Observation Letters

Novel glycine substitution G2037R of *COL7A1* in a Chinese boy with pretibial epidermolysis bullosa treated with oral olopatadine hydrochloride and topical Vitamin E

Sir,

Epidermolysis bullosa has been divided into distinct subtypes depending on the level of tissue separation in the dermal-epidermal basement membrane zone; mainly classified as epidermolysis bullosa simplex, junctional epidermolysis bullosa and dystrophic epidermolysis bullosa.[1] The site-specific structural abnormalities are correlated to the genetic dysfunction of different genes, such as K5/K14 mutations in epidermolysis bullosa simplex, mutations of laminins in junctional epidermolysis bullosa and *COL7A1* mutations in dystrophic epidermolysis bullosa. So far, only six mutations have been detected in pretibial dystrophic epidermolysis bullosa, according to the literature.[2,3] We found a novel glycine substitution mutation (G2037R) in exon 73 in a sporadic pretibial dystrophic epidermolysis bullosa patient, whose symptoms were well controlled with a combination treatment regime of oral olopatadine hydrochloride and topical Vitamin E.

An 11-year-old Chinese boy presented to the dermatology clinic with multiple bullous lesions of approximately 0.5–1 cm size, on the abdomen and back; Nikolsky's sign was positive. Several tense and clear blisters, scars and small erosions were also found on the skin around the ankle, knee, hip, elbow and finger joints [Figure 1a]. Some nails were fragile, disfigured and some were absent. His teeth were irregularly arranged, defective or absent [Figure 1b]. Biopsy from a flat papule on the left shin revealed epidermal hyperkeratosis, keratin cysts, irregular acanthosis, hyperplasia and subepidermal cleft formation containing a mild-to-moderate perivascular and interstitial eosinophilic, neutrophil and lymphocytic infiltrate within the proliferative collagen fibers in the papillary dermis [Figure 1c].

After starting treatment with oral olopatadine hydrochloride and topical Vitamin E, the pruritus was well controlled, as evidenced by reduced excoriations at the lesional sites. After 2 weeks of treatment, new blisters no longer appeared and the older lesions showed signs of healing. In addition, the nails became clearer and the skin became more smooth and elastic [Figure 1d].

Genetic studies were performed on the patient and a heterozygous missense mutation was identified in the proband by directly sequencing the polymerase chain reaction products, designated as c. 6109 G>A or p.G2037R in exon 73 of *COL7A1* gene [Figure 2a]. His parents carried an unaffected homozygous allele [Figure 2b]. The mutation G2037R was not found in his parents and 100 unrelated, unaffected control individuals. This mutation is predicted to be "probably damaging" with a score of 1.000 by polyphen-2 (polymorphism phenotyping-2 http://genetics.bwh.harvard.edu/pph 2/). A three-dimensional molecular modeling of the mutant *COL7A1* protein was predicted by a web-based software I-TASSER (University of Kansas, Lawrence, Kansas, USA) [Figure 3].

Herein, we studied a Chinese case with pretibial dystrophic epidermolysis bullosa, where the proband was found to have a heterozygous glycine substitution p.Gly2037Arg. We also found that the combination of olopatadine hydrochloride and topical Vitamin E was effective in reducing the itch and helped in achieving disease control.

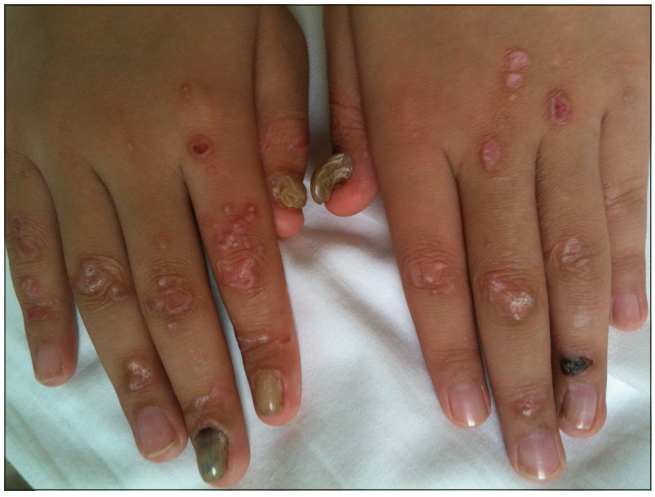

Figure 1a: Clinical presentation and histological features. Relaxed blisters and scars scattered on hands

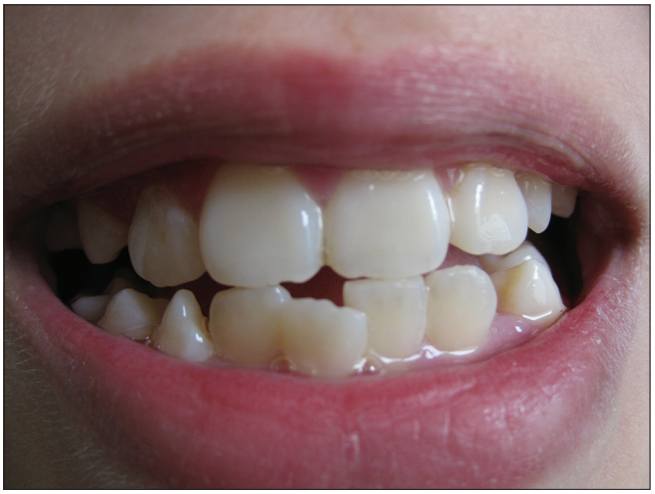

Figure 1b: His teeth are irregularly positioned and/or absent

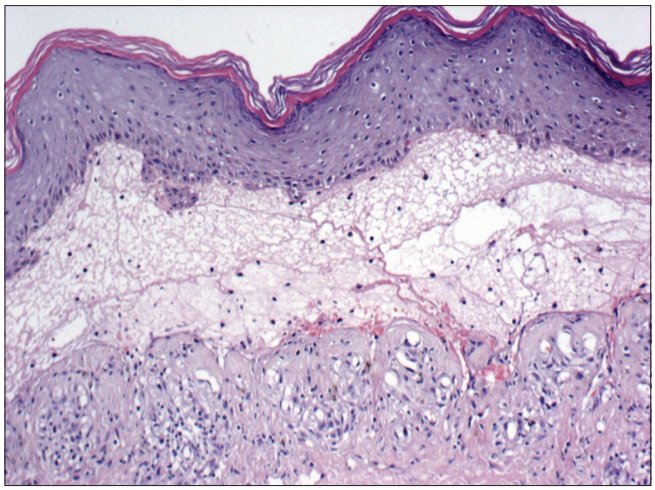

Figure 1c: H and E staining revealed epidermal hyperkeratinization, subepidermal bulla formation and infiltration of numerous inflammatory cells (×100, 100 μm)

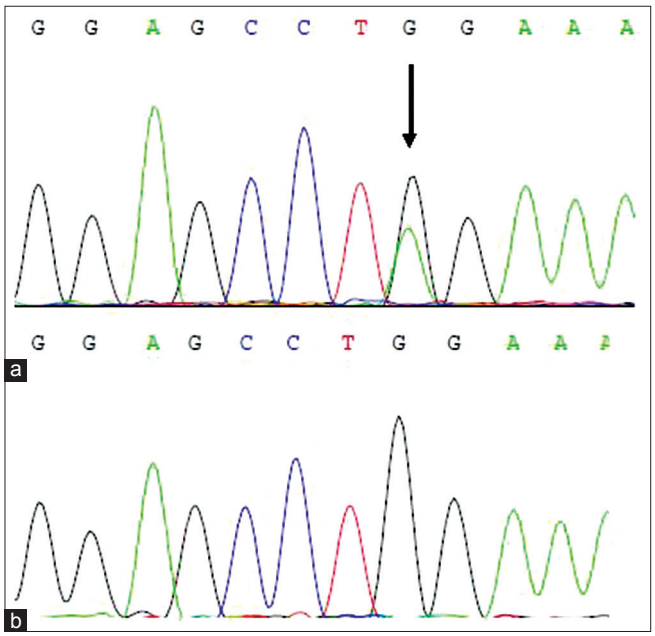

Figure 2: Detection of *COL7A1* mutation. (a) After direct sequence analysis of 118 exons and exon-intron boundary of *COL7A1* gene, a nucleotide substitution was found in exon 73 of the patient, designated as c. 6109G>A, causing change of the 2037th amino residue from glycine (GGA) to arginine (AGA). (b) The same genomic change were not seen in a population of matched, unrelated healthy controls

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Conflicts of interest

There are no conflicts of interest.

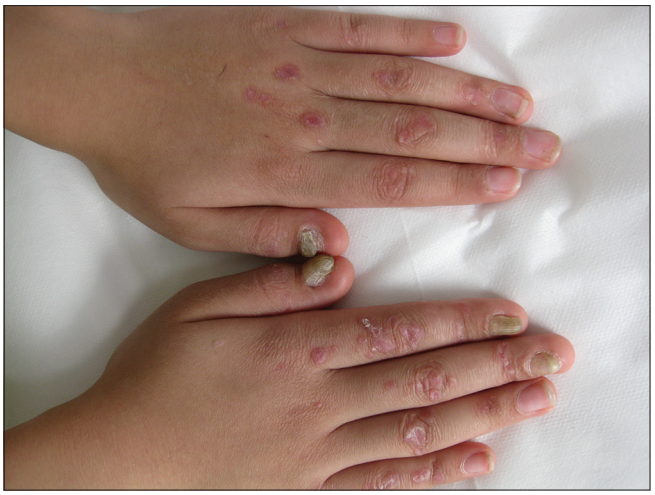

Figure 1d: The cutaneous lesions were much improved after 5-month treatment with olopatadine and Vitamin E

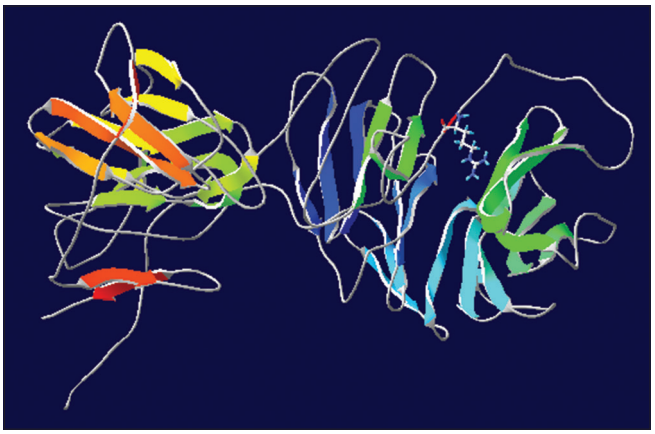

Figure 3: The three-dimensional molecular modeling of the mutant COL7A1 protein

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