



A Case of Pretibial Epidermolysis Bullosa with Novel Mutations of the *COL7A1* Gene

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Dear Editor:

Pretibial epidermolysis bullosa (PEB) was first described by Kuske in 1946¹. The author reported two cases of PEB with recurrent blisters in a middle-aged man and his son. PEB is a rare subtype of dominant dystrophic epidermolysis bullosa (DDEB). Symptoms of DDEB usually appear in infancy, and severe blistering can be life-threatening. On the other hand, PEB is characterized by mild blistering, erosions, and milia localized to the shins. The age of onset is variable, and some patients do not develop signs and symptoms until adulthood. In previous studies, nine patients with mutations in the *COL7A1* gene have been reported²⁻⁵. Herein, we report a case of late-onset PEB and new mutations in the *COL7A1* gene.

An 86-year-old Japanese male presented with a 1-month history of recurrent blisters on the shins. Several erythema, tense blisters, erosions, and scars after healing were present on his shins (Fig. 1A, B). All of his toenails were dystrophic (Fig. 1C). His fingernails, teeth, and hair were not involved. Toenail dystrophy had persisted from his childhood, and his father

also had the condition.

Blood investigations, including a complete blood picture, liver and renal functions, antinuclear antibody, anti-BP180 antibody, and immunoglobulin (Ig) patterns, reported normal results.

A skin biopsy showed a subepidermal bulla with poor inflammatory cell infiltration. The roof of the blister was intact. Mild infiltration of lymphocytes, neutrophils, and histiocytes was observed (Fig. 1D). At the epidermal side and the dermal side of the blister, direct immunofluorescence showed no deposition of IgG, IgM, IgA, and C3. Immunohistochemistry using an anti-collagen type VII monoclonal antibody revealed that staining was less intense at the basement membrane (Fig. 1E, F). Total RNA was extracted from peripheral blood, and cDNA was synthesized. Direct sequencing was performed to detect mutations in the *COL7A1* gene. We identified two novel glycine substitution mutations, namely c.5264G>T (p.Gly1755Val) and c.5345G>C (p.Gly1782Ala), in exons 59 and exon 61, respectively. Both mutations have not been previously reported (Fig. 1G).

After starting treatment with topical corticosteroid and vitamin D3 ointments, no blisters appeared. Milia occurred after lesions improved with topical benzoyl peroxide.

In the nine cases previously reported, the age of onset of blisters and erosions on the shins ranged from 1 month to 52 years. Here, we present the oldest age of onset of blisters and erosions on the shins. Seven of the nine previously reported cases involved toenail dystrophy (Fig. 1H)²⁻⁵. This case also involved toenail dystrophy that started in childhood. Toenail

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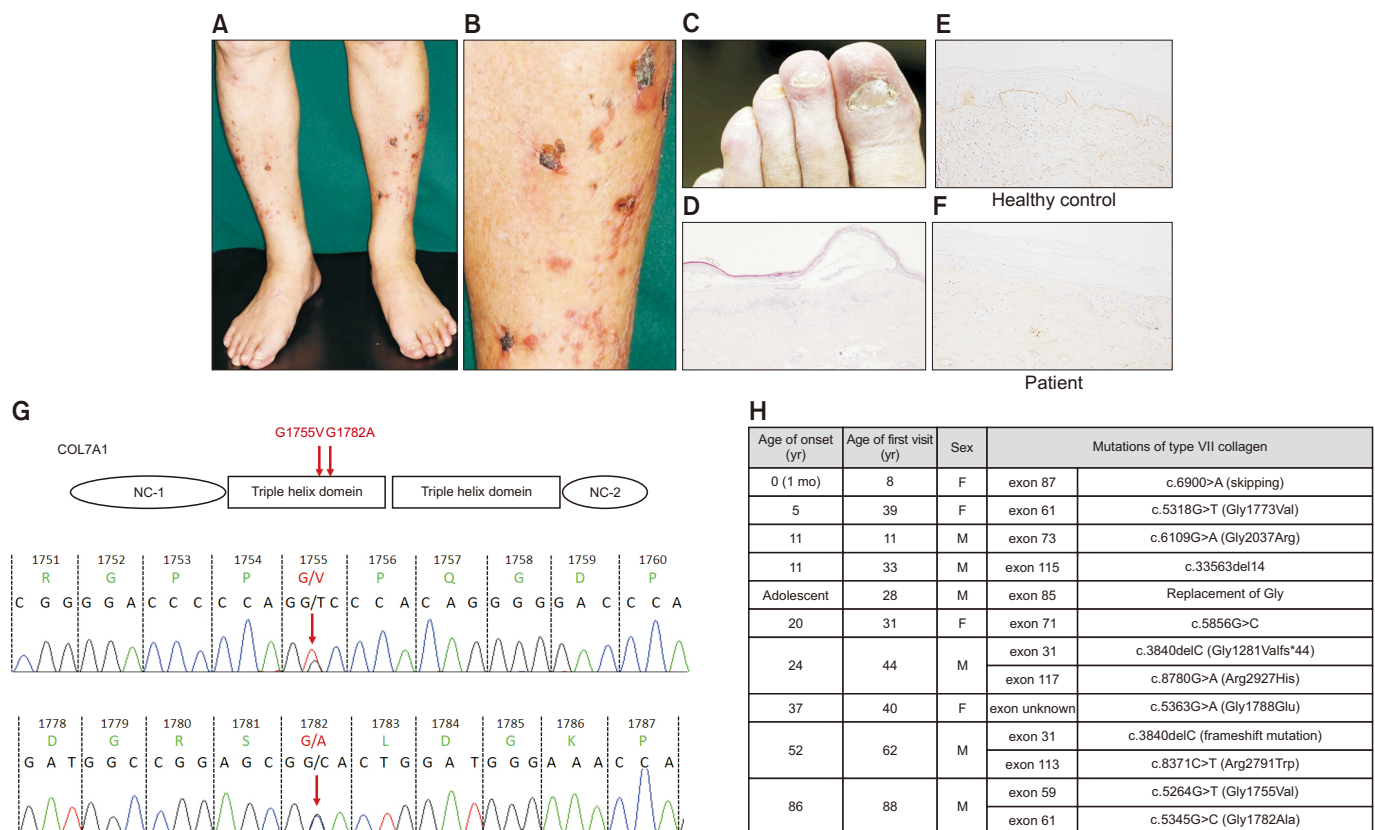


Fig. 1. Clinical features of this case. (A, B) Several erythema, tense blisters, erosions, and scars are observed on the shins. (C) All of the toenails are dystrophic. (D) Histopathology shows subepidermal bulla with poor inflammatory cell infiltration (H&E, original magnification $\times 40$). (E, F) Collagen type VII staining is less intense at the basement membrane (DAB staining, original magnification $\times 100$). (G) Sequencing identified two novel point mutations in type VII collagen (*COL7A1*). (H) Table of pretibial epidermolysis bullosa cases regarding age of onset and mutations in *COL7A1*. We received the patient's consent form about publishing all photographic materials. F: female, M: male.

dystrophy beginning in childhood may be a clue for PEB diagnosis. We report of two novel glycine substitution mutations in *COL7A1* gene, c.5264G>T (p.Gly1755Val) and c.5345G>C (p.Gly1782Ala) in exons 59 and 61, respectively, that occurred in late-onset PEB. It is possible that the both mutations are on the same father-derived allele, but have relatively low impact on the anchoring fibril formation to generate mild phenotype. Another possibility is that one mutation is the father-derived dominant mutation and another mutation might be a silent glycine substitution mutation from his mother.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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Pancreatitis, Panniculitis, and Polyarthrititis Syndrome with a Fatal Course

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Dear Editor:

Pancreatitis, panniculitis, and polyarthrititis (PPP) syndrome is a rare disease characterized by pancreatic disease, panniculitis presenting as tender erythematous nodules especially on the lower extremities, and polyarthrititis showing swelling and inflammation without evidence of infection¹. Prompt diagnosis is crucial because of its poor prognosis and high mortality with delayed treatment².

An 64-year-old male visited the emergency department with pain on both legs for five days. He had history of frequent alcohol consumption and hypertension. The laboratory examination revealed leukocytosis (28,690/ μ l) with neutrophil dominance (88.7%), elevated amylase (9,055 U/L; 28~100 U/L), lipase (2,089 U/L; 13~60 U/L), C-reactive protein (12.94 mg/dl; 0~0.5 mg/dl), creatinine (2.71 mg/dl; 0.7~1.2 mg/dl), and blood urea nitrogen (41.0 mg/dl; 6~20 mg/dl). The peripheral blood cell morphologic analysis revealed normocytic normochromic anemia and neutrophilia with left-shifted maturation. The blood test revealed no evidence of viral infections, autoimmune diseases, or hematologic malignancies. There was no fever or abdominal pain, but abdominal computed tomography showed acute pancreatitis. He was admitted to the department of internal medicine and was consulted to the dermatology department for tender erythematous subcutaneous nodules with periarticular swelling on the knees and ankles (Fig. 1). A skin biopsy of the left ankle showed lobular

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