A Case of Netherton Syndrome Responsive to 1% Topical Pimecrolimus Cream

Netherton syndrome is a rare autosomal recessive disorder associated with mutation of the *SPINK5* gene. Its typical manifestations are the triad of ichthyosis, hair shaft abnormality, and atopic diathesis. We report a case of Netherton syndrome and suggest topical pimecrolimus as a well-tolerated agent for truncal lesions.

A 17-year-old male patient presented with skin lesions involving the whole body and hair present shortly after his birth. On physical examination, there were polycyclic serpiginous patches with peripheral scales on the extremities (Fig. 1A, 1B). Erythematous lesions resembling atopic dermatitis were present on the popliteal fossa area; however, they were mild and without lichenification. Also, diffuse erythema was noted on the face with a positive Hertoghe sign and brittle hair (Fig. 1C). Clinically, the lesions with geographic, sharply defined erythema on the trunk were compatible with ichthyosis linearis circumflexa (ILC). Pathological findings revealed hyperkeratosis, acanthosis, and parakeratosis along with perivascular cellular infiltration, mostly lymphocytic, in the upper dermis (Fig. 2A). Also, a closer inspection of the patient's hair with light microscopy and scanning electromicrography yielded findings suspicious for trichorrhexis invaginata (Fig. 2B). Complete blood count and routine blood chemistry were all within normal limits; however, total IgE was elevated (3,449 IU/mL) and allergen-specific IgE to *Dermatophagoides farinae* was strongly positive (class 6) on ImmunoCAP®. The combination of ichthyosis, hair shaft abnormality, and atopic tendency satisfied the diagnostic triad of Netherton syndrome.

For treatment, 1% topical pimecrolimus ointment was applied once daily for 6 months. No adverse events occurred, and the most prominent changes occurred over the extremities with a reduction of scaly hyperkeratotic plaques (Fig. 1D, 1E). However, the facial erythema persisted despite the applica-

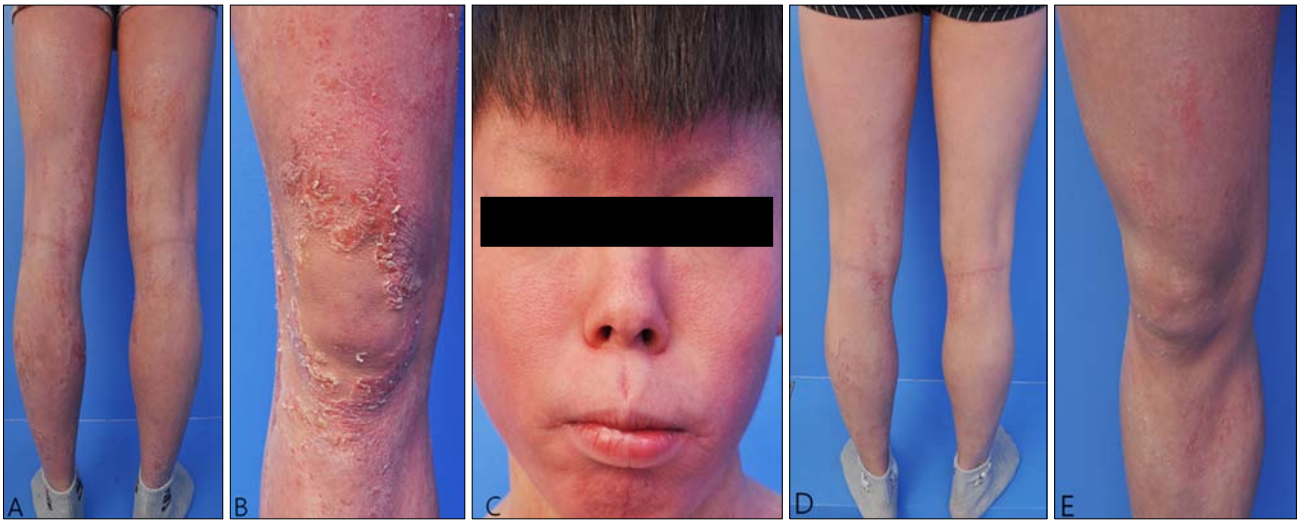

Fig. 1. (A) and (B) Serpiginous polycyclic lesions with erythema and double-edged scales are clinically compatible with ichthyosis linearis circumflexa (ILC). (C) Erythematous face with Hertoghe sign and brittle quality of hair is also observed. (D) and (E) Reduced scaling and erythema for ILC on extremities after topical pimecrolimus application once daily for six months.

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Corresponding author: Kwang Hoon Lee
Department of Dermatology and Cutaneous Biology Research Institute, Yonsei University College of Medicine, 50-1, Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea
Tel: 82-2-2228-2080, Fax: 82-2-393-9157, E-mail: kwanglee@yuhs.ac

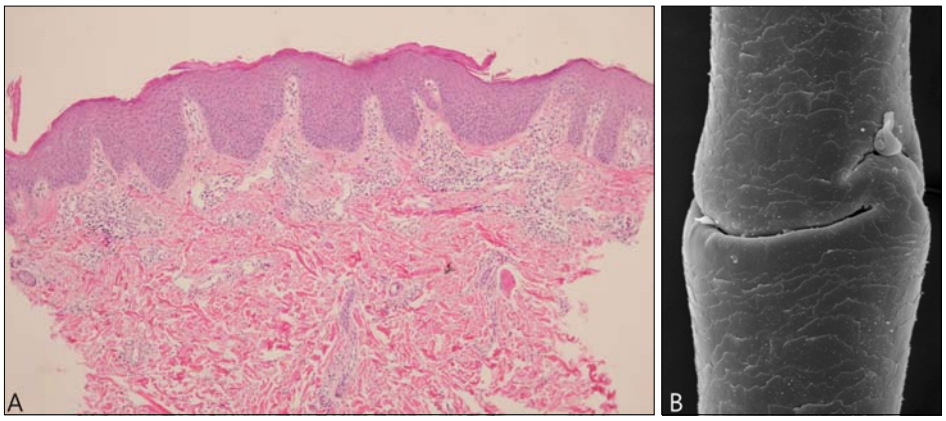

Fig. 2. (A) Hyperkeratotis, acanthosis, and parakeratosis with perivascular cellular infiltration, mostly lymphocytic, is found in upper dermis from trunk lesion suspicious for ILC (H&E, ×200). (B) Closer inspection of hair with scanning electromicrography (SEM) revealed finding suspicious for trichorrhexis invaginata (SEM, ×600).

tion of pimecrolimus. There was an approximately >50% reduction of the Netherton Area and Severity Assessment score from the initial value.

There is no set guideline for the treatment of Netherton syndrome. Topical steroid, topical pimecrolimus, tacrolimus, calcipotriene, 12% ammonium lactate, systemic retinoid, and NB-UVB are some of the options available. Among these treatments, pimecrolimus has been suggested as an effective choice for ILC[1]. Treatment with pimecrolimus for 18 months caused a dramatic reduction in disease severity and pruritus score compared with baseline[2]. Also, despite concerns of decreased protease inhibition within the epidermis and defective barrier function increasing the risk of transepidermal water loss, skin infection, and, most important, systemic absorption of topical drugs[3], treatment of 99% of the body surface area with pimecrolimus did not result in its increased level in blood, assuring its relative safety[4].

The atopic dermatitis on flexural sites and ichthyosis on the trunk and extremities in our patient showed improvement after treatment with pimecrolimus. However, no effect on facial erythema was seen. Diffuse erythema on the face is commonly noted in Netherton syndrome. Yet, it is still unclear whether the major contributory factors for persistent erythema are a result of an ineffective barrier, vasculature abnormality, or environmental effects.

We report an educational case reminding of the classical triad of Netherton syndrome and showing the effectiveness of topical pimecrolimus. Our patient showed comparable results to those reported in Western countries; however, we additionally suggest the need for future studies aimed at uncovering the mechanism of facial erythema refractory to treatment.

Key Words: Netherton syndrome, Ichthyosis linearis circumflexa, Pimecrolimus

Hemin Lee, Jung U Shin, Kwang Hoon Lee
Department of Dermatology and Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul, Korea
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