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LETTER TO THE EDITOR

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Two cases of ichthyosis and their EPR analyses of stratum corneum

Dear Editor,

Ichthyosis is an inherited skin disorder characterized by generalized scaling and hyperkeratosis. Lamellar ichthyosis (LI) (OMIM number 242100) has been named "ichthyosis congenita type II" by the Heidelberg group on the basis of electron microscopic findings.[1] In approximately half of all cases of LI, the cause is absence of transglutaminase-1 (TGM1).[2] Superficial epidermolytic ichthyosis (SEI, OMIM 146800), previously known as ichthyosis bullosa of Siemens (IBS), is a rare autosomal dominant skin disorder caused by mutations in the keratin 2 (*KRT2*) gene.[3] We investigated stratum corneum (SC) radicals of the patients with ichthyosis using the electron paramagnetic resonance (EPR).

1 | CASE 1

The patient is a 40-year-old Japanese man who was born as a "collodion baby" at birth and later developed large thick brown hyperkeratotic scales on the entire body with marked ectropion, mild palmoplantar keratoderma, and mild erythema (Figure 1A,B). Skin biopsy on the eighth day of his life revealed a thickened SC without parakeratosis. There was only one layer of the granular degeneration in the epidermis (Figure 1C). There was a decrease in the expression of the TGM1 staining (Figure 1D), but there was no change in the expression of the keratin staining (Figure 1E). The lipid droplets and corneodesmosome were observed in the patient with LI (Figure 1F-H), and it was presumed that there was a qualitative change in the intercellular lipid in the SC. The mutations (R348X/Y365D) in the TGM1 gene were identified.[2]

2 | CASE 2

A 10-year-old Japanese boy was referred to our department with a history of skin rash on his extremities since early childhood. There was no definite history of blistering. Physical examination revealed dark-to-light gray hyperkeratosis covering the extremities, superficial denuded areas, and hypopigmented spots (Figure 1J-L). Skin biopsy specimen obtained from his right ankle revealed marked hyperkeratosis and vacuolated keratinocytes with large keratohyalin granules in the upper spinous layer and granular layer (Figure 1M,N). The tonofilaments in the prickle layer formed clumps in the cells (Figure 1O). The mutations (p.N186S) in the *KRT2* gene were identified.[3]

EPR is a technique for measuring the free radicals in a sample at any temperature.[4] The motion of the unpaired spin is affected by the radical moiety and appears in the EPR spectral pattern. The spin probes, which contain the unpaired spin, permeate the intercellular lipid region of the SC.[4]

SC was obtained from skin lesions on the legs and subjected to the EPR assay by using the method previously described.[4,5] The median of the magnetic field was 336 mT. The spectral patterns of Case 1 and Case 2 were similar to those of the previous controls, except for the intensity (Figure 1P).

The EPR method was able to detect abnormalities of keratin in psoriasis[4]. However, our cases of congenital ichthyosis were not normalized. These results suggest the possibility that psoriasis and congenital ichthyosis might have different mechanisms of hyperkeratosis formation.

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DECLARATIONS

Approval of the research protocol: The Hirosaki University Internal Review Board approved the research.

INFORMED CONSENT

The Registry and Registration No. of the study/trial is 2016-252.

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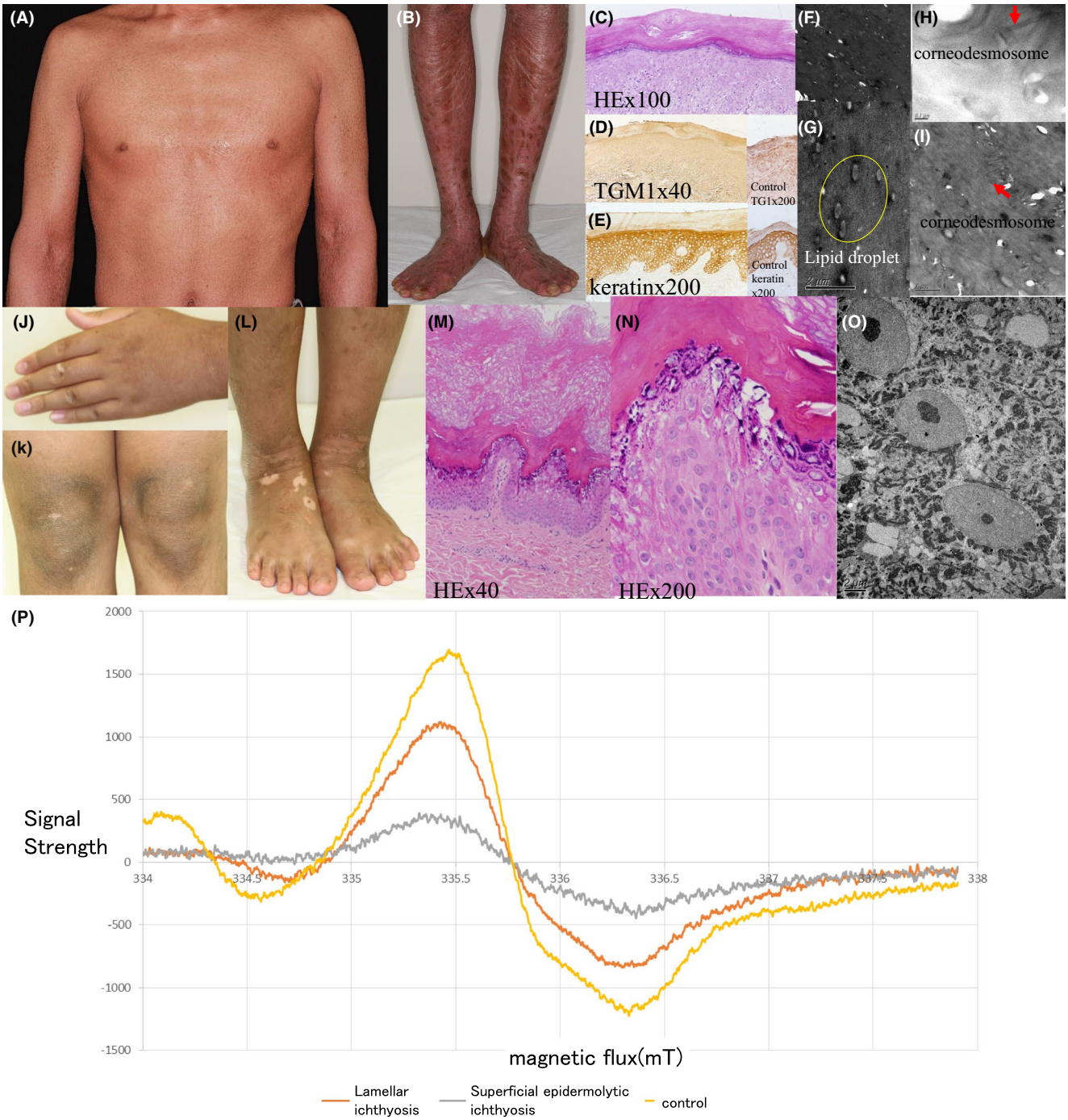

FIGURE 1 Clinical and laboratory findings. A and B, Physical examination shows large thick brown hyperkeratotic scales on the entire body with marked ectropion, mild palmoplantar keratoderma, and mild erythema, typical of the LI phenotype. C, Skin biopsy on the eighth day of his life reveals a thickened stratum corneum (SC) without parakeratosis. There was only one layer of the granular degeneration in the epidermis. D, There was a decrease in expression of the transglutaminase-1 staining. E, Immunohistochemical staining is negative for keratin. F-I, The lipid droplets and corneodesmosome are observed in the patient with LI. J-L, Physical examination reveals dark-to-light gray hyperkeratosis covering the extremities, superficial denuded areas, and hypopigmented spots. M and N, Skin biopsy specimen obtained from the right ankle of the patient reveals marked hyperkeratosis and vacuolated keratinocytes with large keratohyalin granules in the upper spinous layer and granular layer. O, The tonofilaments in the prickle layer formed clumps in the cells. P, The spectral patterns of Case 1 and Case 2 are similar to those of the previous controls, except for the intensity

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Niemi KM, Kanerva L, Kuokkanen K. Recessive ichthyosis congenita type II. Arch Dermatol Res. 1991;283:211–8.
2. Kon A, Takeda H, Sasaki H, Yoneda K, Nomura K, Ahvazi B, et al. Novel Transglutaminase 1 Gene Mutations (R348X/Y365D) in a Japanese Family with Lamellar Ichthyosis. J Invest Dermatol. 2003;120:170–2.
3. Akasaka E, Minakawa S, Rokunohe D, Toyomaki Y, Matsuzaki Y, Sawamura D, et al. Superficial epidermolytic ichthyosis caused by a novel KRT2 mutation. J Dermatol Sci. 2015;79:86–8.
4. Nakagawa K, Minakawa S, Sawamura D. Spectroscopic evidence of abnormal structure of psoriasis vulgaris stratum corneum. J Dermatol Sci. 2012;65:222–4.
5. Nakagawa K. Electron paramagnetic resonance investigation of stratum corneum lipid structure. Lipids. 2010;45:91–6.