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A 2-Year-Old Girl With Skin Fragility

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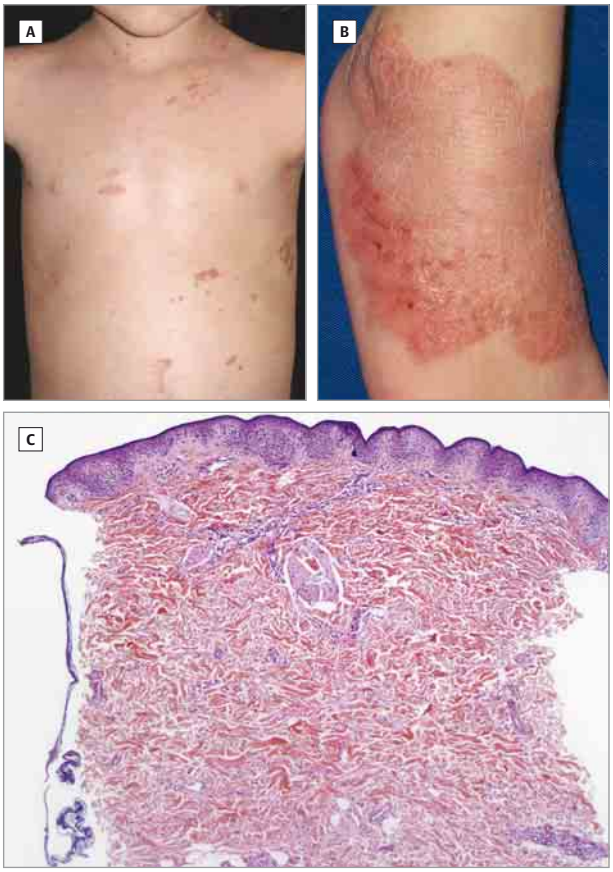

Figure. A, Clinical photograph of a disease outbreak. Skin fragility can be seen as superficial erosions distributed predominantly around the trunk, some with geometric shape. B, Photograph showing localized affectation of the disease. Erythemato-desquamative well-demarcated plaque with peeling borders on right foot. C, Hematoxylin-eosin staining (original magnification ×40) of healthy skin. Remarkable detachment of the entire stratum corneum and mild psoriasiform epidermis hyperplasia with no other significant findings.

A 2-year-old girl was referred to our department for skin fragility since early infancy. She had 2 older brothers, and the family had no medical history of note. Physical examination revealed mild xerosis with superficial skin erosions and erythematous residual macules from previous erosions. Some of the lesions had an unusual linear geographic contour and were predominantly located at areas of friction (**Figure**, A and B). Hair, nails, and mucous membranes were normal. There was no history of blistering. The mother explained that she often found the child peeling off skin with marked facility. Symptoms improved in winter and worsened in summer. Physical and mental developments were normal. Serological markers for celiac disease were negative. A skin biopsy was performed (Figure, C).

WHAT IS THE DIAGNOSIS?

- **A.** Kindler syndrome
- **B.** Dermatitis artefacta
- **C.** Epidermolysis bullosa simplex superficialis
- **D.** Peeling skin disease

Diagnosis

D. Peeling skin disease

Microscopic Findings and Clinical Course

A biopsy specimen from normal skin was obtained by rubbing with a pencil eraser. Hematoxylin-eosin staining and immunofluorescence mapping showed complete separation of the stratum corneum with a clean split just above the stratum granulosum. Faint psoriasiform hyperplasia and a mild perivascular and interstitial mononuclear infiltrate were observed in the upper dermis. Results from immunofluorescence mapping were normal for collagen IV and VII, for α6 and β4 integrines and for laminine-332. The subcorneal split is usually the key for the diagnosis of peeling skin disease (PSD).[1] A genetic study was performed of the *COL7A1* and *CDSN* genes with polymerase chain reaction technique and automatic sequencing with Big Dye Terminators in the genetic analyzer ABI3100. This test revealed 2 heterozygous mutations not previously described in exon 2 of the *CDSN* gene, confirming the diagnosis of PSD. The patient is now 5 years old, and her disease is well controlled with hygienic measures and topical treatment.

Discussion

Peeling skin disease, previously called peeling skin syndrome, is a recessively inherited ichthyosiform genodermatoses. It is characterized by skin fragility and chronic or recurrent superficial peeling and is classified as a nonsyndromic ichthyosis.[2] Severity is variable. According to its distribution, the disorder is divided into acral and generalized forms. Acral PSD is the result of mutations in the transglutaminase 5 (*TGM5*) gene.[3] Generalized PSD has been subclassified into noninflammatory and inflammatory forms. Mutations in the corneodesmosin (*CNDS*) gene have been detected in inflammatory forms. This gene codifies the corneodesmosin protein responsible for stabilizing the stratum corneum and its adhesion to the stratum granulosum. The gene of the noninflammatory form is currently unknown.[4]

Diagnosis of PSD is often delayed owing to late presentation in less severe cases. It is possibly considered an underdiagnosed disease because of its low clinical expression and the few cases described in the literature. Diagnosis is made exclusively by genetic study. Peeling skin disease can often be well managed with topical treatments and hygienic measures alone. Oral treatments, such as retinoids, methotrexate, or systemic corticosteroids, have been proposed in severe cases without a sustained clinical response. Prognosis is not well known owing to the limited number of cases, but it seems to improve with age.

Differential diagnosis of PSD includes mainly the group of inherited epidermolysis bullosa (EB) disorders. Skin fragility occurs in both entities but histological and direct immunofluorescence findings usually help to differentiate them.[5] In EB, the separation of keratinocytes occurs at several levels: basal keratinocyte (EB simplex type), dermoepidermal junction (junctional EB), and superficial dermis (dystrophic EB). In Kindler syndrome the division can be seen in both dermoepidermal junction and superficial dermis.[6] However, the separation in PSD is within keratinocytes at the junction of the stratum granulosum and stratum corneum.[1] The only indistinguishable subtype of EB according to the level of cleavage is epidermolysis bullosa simplex superficialis.[1] Nevertheless, in this form of EB, there are several clinical findings that are usually absent in PSD, such as atrophic scarring, onychodystrophy, and milium cysts.[7]

In conclusion, PSD is a rare and misdiagnosed genodermatosis, classified as a nonsyndromic ichthyosis, which we should suspect in young patients with recurrent or chronic skin fragility and a subcorneal split in the skin biopsy. Although diagnosis can be confirmed only by genetic study, the association of these clinicopathological findings should suggest this diagnosis.

ARTICLE INFORMATION

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