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Homozygous Deletion Mutation of the *FERMT1* Gene in a Chinese Patient with Kindler Syndrome

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Dear Editor:

Kindler syndrome (KS, OMIM173650) is a rare autosomal recessive genodermatosis characterized by trauma-induced skin blistering, cutaneous atrophy, progressive poikiloderma and photosensitivity[1]. KS is caused by mutation in the *FERMT1* gene[1]. This gene encodes kindlin-1, which regulates not only keratinocyte adhesion through β_1-class integrins but also proliferation and differentiation of cutaneous stem cells by promoting $\alpha_v\beta_6$ integrin–mediated transforming growth factor-β activation and inhibiting Wnt ligand expression[2].

A 12-year-old Chinese boy presented with recurrent blistering after mild trauma from the age of 1 year. There is no family history. Physical examination revealed generalized skin atrophy with some scattered resolving blisters on the extremities and poikiloderma on the face and neck (Fig. 1). He has also suffered from pruritus and photosensitivity. A skin biopsy from non-blistered area on his leg revealed hyperkeratosis and epidermal atrophy (Fig. 2A). Immunofluorescence (IF) mapping of a blister showed that keratins 5 and 14 were localized at the roof of the blister while laminin 5 and type IV collagen were localized at the base (Fig. 2B, C). Electron microscopic findings of non-blistered skin revealed widening of the lamina lucida and reduplication of the lamina densa (Fig. 2D). DNA extracted from the patient's blood was processed for direct nucleotide sequencing and we detected a homozygous dinucleotide deletion mutation at c.994_995delCA in exon 8. The mutation causes frameshift and a premature stop codon (Fig. 2E). Based on these results, we diagnosed the patient with KS.

KS usually manifests at birth with trauma-induced skin blistering that is more prominent on the extremities and

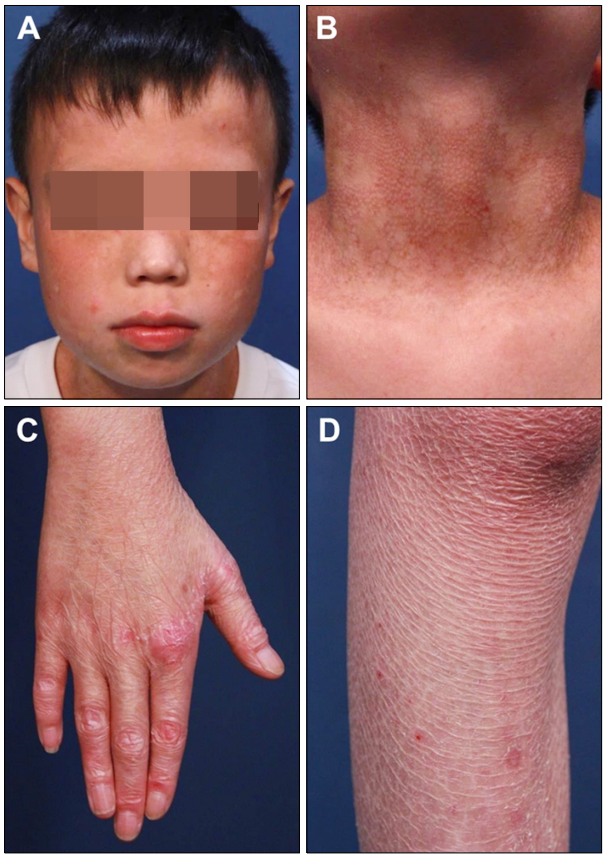

Fig. 1. Clinical features of the patient. (A, B) Poikiloderma on the face and neck. (C) Atrophic change on the dorsal aspect of hand. (D) Skin atrophy with resolving blisters on the leg.

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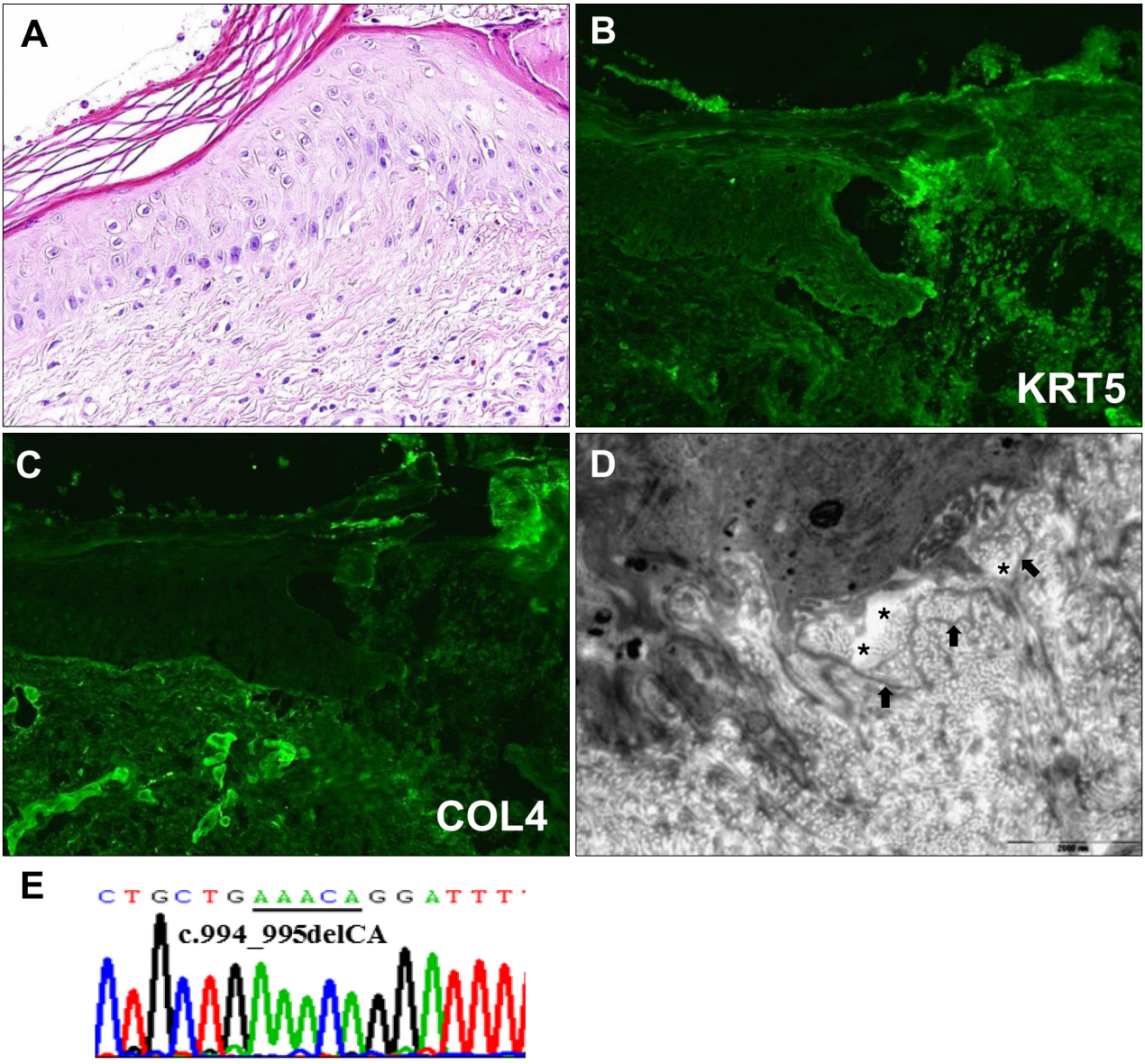

Fig. 2. (A) Histological examination. Hyperkeratosis and epidermal atrophy (H&E, ×400). (B, C) Immunofluorescence mapping shows separation between keratin 5 (KRT5) and type IV collagen (COL4). KRT5 is localized at the roof of the blister (B) while COL4 is localized at the base (C). (D) Electron microscopic features. Stretches of lamina lucida (asterisks) and reduplication of lamina densa (arrows) (bar=2,000 nm). (E) Genetic analysis of the *FERMT1* gene shows homozygous mutation at c.994_995delCA.

tends to regress with age[3]. However, as patients age, skin atrophy localized to the dorsal aspects of the hands and feet become generalized and progressive skin poikiloderma manifests. Most patients also show photosensitivity[3]. Although our patient had no history of mucosal lesions, mucosal involvement is common[1].

Histopathology and IF mapping of a blister are not informative for diagnosis because the plane of cleavage can be variable at the level of the basement membrane zone[1]. Transmission electron microscopy of the non-blistered skin shows extensive reduplication of the lamina densa which is a characteristic diagnostic feature of KS[4]. The diagnostic golden standard is sequencing of the *FERMT1* gene[1].

To date, more than 60 *FERMT1* gene mutations and 150 KS patients have been reported and one Chinese and 4 Japanese patients have been reported in Eastern Asia[5] (https://grenada.lumc.nl/LOVD2/mendelian_genes/home.php?select_db=FERMT1). Most mutations cause premature termination of translation, therefore loss of kindlin-1 function and most patients are related with consanguineous marriages[3]. Recently, Youssefian et al.[4] first reported the

c.994_995delCA mutation in a 19-year-old Iranian female patient. Interestingly, that patient had no mucosal involvement except dental plaques. This may imply an association between the mutation and mucosal-sparing features. Has et al.[3] suggested genotype-phenotype correlations in KS because some patients with a missense mutation or in-frame deletion demonstrate a mild phenotype. However, only two cases including ours have been reported to date and our patient might be too young to have developed mucosal lesions. Further studies are needed to clarify this association.

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A Case of Facial *Sarcoptes scabiei* in a Female Child

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Dear Editor:

Scabies in infants and young children differs from adult scabies infection and is frequently misdiagnosed[1].

An 8-year-old female presented with erythematous scaly pustules on her cheeks that start 3 months prior and had spread to her forehead. She was diagnosed at a local clinic with folliculitis, at which time she was treated with anti-

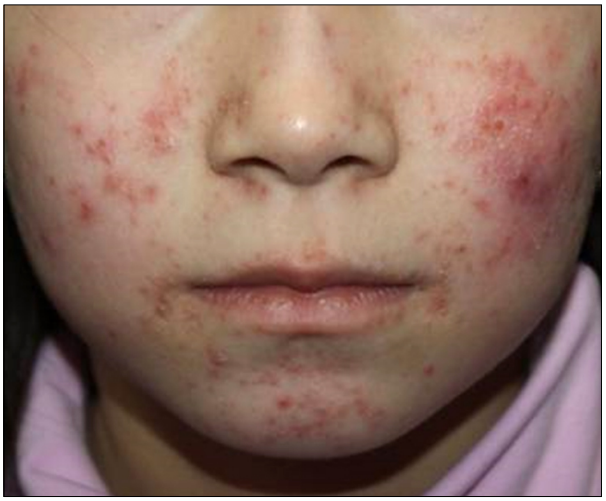

Fig. 1. Scattered, 2～3 mm sized, erythematous scaly pustules and a firm nodule on the face.

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