A 27-year-old Japanese woman presented with small atrophic hyperpigmented macules on her extremities since early childhood. The macules spread across her body and increased in number following Blaschko’s lines (Fig. 1A, B). The skin lesions gradually coexisted with the development of hypopigmentation, nodular fat herniation, verrucoid papillomas, and telangiectasia (Fig. 1C). Dermoscopy of the hyper/hypopigmentation showed multiple light-brown macules with a delicate pigment network, as well as white scar-like hypopigmentation and thin telangiectasia, mimicking the features of poikiloderma (Fig. 1D). Dermoscopic examination of nodular herniation demonstrated aggregation of yellowish-white clods (Fig. 1E). There were no limb abnormalities, or ocular or dental involvement. No other family members were affected.

What is your diagnosis? See next page for answer.

Fig. 1. Multiple hyperpigmented macules on (A) the back and (B) the lower legs following Blaschko’s lines. (C) Verrucoid papillomas (arrow) and nodular fat herniations (arrowhead) on the right axilla. (D) Dermoscopic examination demonstrates light-brown macules with a delicate pigment network and white scar-like hypopigmentation with thin telangiectasia on the abdominal skin. (E) Nodular fat herniations on the right axilla demonstrate aggregation of yellowish-white clods.
**ANSWERS TO QUIZ**

**Life-long Skin Eruptions along Blaschko’s Lines in a 27-year-old Woman: A Commentary**

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**Diagnosis: Focal dermal hypoplasia**

Histopathological examination of a skin biopsy from the lower leg revealed irregular acanthosis with extension of subcutaneous fat toward the upper dermis (Fig. 2A). Hyper/hypopigmentation on the abdominal skin showed epidermal atrophy with basal pigmentation, dermal atrophy, and a perivascular lymphocytic infiltrate with slight oedema in the papillary dermis (Fig. 2B). Based on the above clinical and histopathological findings, a diagnosis of focal dermal hypoplasia (FDH) was made. After obtaining ethics approval and informed consent, genetic analysis was performed using genomic DNA from formalin-fixed paraffin-embedded (FFPE) lesional lower leg tissue and blood lymphocytes of the patient, in accordance with the principles of the Declaration of Helsinki. The FFPE tissue was prepared originally for routine light microscopy and contained the epidermis, dermis, and part of subcutaneous fat. Sanger sequencing revealed a new heterozygous duplication of 8 base pairs in exon 11 of the *PORCN* gene (c.1047_1054dup, p.Leu352Argfs*50) from the lesional skin, whereas the signal of the mutated allele was much weaker than the wild-type signal from blood lymphocytes, suggesting that discrepancy of signal intensities demonstrates the presence of postzygotic mosaicism in this patient (Fig. 2C). Currently, there is no satisfactory treatment for FDH. The hyperpigmented lesion on the patient’s upper arm was tentatively treated once with a Q-switched ruby laser, with a partial improvement 1 year after the treatment.

FDH is a rare X-linked dominant disorder with developmental abnormalities in ectoderm and mesoderm tissues, characterized by widespread skin aplasia along Blaschko’s lines, as well as the limbs, ocular and dental malformations. Skin manifestations may include linear skin atrophy, hyper/hypopigmentation, nodular fat herniation, telangiectasia, ridged dysplastic nails, and verrucoid papillomas. The molecular basis of FDH was shown to result from mutations in *PORCN*, encoding endoplasmic reticulum proteins putatively serving as porcupine O-acyltransferase, which is involved in Wnt ligand secretion (1, 2). Following gastrulation, embryonic cells of ectoderm and mesoderm strongly influenced by Wnt signalling will differentiate to form the epidermis and dermis, respectively. Deletion of *Porcn* in mice exhibited developmental abnormalities in skin and limbs, resembling those observed in human FDH (3). The marker for hair follicle development *Lef1* and the mesenchyme marker *PDGFRA* are normally expressed in the basal keratinocytes and the dermis, respectively. Expressions of both *Lef1* and *PDGFRA* were reduced or absent in mouse *Porcn* mutant embryos. *PORCN* is thus essential for the initiation of epidermal and dermal developments, like other Wnt signalling molecules, although distinct distribution of *PORCN* in skin remains to be fully elucidated.

We report here a case of FDH without any extracutaneous features, caused by the postzygotic *PORCN* mutation. Postzygotic mutations of the late gastrula could generally lead to a mild phenotype with focal lesions restricted to specific organs, which is consistent with the mild features in this case, whereas the mosaic state in this case may also affect the gonads. Epidermolytic naevus due to mutations in *KRT1/10* is known to be rarely passed on as epidermolytic ichthyosis in the next generation. A recent next-generation sequencing study revealed that 3.9% of the sperm in a male patient with epidermal naevus accounted for 0.5% of his

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**Fig. 2.** (A) Skin biopsy specimen from the lower leg shows irregular acanthosis with extension of subcutaneous fat toward the upper dermis. (B) Hyper/hypopigmentation on the abdominal skin shows epidermal atrophy with basal pigmentation, dermal atrophy, and a perivascular lymphocytic infiltrate with slight oedema in the papillary dermis. (C) Sanger sequencing of the lesional skin reveals a new heterozygous 8-bp duplication, c.1047_1054dup (GGTCTGTC) in exon 11 of *PORCN*. The signal of the mutated allele in blood is much weaker than the wild-type signal.
whole-body surface, had the postzygotic KRT10 mutation, which was passed on in the germline of his daughter, leading to a phenotype of epidermolytic ichthyosis (9). This observation is important for the purpose of genetic counselling, because the presence of mild FDH implies a risk of simultaneous gonadal mosaicism that may cause the full-blown phenotype in the next generation. Genetic counselling is therefore complex, and is not recommended to be attempted by dermatologists alone. Individuals and families with FDH should be referred to clinical genetics’ services for counselling by trained counsellors who have an up-to-date knowledge of the inheritance potential of specific postzygotic mutations (10).

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