Erythroderma in a neonate

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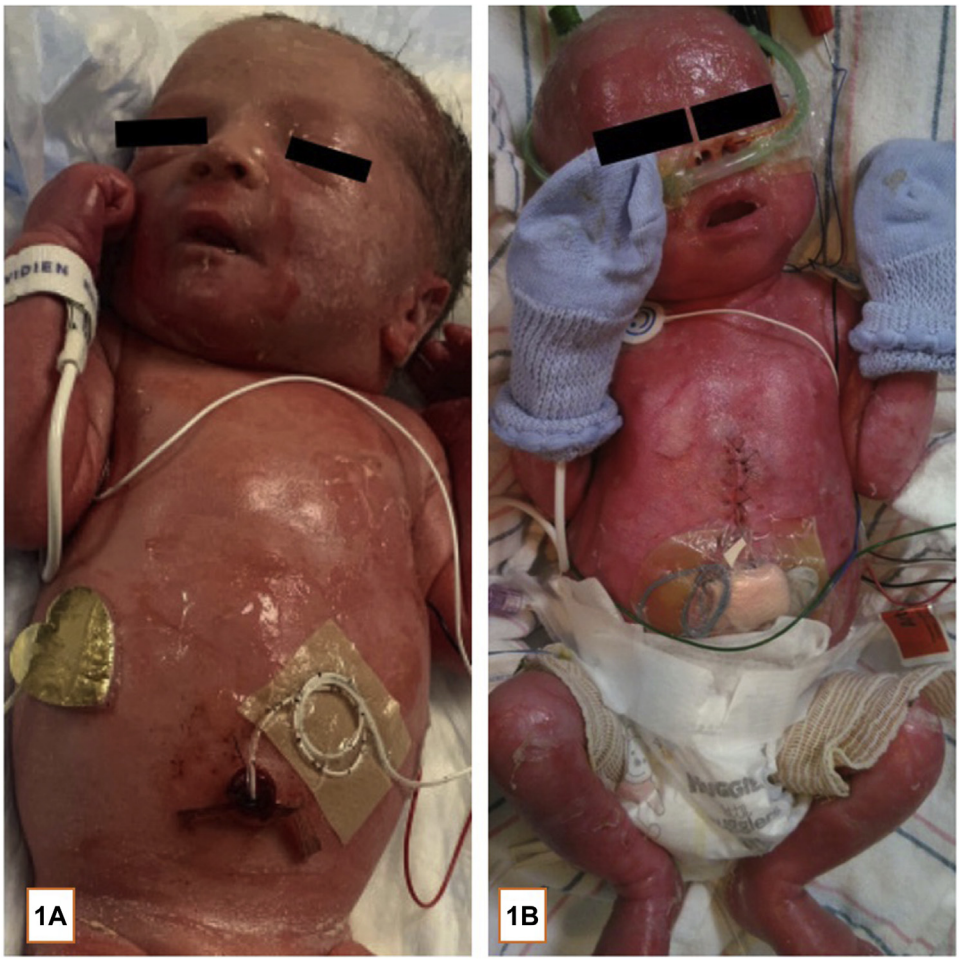

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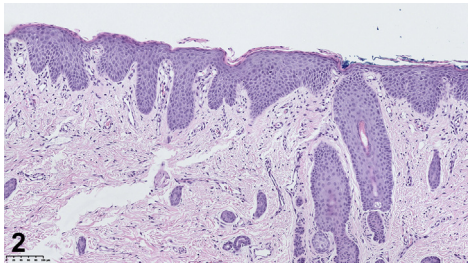

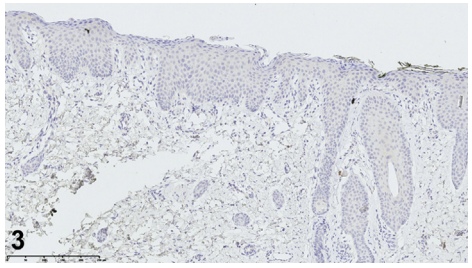

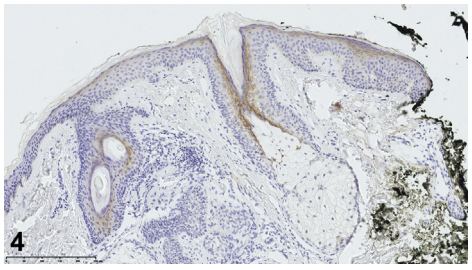

A newborn boy with no family history of erythroderma or ichthyosis presented with fine, superficial scale overlying diffuse mild erythema (Fig 1, *A*). At 5 weeks of age, he demonstrated worsening erythroderma with superficial desquamation (Fig 1, *B*). A complete blood cell count with differential count showed an elevated level of eosinophils. A punch biopsy was performed that demonstrated psoriasiform hyperplasia of the epidermis with enlarged nuclei in the stratum corneum and almost complete absence of the stratum granulosum. Immunostaining for lymphoepithelial Kazal-type–related inhibitor (LEKTI) was performed and showed the absence of staining in the epidermis and the epithelium of hair follicles (Figs 2 and 3) compared with the control (Fig 4).

Question 1: Based on the clinical presentation and histology, what is the most likely diagnosis?

A. Severe dermatitis, multiple allergies, and metabolic wasting syndrome

B. Autosomal recessive congenital ichthyosis, lamellar type

C. Netherton syndrome (NS)

D. Acrodermatitis enteropathica

E. Generalized inflammatory (type B) peeling skin syndrome

Answers:

A. Severe dermatitis, multiple allergies, and metabolic wasting syndrome — Incorrect. This syndrome results from a mutation in the gene encoding desmoglein. Erythroderma, ichthyosis, and nail dystrophy are present in the first week of life. Features include multiple food allergies, high serum immunoglobulin E levels, recurrent infections, and metabolic wasting.

B. Autosomal recessive congenital ichthyosis, lamellar type — Incorrect. Autosomal recessive congenital ichthyosis encompasses a heterogeneous group of ichthyoses inherited in an autosomal recessive manner. Most neonates with autosomal recessive congenital ichthyosis of the lamellar subtype are born with a collodion membrane; erythroderma is not a typical feature.[1]

C. Netherton syndrome (NS) — Correct. NS is a rare autosomal recessive disorder characterized by ichthyosiform erythroderma, trichorrhexis invaginata, and atopic manifestations.

The gene that encodes the serine protease inhibitor, *LEKTI*, is mutated. The absence of LEKTI expression by immunohistochemistry supports the early diagnostic confirmation of NS with 100% sensitivity and specificity. Psoriasiform hyperplasia and compact parakeratosis with large nuclei are frequently observed on routine histopathology.[2]

D. Acrodermatitis enteropathica — Incorrect. Acrodermatitis enteropathica presents with perioral or anogenital erosive or scaly plaques. It is due to a defective zinc transporter protein, SLC39A4, resulting in impaired enteral zinc absorption. Infants respond to zinc supplementation.

E. Generalized inflammatory (type B) peeling skin syndrome — Incorrect. Peeling skin syndrome is an autosomal recessive disorder that presents at birth or in early childhood with widespread peeling, erythroderma, pruritus, and atopy. The stratum corneum is easily peeled in patients with peeling skin syndrome. Histopathology shows the absence of corneodesmosin in the epidermis rather than the absence of LEKTI as observed in NS.[3]

Question 2: Which treatment is most likely to lead to significant improvement in the cutaneous manifestations of this condition?

A. Topical corticosteroids

B. Secukinumab

C. Topical tacrolimus

D. Guselkumab

E. Natalizumab

Answers:

A. Topical corticosteroids — Incorrect. Topical corticosteroids provide minimal improvement in NS. There is also a risk of increased systemic absorption due to a significant barrier defect, placing patients at risk of the development of Cushing syndrome.[4]

B. Secukinumab — Correct. The molecular profile of NS shows an elevated level of interleukin (IL)-17, similar to that observed in psoriasis. Secukinumab is an anti—IL-17A monoclonal antibody that has been shown to be effective for patients with an erythrodermic phenotype of NS, leading to a significant decrease in pruritus, rapid improvement of ichthyosis linearis circumflexa, and clearance of erythematous scaly plaques.[5]

C. Topical tacrolimus — Incorrect. Due to the severe barrier defect in NS, systemic absorption increases the potential for adverse effects.[4]

D. Guselkumab — Incorrect. Guselkumab is a monoclonal antibody targeting IL-23 and is approved for plaque psoriasis. Although the helper T cell type 17/IL-23 pathway is upregulated in NS, IL-17 inhibition has been reported as effective, rather than IL-23 inhibition.

E. Natalizumab — Incorrect. Natalizumab is a monoclonal antibody targeting $\alpha 4$ integrin on white blood cells and is used to treat relapsing forms of multiple sclerosis and refractory Crohn's disease.

Question 3: Which histopathologic patterns are most commonly described in patients with NS?

A. Ichthyosiform hyperplasia, absent stratum corneum, and acantholysis

B. Ichthyosiform hyperplasia with decreased or absent granular layer

C. Psoriasiform hyperplasia with absent spinous layer

D. Psoriasiform hyperplasia, absent spinous layer, and acantholysis

E. Psoriasiform hyperplasia, decreased or absent granular layer, and splitting of the subcorneum

Answers:

A. Ichthyosiform hyperplasia, absent stratum corneum, and acantholysis — Incorrect. Ichthyosiform hyperplasia is defined as compact orthohyperkeratosis, a normal or thickened granular layer, and few or no inflammatory cells in the dermis. This is not observed in NS. Instead, psoriasiform or nonspecific hyperplasia has been reported. The stratum corneum is rarely absent in NS. More commonly, parakeratosis is observed. Acantholysis is observed in pemphigus vulgaris, not in NS.[2]

B. Ichthyosiform hyperplasia with decreased or absent granular layer — Incorrect. While the granular layer is often absent in NS, ichthyosiform hyperplasia is not observed.

C. Psoriasiform hyperplasia with absent spinous layer — Incorrect. Although psoriasiform hyperplasia is observed in NS, the spinous layer is mostly reported to have dyskeratosis rather than being absent.

D. Psoriasiform hyperplasia, absent spinous layer, and acantholysis — Incorrect. Although psoriasiform hyperplasia is observed in NS, the spinous layer is not reported to be absent. Acantholysis is observed in pemphigus vulgaris.

E. Psoriasiform hyperplasia, decreased or absent granular layer, and splitting of the subcorneum — Correct. In a study of 80 skin biopsies from patients with NS confirmed using LEKTI staining, psoriasiform hyperplasia, decreased or absent granular layer, and splitting of the subcorneum were among some of the most common findings that can be useful for suggesting a diagnosis of NS.[2]

Abbreviations used:

IL: interleukin
LEKTI: lymphoepithelial Kazal-type—related inhibitor
NS: Netherton syndrome

Conflicts of interest

None disclosed.

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