

## Porokeratotic Eccrine Ostial and Dermal Duct Naevus and Aberrantly Regulated Keratinization

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Porokeratotic eccrine ostial and dermal duct naevus (PEODDN) (porokeratotic eccrine naevus) is an uncommon naevus characterized by a hyperkeratotic streak or hyperkeratotic streaks following Blaschko's lines (1–3). Histopathological features include cornoid lamellae protruding from dilated eccrine ducts. PEODDN is a mosaic form of keratitis-ichthyosis-deafness (KID) syndrome caused by a mutation in *GJB2* encoding a gap junction protein connexin-26 (Cx26) (3). Connexin proteins are components of gap junctions of aqueous pores, which allow intercellular exchanges of ions and small molecules (4). Gap junctions mediate intercellular communications in various physiological processes, including cell growth and differentiation.

Connexin proteins assemble into hemichannels (connexons) and intercellular channels (gap junctions) (5). The mutation in *GJB2* causes various disorders, including KID syndrome, Vohwinkel syndrome (VS), Bart-Pumphrey syndrome (BPS), and non-epidermolytic palmoplantar keratoderma (NEPPK) with deafness. KID syndrome is associated with the aberrant function of gap junction (5). VS, BPS and NEPPK with deafness are related to the decreased function (5).

Aberrant expression of K10, K14 and loricrin were illustrated in 2 cases of PEODDN (3), although proper expression of keratins and filaggrin were shown in cases of NEPPK with deafness (6). The aberrant function of gap junction would induce abnormal expression of keratins and keratinization-associated proteins. The theory prompted us to investigate keratins and filaggrin expression in our case of bilateral systematized PEODDN.

### CASE REPORT

A 1-year-old Japanese boy was referred to us with congenital asymptomatic skin lesions. Their relative sizes and distribution had been stable. The family had no history of such a skin disorder or parental consanguinity. Physical examination revealed asymptomatic, slightly hyperkeratotic streaks on the bilateral trunk and extremities following the lines of Blaschko (Fig. 1a, 1b). A biopsied specimen was taken from the left lateral abdomen. Keratin expression was examined with keratin (K) 1, K7, K8, K10, K14, K15, K16, K17, K18, K19, and K20, as described (7). Filaggrin expression was examined with an antibody reacting to profilaggrin and filaggrin, as described (7).

Haematoxylin and eosin staining revealed cornoid lamella-like columns (CLLCs) with dilated acrosyringi-

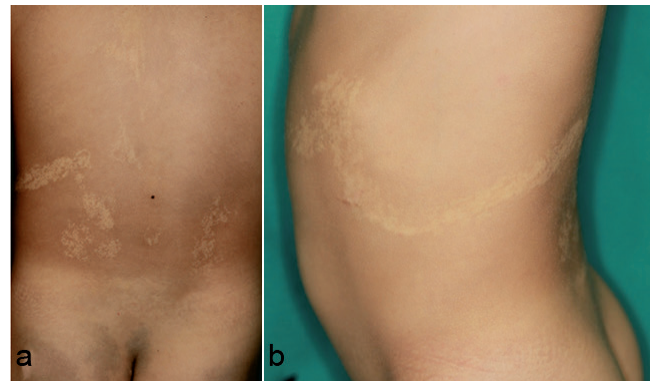


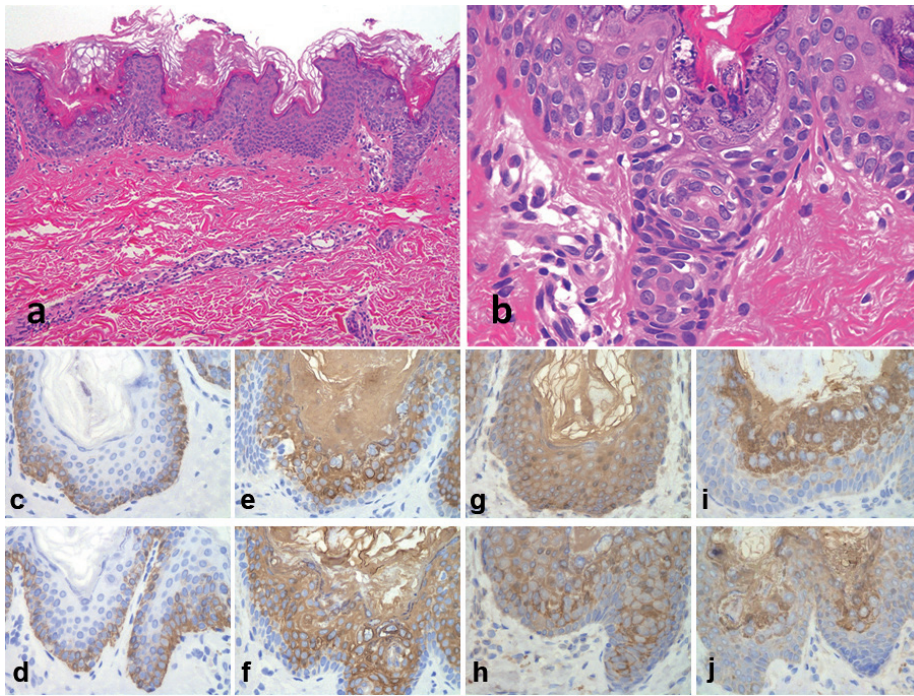
Fig. 1. (a, b) Asymptomatic, slightly hyperkeratotic streaks following the lines of Blaschko in the patient at the age of 2 years.

ums within the epidermal invaginations, wavy epidermis with acanthosis, and basket-weave hyperkeratosis (Fig. 2a). High magnification showed diminished or no granular layer and focal vacuolization in the upper keratinocytes adjacent to CLLCs in the epidermis and in the dilated acrosyringium (Fig. 2b). K14 was expressed in the basal layer of the epidermis and partly in the adjacent suprabasal layer (Fig. 2c, 2d). K10 was not expressed in the basal and approximately half of the suprabasal layers, but was completely expressed from the lower spinous layer to CLLCs (Fig. 2e, f). K1 was expressed in the basal layer, spinous layer and CLLCs, although it was expressed less in the basal layer than in the suprabasal layer (Fig. 2g, h). Filaggrin/profilaggrin was excessively expressed in the middle to upper spinous layer, but was not present in CLLCs (Fig. 2i, j). K7, K8, K15, K16, K17, K18, K19 and K20 were not expressed in the epidermis.

### DISCUSSION

We diagnosed the bilaterally distributed, multiple linear lesions with bilateral systematized PEODDN as the presence of CLLCs with dilated acrosyringia within the epidermal invagination. We confirmed 4 anomalous features: persistent expression of K5 to the suprabasal layer; delayed expression of K10 from the lower spinous layer; early expression of K1 from the basal layer; and early intense expression of filaggrin/profilaggrin from the middle spinous layer.

We evaluated the previously reported immunofluorescent stains for K10 and K14 in two PEODDN cases (3), and judged that K10 was mostly expressed from the



*Fig. 2.* Histopathological figures of the biopsied specimen. (a) A specimen showed cornoid lamella-like columns (CLLCs). (b) High magnification of the dilated acrosyringium. (haematoxylin and eosin stain, original magnification: (a)  $\times 40$ , (b)  $\times 400$ .) Histochemical staining with (c, d) K14, (e, f) K10, (g, h) K1, and (i, j) filaggrin/profilaggrin (original magnification:  $\times 400$ ).

lower spinous layer in both two cases, and that K14 was expressed in the basal layer and suprabasal layer in one case, and in the basal layer and focally in the spinous layer in another case. In the previous and our cases of PEODDN, expression of keratins is dysregulated from early to terminal keratinization. We conjecture that aberrant keratin expression would be associated with the dysregulated gap junction.

In porokeratosis, some keratinocytes in the spinous layer possess an eosinophilic cytoplasm as a result of premature keratinization (8). The underlying granular layer is diminished or absent. In PEODDN, we believe that filaggrin/profilaggrin is already present in the middle spinous layer, resulting in premature keratinization and formation of CLLCs.

In conclusion, we describe here a patient with bilateral systematized PEODDN with histochemical features, unusual persistent expression of K14 as an early differentiation marker, abnormal delayed expression of K10 and early expression of K1 as subsequent differentiation markers, and extraordinary early and excess expression of filaggrin/profilaggrin as a terminal differentiation marker. The aberrant function of gap junction in PEODDN would be associated with dysregulated expression of keratins and filaggrin/profilaggrin.

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*The authors declare no conflicts of interest.*

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