerbating skin lesions characterized by keratotic, crusted papules with a greasy, warty texture, predominantly on the body, upper and lower limbs, along with V-shaped nails and papules with a central depression on the lips and oral mucosa.

After addressing the acute issues, we performed a lesional skin biopsy, which showed the following histological findings: epidermis with mild acantholysis, foci of acantholysis with suprabasal clefts, and dermis with a lymphocytic infiltrate (Figure 1), confirming the diagnosis of DD.

For further evaluation of iron deficiency anemia and the extent of oral mucosal lesions, an upper gastrointestinal endoscopy was performed. This revealed grade D peptic esophagitis with areas of hyperkeratotic lesions. Biopsy specimens were taken from the upper esophagus and gastroesophageal junction. The histological findings in the upper esophagus mucosa were similar to the skin biopsy, with acanthosis and papillomatosis, small areas of acantholysis, suprabasal clefts, and fibrino-leukocytic and necrotic exudates.

Histological findings in the gastroesophageal junction were more nonspecific, showing slight acanthosis and chronic inflammatory infiltrates without active dysplasia but with areas of metaplasia (Figure 2).

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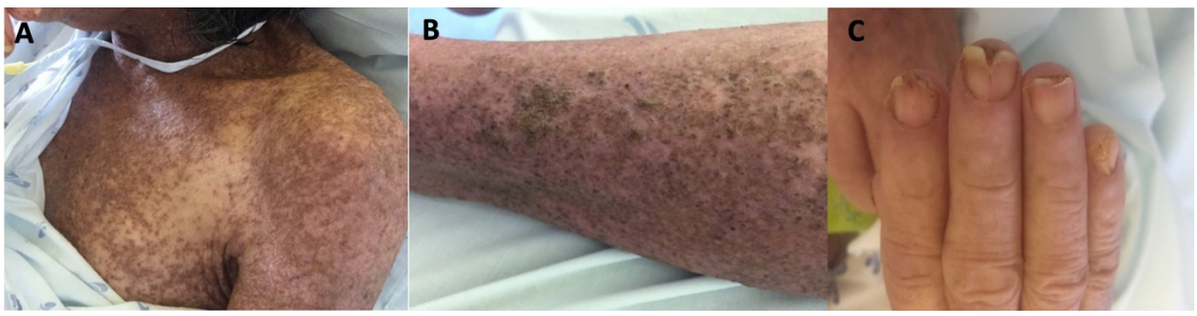

Figure 1. Extended confluent papular, hyperkeratotic lesions and crusted plaques on the body (A) and lower limbs (B). Notching of the free nail border: V-shaped nails (C).

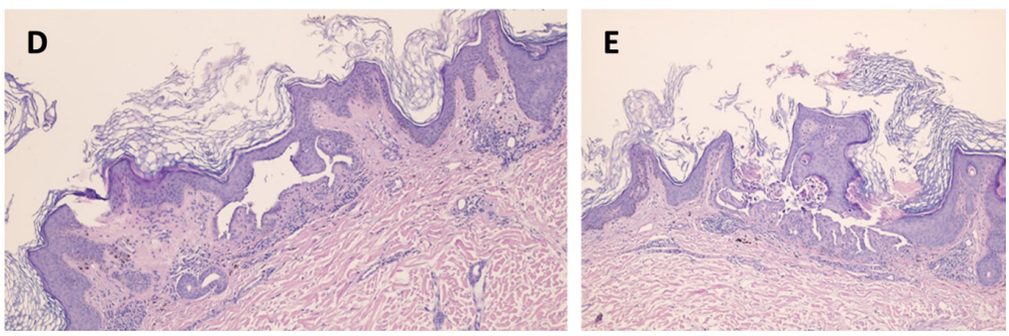

Figure 2. Histological examination of the lesional skin showing mild acantholysis, foci of acantholysis with suprabasal clefts, and dermis with a lymphocytic infiltrate (D, E).

The patient and her family were referred to the dermatology and gastroenterology departments for further management and genetic counseling.

DISCUSSION

Some extracutaneous manifestations of Darier's disease have been described, with neuropsychiatric disorders being the most common. However, only a few cases have documented esophageal mucous membrane involvement. This could be due to the pleiotropic effect of ATP2A2 mutations in other cells. The ATP2A2 gene encodes the calcium ATPase pump (SERCA2b) in the endoplasmic reticulum, which is present in all body cells, suggesting that this genetic disorder could potentially induce extracutaneous manifestations.

We present the case of a woman with a delayed diagnosis of her skin condition, which also involved the esophagus and revealed areas of metaplasia. Some studies have suggested an association between mutations in the ATP2A2 gene and the development of squamous cell carcinoma in patients with esophageal involvement. In this patient, the findings of metaplasia prompted closer monitoring due to a higher risk of esophageal cancer. Unfortunately, the patient passed away, and we were unable to extend the genetic study to all family members.

This case is one of the few published instances of Darier disease (DD) with documented extracutaneous involvement, highlighting that DD is not solely a dermatological condition. Further investigation of other DD cases is necessary to elucidate the underlying pathological mechanisms of the disease, improve our understanding of its implications, and explore new therapeutic approaches.

CONFLICT OF INTEREST
The authors declare no conflicts of interest.

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This research did not receive any funding.

ETHICAL ASPECTS
The ethical standards of the Research Committee and the Declaration of Helsinki (1975) were followed during the conduct of this study.

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