Familiar palmoplantar keratoderma, flaccid blisters, and widespread scaling

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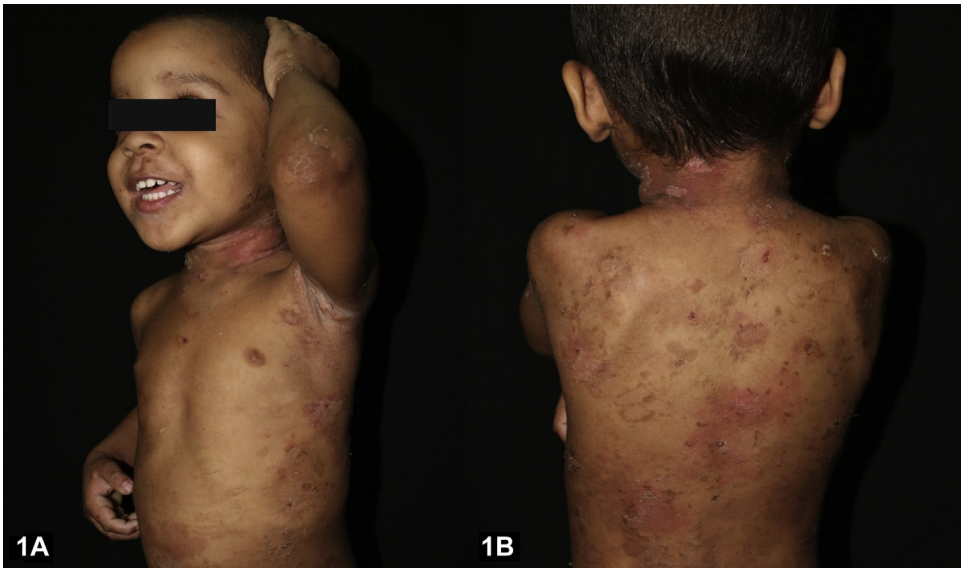

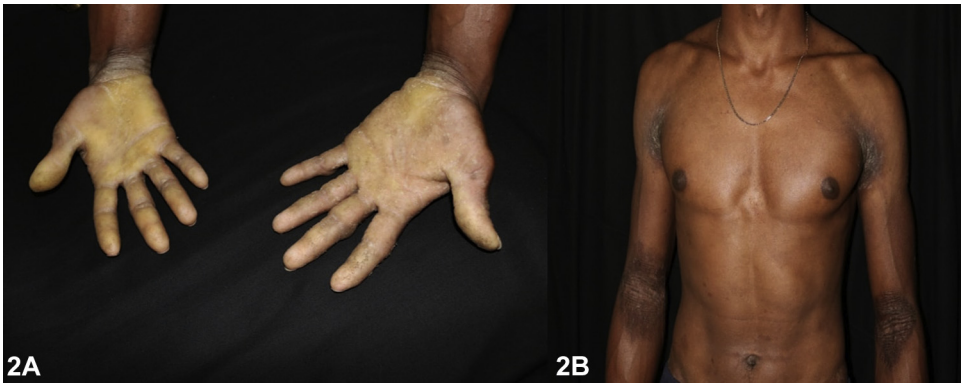

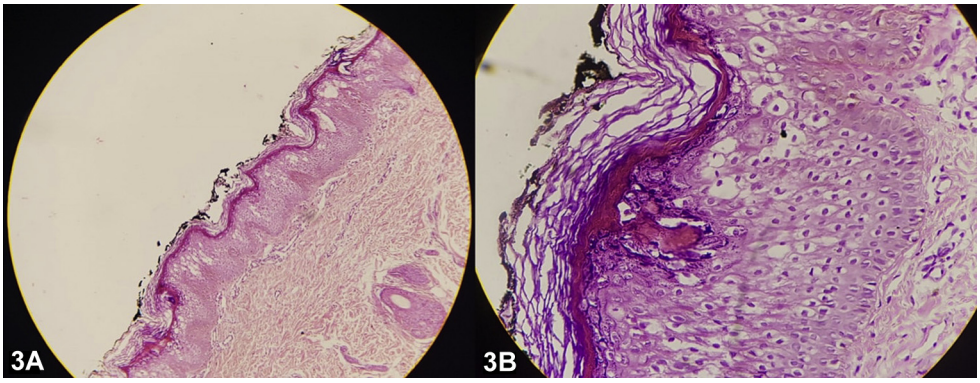

A 3-year-old boy presented with diffuse xerosis, palmoplantar keratoderma, and widespread erosion, especially over joint flexures, neck, and trunk (Fig 1). He was accompanied by his father, a 25-year-old man who exhibited corrugated hyperkeratotic plaques on the trunk and limbs combined with palmoplantar keratoderma (Fig 2). The father claimed that both he and his son had congenital epidermolysis bullosa, and that his son's condition was noticed at birth, for he had multiple flaccid blisters. A 4-mm punch biopsy specimen of the boy was obtained and histopathology found epidermis with vacuolar degeneration, hyperkeratosis, papillomatosis, hypergranulosis, and acanthosis (Fig 3).

Question 1: What is your diagnosis?

A. Congenital Epidermolysis Bullosa (CEB)

B. Epidermolytic ichthyosis (EI)

C. Ichthyosis bullosa of Siemens

D. Congenital ichthyosiform erythroderma

E. Peeling skin syndrome (PSS)

Answers:

A. CEB — Incorrect. CEB comprises a group of mechanobullous genodermatosis with varied inheritance patterns marked by the separation between the epidermal and dermal layers of the skin. Clinically, it can be expressed at birth with generalized blistering. However, the differences become more prominent throughout the years, as CEB is not associated with hyperkeratosis.

B. EI — Correct. EI is a rare autosomal dominant keratinization disorder caused by either keratin 1 or keratin 10 mutations. Named after its distinctive histopathologic findings of epidermolysis and hyperkeratosis, this disease is characterized by the presence of erythroderma, blisters, and desquamation at birth. Palmoplantar keratoderma may occur as the aforementioned features gradually give place to hyperkeratotic plaques and hyperkeratosis becomes more evident.[1,2]

C. Ichthyosis bullosa of Siemens — Incorrect. Ichthyosis bullosa of Siemens results from a keratin 2e defect. It presents with blistering, mild hyperkeratosis of extremities, and superficial peeling of the skin, a distinctive feature called the *Mauserung phenomenon* that is absent in other forms of ichthyosis.

D. Congenital ichthyosiform erythroderma — Incorrect. Congenital ichthyosiform erythroderma is an autosomal recessive condition that can present as a Collodion baby with fine white scales and erythroderma. Also known as nonbullous congenital ichthyosiform erythroderma, this disease is not associated with blistering.

E. PSS — Incorrect. Peeling skin syndrome is a rare autosomal recessive disorder, the cause of which is unknown. PSS presents with widespread painless peeling. Histologic examination of the lesions finds hyperkeratosis and subcorneal skin cleavage without vacuolar degeneration.

Question 2: What skin structure is altered in this disease?

A. Steroid sulfatase

B. Keratin 5/keratin 14

C. Filaggrin

D. Transglutaminase 5

E. Keratin 1/keratin 10

Answers:

A. Steroid sulfatase — Incorrect. Hereditary deficiency of steroid sulfatase enzyme leads to X-linked ichthyosis, a disease that mostly affects extensor surfaces, neck, trunk, and lower extremities.

B. Keratin 5/keratin 14 — Incorrect. Keratin 5 and keratin 14 mutations are associated with epidermolysis bullosa simplex, a type of congenital epidermolysis bullosa in which the epidermal and dermal layers of the skin are separated at the basal keratinocyte level.

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C. Filaggrin — Incorrect. Mutations in the filaggrin gene are responsible for ichthyosis vulgaris, a disorder clinically expressed by xerosis, palmoplantar hyperlinearity, scaling, and keratosis pilaris.[3]

D. Transglutaminase 5 — Incorrect. Transglutaminase 5 mutations are related to a localized form of PSS known as acral peeling skin syndrome, which involves the continuous shedding of the skin on hands and feet.

E. Keratin 1/keratin 10 — Correct. Both keratin 1 and keratin 10 mutations can justify EI. These genes, respectively located on chromosomes 17q12-21 and 12q11-13, are expressed in the suprabasal layers of epidermis, inhibiting cell proliferation and playing a pivotal role in the cytoskeleton organization. Hence, the lack of gene expression leads to hyperkeratinization. Blistering is common in early EI. Furthermore, EI can occur with or without palmoplantar keratoderma, a finding mostly associated with keratin 1 mutations.[1,2]

Question 3: What is the natural course of the disorder?

A. The lesions eventually give place to an erythroderma.

B. The number of flaccid blisters increase and they become the primary clinical feature of the disease.

C. The hyperkeratotic plaques degenerate into skin cancer.

D. Blisters fade as hyperkeratosis becomes more evident.

E. The life expectancy of the patient decreases, as EI has no treatment and no cure.

Answers:

A. The lesions eventually give place to an erythroderma — Incorrect. Varying degrees of erythema may be present at birth in patients with EI. Nevertheless, this clinical feature fades over the years.[1,2]

B. The number of flaccid blisters increases and they become the primary clinical feature of the disease — Incorrect. What happens is exactly the opposite, because the blisters and the erythema improve, and hyperkeratosis becomes the main characteristic of the disease. Nevertheless, because blisters are frequently observed as soon as the patient is born, it is important to exclude other generalized neonatal blistering disorders before diagnosing EI.[1,2]

C. The hyperkeratotic plaques degenerate into skin cancer — Incorrect. There is no clear association between EI and cancer. Nonetheless, the treatment of this hyperproliferative disorder with psoralen ultraviolet A must be avoided, for it has been linked to an increased risk of nonmelanoma skin cancer.[4]

D. Blisters fade as hyperkeratosis becomes more evident — Correct. Hyperkeratosis is a hallmark of EI. Although flexural surfaces often display verrucous plaques, extensor surfaces usually have a cobblestone appearance. A complete involvement of the body may occur; however, the face is often less affected.[1,2,5]

E. The life expectancy of the patient decreases, as EI has no treatment and no cure — Incorrect. Despite being an incurable disease, EI has several therapeutic options, such as keratolytics, emollients, topical vitamin D derivatives, and retinoids.[2] Overall, life expectancy is not affected, and a proper treatment can lead to complete disease remission.

Abbreviations:

EI: epidermolytic ichthyosis
CEB: congenital epidermolysis bullosa
PSS: peeling skin syndrome

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