Case Report

Pretibial dystrophic epidermolysis bullosa*

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Abstract: Epidermolysis bullosa is a group of mechano-bullous genetic disorders caused by mutations in the genes encoding structural proteins of the skin. Dystrophic epidermolysis bullosa is caused by mutations in the COL7A1 gene encoding collagen VII, the main constituent of anchoring fibrils. In this group, there are autosomal dominant and recessive inheritances. The pre-tibial form is characterized by the presence of blisters, milia, atrophic scars and lesions similar to lichen planus. The diagnosis is clinical and laboratory and subtypes are distinguished by means of immunohistochemical and ultrastructural studies, in addition to genetic differentiation. Electron microscopy and immunomapping are used in the diagnosis.
Kewbords: Collagen type VII; Epidermolysis bullosa dystrophica; Lichen planus

INTRODUCTION

Epidermolysis bullosa (EB) is a heterogenous group of mechano-bullous genetic disorders caused by mutations in the genes that encode structural proteins of the skin.[1] Clinically, there are four main types of EB: simple, junctional, dystrophic, and Kindler syndrome; however, the classification of EB continues to include new clinical and pathological entities, with 30 clinical subtypes recognised.[2] The diagnosis of EB is made on clinical and laboratory grounds, but it is always important to take into consideration family history and parent consanguinity.[3] EB's subtypes can only be differentiated through immunohistochemical and ultrastructural studies, in addition to genetic differentiation, which is not available in most of the large centres.[3] Both electronic microscopy and immunomapping are used, successfully, for the diagnosis of EB. Each technique will allow the diagnosis of the cleavage level in the skin: intra-epidermal, in the lamina lucida and sub-lamina densa.[4]

Dystrophic EB (DEB) is caused by mutations in the gene COL7A1, which is responsible for encoding collagen VII, main constituent of the anchoring fibrils, which participate in the adherence of the lamina densa to the dermis.[5] The main clinical feature of DEB is scarring resulting from tissue loss, because the cleavage happens below the lamina densa. In this group, there are autosomal dominant and recessive forms.[5]

CASE REPORT

A female 42-year-old patient born in and living in São Paulo, physical education teacher, had a history of bullous lesions in areas of trauma since she was six months old, besides nail dystrophy. The patient presented at our department in March 2015 due to the exacerbation of the bullous lesions, associated with intense pruritus. She reported that her brother had the same lesions since

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the first months of life, but she denied other family members with a similar condition.

On dermatological examination, the patient had vesicles and tense bullae, some ruptured and some serohematic crusts overlying an erythematous base, affecting the whole lower limbs (Figure 1). Milia were seen on the extremities and polygonal violaceous papules on the upper limbs and abdomen, resembling lichen planus, and nail dystrophy (Figures 2 and 3). The inspection of the oral cavity revealed the presence of multiple cavities. Histopathology of an erythematous papule of the forearm demonstrated the presence of a subepidermal bullous dermatitis and the immunomapping was consistent with dominant dystrophic epidermolysis bullosa (Figure 4).

Due to the presence of inflammation and intense pruritus, she was treated with prednisone, loratadine, hydroxyzine, and doxepin. Since there was little improvement, she started treatment with phototherapy. She had eight sessions of narrowband UVB and showed progressive improvement of the pruritus and, consequently, of the blisters.

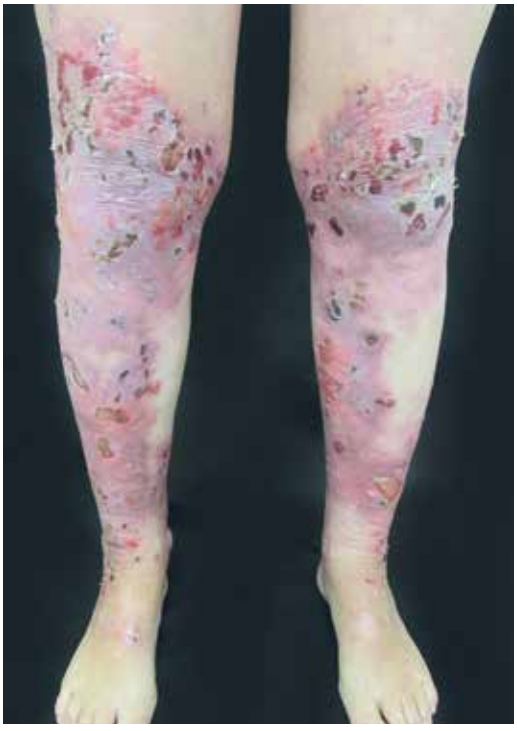

Figure 1: Vesicles and blisters overlying an erythematous base

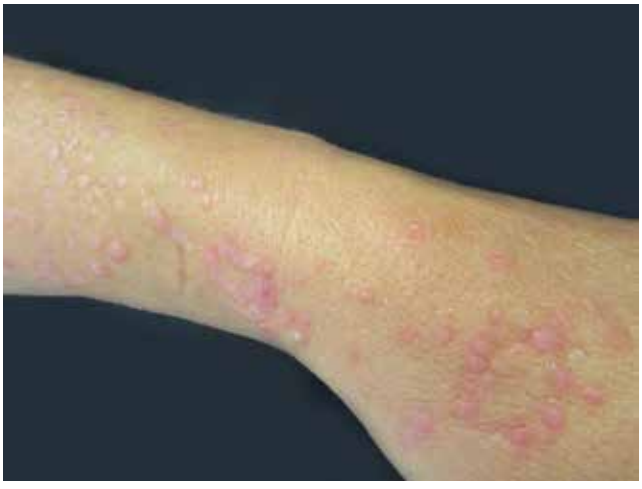

Figure 2: Lesions similar to lichen planus

DISCUSSION

Dystrophic EB (DEB) can be dominant or recessive. In both, the genetic abnormality is in the COL7A1 gene, that includes collagen type VII.[4] The result of this anomaly is the modification in the structure and number of anchoring fibrils, of which collagen type VII is part of, leading to the loss of adherence between epidermis and dermis.[6] Due to cutaneous fragility, the lesions are preferably lo-

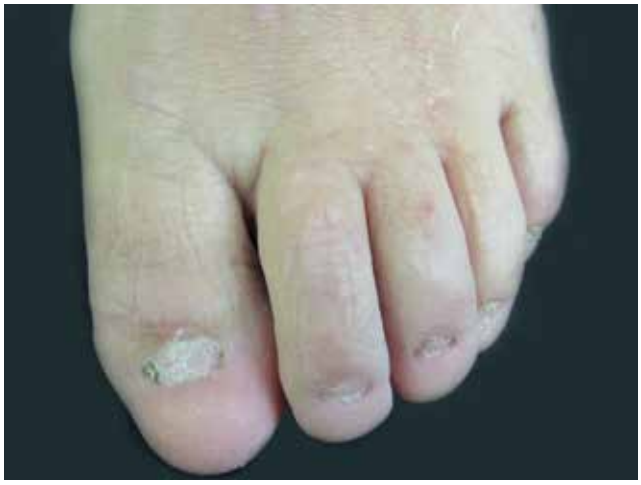

Figure 3: Nail dystrophy

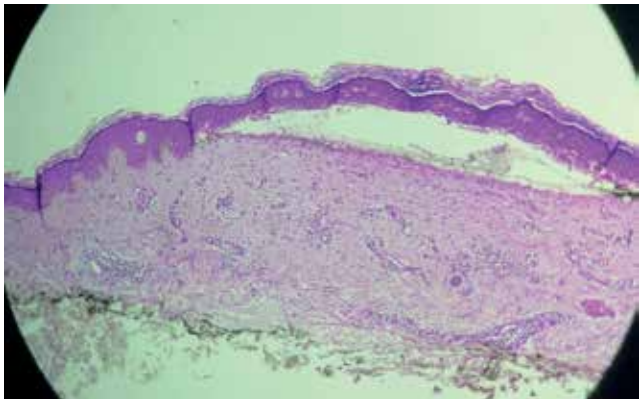

Figure 4: Histopathology: subepidermal cleavage (PAS; X100)

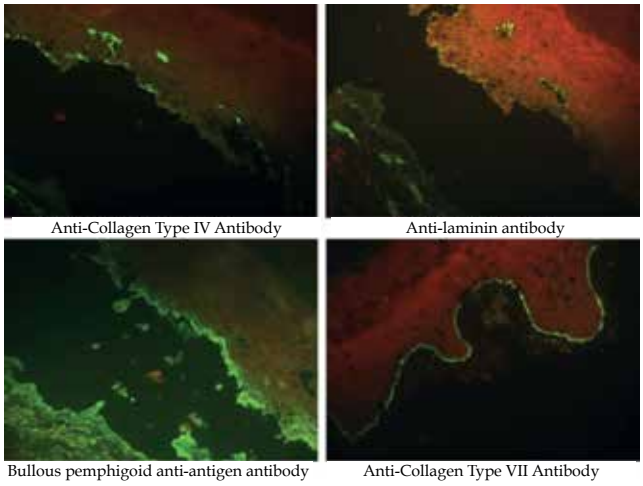

Figure 5: Immunomapping: main antibodies with fluorescence in the epidermal side of the cleavage. The demarcation of the antigens in the roof of the blister suggests cleavage below the lamina densa

cated on the pretibial regions, but they can also affect the forearms, dorsum of the hands and feet, and also the nails. The intense pruritus contributes to the formation of lesions. The lesions usually appear during childhood, but can continue till the third decade of life.[6]

Clinically, dominant DEB has the following types: 1) generalized, 2) acral, 3) pretibial, 4) pruriginosa, 5) nails only and 6) bullous dermatolysis of the newborn.[4] Pretibial DEB is a rare variant, clinically differentiated from the other forms by the presence of more localized lesions, with blisters and erosions, scarring, milia, frequent pruritus and nail dystrophy.[7] In our case, the patient also had, besides these lesions, violaceous polygonal flat papules on the lower limbs and abdomen, similar to lichen planus. Those lesions are present exclusively in the pretibial form, supporting this diagnosis.[4]

Regarding immunomapping, in dominant DEB, the deposition of fluorescence occurs on the roof of the blister (epidermal side) with the presence of four main antibodies against the following markers: collagen type IV, bullous pemphigoid antigen, laminin and collagen type VII. All the antibodies will mark the roof of the blister, demonstrating cleavage in the sublamina densa. In some cases, fluorescence on the roof and floor of the blister with anti-collagen type VII antibody can be seen. The reduced or absent fluorescence with anti-collagen type VII antibody will differentiate the recessive and dominant forms, since its absence allows the accurate diagnosis of the recessive form, which is a severe variant of EB.[3]

In our case, the diagnosis of pretibial DEB was made by the clinical picture, the presence of blisters, milia, nail dystrophy and lesions resembling lichen planus, and also through immunomapping, with the presence of fluorescence of all antibodies in the roof of the blister, consistent with dominant dystrophic EB (Figure 5).

There are no effective treatments nor cure for EB. The treatments include multidisciplinary health care and social well-being. Some forms of EB need daily dressings, maintenance of mobility, appropriate nutrition and care to limit complications, such as skin infections, scar formation, dental cavities, dysphagia, constipation and skin cancer.[3] In the reported case, the lack of control of the pruritus with symptomatic medications led to initiation of phototherapy with narrowband UVB, with improvement of the pruritus and of the lesions.

This report illustrates the difficulty in the diagnostic and therapeutic approach of this rare dermatosis.❑

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