asymmetrical skull geometry, brachygnathia and clinodactyly of the fifth digits of both hands (Fig. 1b). Due to the brachygnathia, he displayed misaligned teeth, but there were no abnormal or missing teeth. On the skin examination, along with the firm black nodule on the nose (Fig. 1c), slight hypotrichosis (Fig. 1a), multiple cherry angiomas (Fig. 1d) and seborrheic keratoses were observed. He complained of hypohidrosis, hearing loss in the right ear and myopia. Dual-energy X-ray absorptiometry displayed severe osteoporosis. Carotid ultrasonography revealed mild stenosis of both carotid arteries. He had a negative family history. A skin biopsy of the nodule on his nose led to a diagnosis of basal cell carcinoma (BCC) (Fig. 1c, inset). In a skin specimen from the back, few sweat ducts were observed. Based on these findings, the differential diagnosis included a subtype of progeria or hypohidrotic ectodermal dysplasia, so we searched causative genes (*EDA1*, *EDAR*, *EDARADD* and *WNT10A*)[2] of hypohidrotic ectodermal dysplasia. The genetic analysis was performed at Hirosaki University Faculty of Medicine under the approval of the ethics committee. Written informed consent from the patient was obtained at Osaka University Faculty of Medicine. We were permitted by the ethics committee of the Osaka University Faculty of Medicine to use the genetic analysis results. Mutational analysis using genomic DNA extracted from the patient's leukocytes revealed a heterozygous c.874A>G mutation in the *WNT10A* gene (NM_025216.2). This point mutation, which has not been reported previously and was not found in 200 normal alleles, causes a missense mutation, p.S292G, which was predicted to change conformation of protein based on Chou–Fasman method.

WNT10A is a member of the wingless signaling pathway that plays a fundamental role in skin and appendage morphogenesis.[1] The *WNT10A* gene is involved in various forms of ectodermal dysplasia.[2] Our patient had a mutation in this gene and displayed ectodermal dysplasia-like manifestation such as hypohidrosis and hypotrichosis; however, he revealed other notable symptoms including severe scoliosis. Patients with *WNT10A* mutations display variable clinical features,[2] but based on previous reports, most of the cases with mutations in this gene tend to have dental changes. Our case was extremely rare because there were no signs of dental disorders, and the patient presented with severe scoliosis, which has never been reported with mutations in this gene. Mutations in components of the Wingless signaling pathways are associated with increased fracture risks, as well as with human skeletal diseases and variation of bone mineral density;[3] so, a mutation in the *WNT10A* gene probably accounts for skeletal disorders including scoliosis in our patient. In addition, dermatologically, our case developed cherry angiomas and BCC. Wingless signaling pathways also play a key role in angiogenesis,[4] and their activities regulate BCC growth,[5] so a mutation in the pathway might have contributed to his cutaneous presentation.

CONFLICT OF INTEREST: None.

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Case of non-Herlitz junctional epidermolysis bullosa with *COL17A1* mutation

Dear Editor,

Non-Herlitz junctional epidermolysis bullosa (JEB-nH; Mendelian Inheritance in Man no. 226650) is an autosomal recessive disorder characterized by generalized blisters, atrophic scars, alopecia, nail dystrophy and dental abnormalities.[1] Several genes, including *COL17A1*, are responsible for JEB-nH. Infants and children with JEB-nH frequently lack many of these clinical manifestations, making it difficult to diagnose in infancy from

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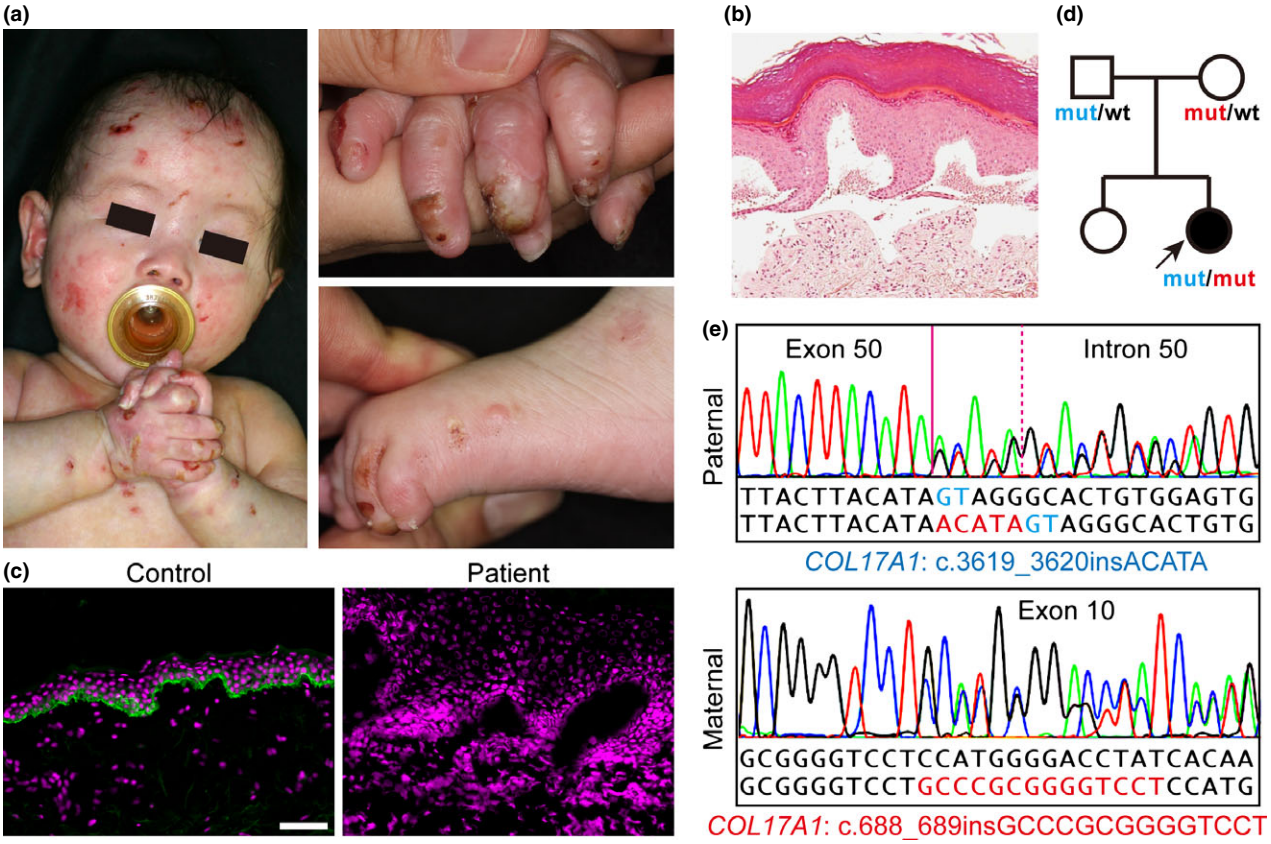

Figure 1. (a) Clinical images of the proband's face, trunk, arms, hand, foot and nails. (b) Skin biopsy from the sole of the proband's foot, displaying subepidermal bulla formation without acantholysis (hematoxylin–eosin, original magnification ×100). (c) Immunofluorescence images of anti-type XVII collagen antibody (D20) staining. While normal control skin showed linear staining at the basement membrane zone (left panel), the proband's skin of the lateral border of the sole displayed total loss of type XVII collagen staining (right panel; bar, 100 μm). (d) Family pedigree. (e) Compound heterozygous insertion mutations in *COL17A1* identified in the family: paternal mutation of c.3619_3620insACATA in exon 50 and maternal mutation of c.688_689insGCCCGCGGGGTCCT in exon 10. Inserted nucleotides are shown in red. In the paternal mutation, splicing donor sequences are shown in pale blue and the border between exon and intron 50 is shown as a solid red line in the wild-type allele. The predicted exon–intron border in the mutated allele is shown by a dotted red line.

clinical features alone.[2] We report a case of JEB-nH diagnosed in infancy from clinical features, immunofluorescence testing and genetic testing.

A 7-month-old Japanese female was admitted to our hospital with recurrent blister formation since birth. The patient had small blisters and erosions on the entire body. The blisters healed with mild atrophic scarring but without milia formation. Several nails had been lost from the hands and feet. The patient's development was normal and without any hair loss (Fig. 1a). There was no familial history of epidermolysis bullosa (EB). Clinically, blister healing without severe skin atrophy or milia formation suggested EB simplex; however, nail loss implied dystrophic EB.

Histological examination of a foot blister revealed acanthosis and subepidermal blister formation without acantholysis (Fig. 1b). Inflammatory cell infiltration was not prominent. Therefore, we performed immunofluorescence studies of basement membrane zone proteins. Normal staining compared with control skin was obtained for type VII collagen (clone, LH7.2), integrin α6 (clone, GOH3), integrin β4 (clone, 3EI), γ2-chain of laminin 332 (clone, GB3), plectin (clone, HD121) and lamina lucida antigen (clone, LH39). In contrast, staining for COL17A1 (clone, D20) was completely absent (Fig. 1c).

We sequenced all the exons of *COL17A1* in the genomic DNA obtained from white blood cells of the patient and parents. We identified two novel small insertion mutations, c.3619_3620insACATA in exon 50 at the 5′-side of the exon–intron border (based on the nucleotide sequence of NM_000494.3) from the patient and father, and c.688_689insGCCCGCGGGGTCCT in exon 10 from the patient and mother, indicating that the patient was a compound heterozygote of these two mutations (Fig. 1d,e). Both mutations were predicted to cause frame-shift and premature termination, resulting in nonsense-mediated mRNA decay, suggesting that the truncated COL17A1 mutant expression level

would be low, which corresponded well with the total loss of COL17A1 immunofluorescence signals. Therefore, we diagnosed the patient with JEB-nH.

Non-Herlitz junctional epidermolysis bullosa is an autosomal recessive, non-lethal variant of junctional EB caused by a deficiency of *COL17A1*, *LAMA3*, *LAMB3* and *LAMC2*.[1,2] Because the most characteristic symptoms of JEB-nH are late onset, clinical diagnosis was difficult and genetic testing was indispensable for a proper diagnosis in this patient. Late-onset non-scarring alopecia is a characteristic finding in JEB-nH. It was speculated from a mouse study that the cell-matrix attachment through COL17A1 is important to maintain the stemness of the hair stem cells located in the hair-bulge area.[3] Close observation of hair changes in this patient will provide a good opportunity to investigate hair stem cell loss in human JEB-nH.

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Mucous membrane pemphigoid with esophageal stricture treated with balloon dilatation

Dear Editor,

Mucous membrane pemphigoid (MMP) is an autoimmune bullous disease that primarily involves the oral mucosa and conjunctiva.[1] Esophageal involvement is less common and can occur a long time after the initial symptoms.[1] Once esophageal involvement does occur, it can cause dysphagia, a life-threatening complication that is difficult to treat.

An 80-year-old woman with no family history of bullous disease presented with recurrent oral mucosal and conjunctival blisters; the blisters had first appeared when the patient was 67 years old. At the age of 73 years, she was diagnosed with MMP, but not esophageal malignancy, by serology and esophageal biopsy at another hospital. She was treated with systemic corticosteroids for 5 years. Because the blisters had not recurred for several years, she decided to stop treatment. However, the blisters gradually recurred, along with odynophagia. At the age of 79 years, the patient could only have semi-solid food and fluids. Her medical history included acute aortic dissection (Stanford A, treated with ascending arch replacement), descending aortic aneurysm (treated surgically), hypertension, and paroxysmal atrial fibrillation.

After she initially presented at another hospital, the patient was transferred to our hospital for treatment. Her height was 164 cm and her body weight was 34 kg. Erosions and crusts were seen on the conjunctiva. Slight cicatrix and adhesion were seen on both lateral angles of the eyes (Fig. 1a). In addition, erosions and scars were seen on the palate, and there were blisters on the buccal mucosa near the right front molar (Fig. 1b). Indirect immunofluorescence study results were negative, and anti-BP180 antibody level was 60 U/mL. A barium study showed an esophageal narrowing at the cervical level that was 13 mm in length, with a minimum diameter of 3 mm (Fig. 1c). Endoscopy revealed adhesion at the epiglottis, blisters of the hypopharynx, and bilateral arytenoid adhesion to the side wall (Fig. 1d). Narrowing and extensive erosion were noted in the upper esophagus (Fig. 1e).

Oral mucosal and conjunctival blisters disappeared after betamethasone syrup (2 mg/day) was started. Concurrently, esophageal dilatations with a balloon catheter (CRE™ Wireguided; Boston Scientific, Natick, MA, USA) and endoscopy (Olympus GIF-XQ260 instrument; Tokyo, Japan) were performed once a week for 7 weeks. The balloon was swelled with water, and water pressure and balloon diameter were correlated. At the sixth dilatation, the esophageal diameter increased to 12 mm. Six months after the start of treatment, no stricture was observed (Fig. 1f), and the patient could ingest

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