

A Case of Dominant Dystrophic Epidermolysis Bullosa with a G2043R Mutation in the Type VII Collagen Gene

Dear Editor,

Dystrophic epidermolysis bullosa (DEB) is a sub-epidermal bulla, characterized by severe itching, lichenoid or nodular prurigo-like lesions, skin erosion, scars, milia, and nail dystrophy, resulting from *COL7A1* mutation. Herein, we report a case of dominant DEB with a G2043R mutation in *COL7A1*.

A 25-year-old Japanese woman was referred to our clinic for recurrent intense pruritis and hypertrophic scars on the abdomen (Figure 1, a). She presented with paper-like scars on her forehead, breast, back, buttock, and extremities (Figure 1, b) with mild toenail hypoplasia (Figure 1, c), but no symptoms on

the fingernails, hair, teeth, or esophagus. She had developed erosions at the ankle joint a few days after birth. Her parents and four siblings had no related symptoms. She had been diagnosed with DEB at 11 months based on clinical and histopathological findings. Erythema, bullae, and skin ulcers had healed with scarring on the extensor surface of the lower legs at 7 years (Figure 1, d). Histopathological findings revealed subepidermal bulla with lymphocyte and eosinophil infiltration in the upper dermis (Figure 1, e). Immunofluorescence staining with type VII collagen antibody showed uneven faint localization at



Figure 1. Clinical manifestations. The patient presented with hypertrophic scarring on the abdomen (a), toenail hypoplasia (b), and paper-like scar on the extremities (c). Erosions with scale-crust on the front side of the lower legs had occurred at age 7 years and subsequently healed (d). Histopathological findings of the abdominal lesion revealed sub-epidermal bulla (e). On immune staining, uneven deposits of type VII collagen were seen at the basement membrane zone (f). Electron microscopy findings showed anchoring fibrils that were scanty, hypoplastic, and unclear (original magnification, 20000) (g).

the basement membrane zone (Figure 1, f). Electron microscopy showed scanty and hypoplastic anchoring fibrils (Figure 1, g). Following ethical approval, informed consent was obtained in compliance with the Declaration of Helsinki guidelines, DNA was extracted from peripheral blood lymphocytes of the patient, and exome sequence analysis was performed. A heterozygous single nucleotide substitution c.6127G>A in exon 73 of *COL7A1* was found, which converts glycine to arginine residue, designated p. G2043R.

Since *COL7A1* is a giant gene with 118 exons and 9276 base pairs, exome sequencing is convenient to determine the mutated gene. In dominant DEB, pathogenic mutations usually occur in glycine substitutions within the type VII collagen triple helix (1). The mutation impedes the trimer formation of collagen and disrupts the normal location of anchoring fibril. The particular localization of mutated collagen VII protein could vary based on the position of mutated glycine residue. In our patient, the mutated collagens were observed sparsely and unevenly at the basement membrane, but can accumulate granularly within the basal keratinocytes (2,3).

G2043R mutation such as in the present case has been previously described with dominant DEB in Italian, Hungarian, Norwegian, Mexican, Scottish, Finnish, American, Chinese, and Japanese cases (1). Given the widespread geographical distribution of this mutation and its occurrence as a *de novo* event like in our case, G2043R can be one of the mutational hotspots in dominant DEB (1). Symptom severity in dominant DEB varies in the same mutation or intra-familial cases, and symptoms regress with age (4). The patient had severe blisters on her legs in early childhood; however, as her age increased, the hypertrophic or atrophic scars on the lower abdomen and extensor surface of her lower legs became the primary skin symptoms. It is presumed that some factor will compensate for the vulnerabilities.

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