Novel heterozygous *COL7A1* mutation in a patient with de-novo dominant dystrophic epidermolysis bullosa pruriginosa

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INTRODUCTION

Dystrophic epidermolysis bullosa (DEB) is a blistering disease linked to a mutation in the *COL7A1* gene, which encodes for type VII collagen, a major component of anchoring fibrils.[1,2] DEB is due to an autosomal dominant or autosomal recessive mutation; the former is commonly associated with a milder form of the disease than the latter.[2] The mutation can be sporadic or hereditary. The common cause of mutation in autosomal dominant DEB is often a heterozygous mutation, which results in an atypical conformation of the anchoring fibrils, thus preventing adhesion of the basement membrane to the dermis.[1-6] Herein, we report a case with a novel mutation leading to autosomal dominant DEB.

Abbreviation used:

DEB: dystrophic epidermolysis bullosa

CASE REPORT

A 47-year-old woman presented to the dermatology clinic with a history of congenital toenail dystrophy and a recurrent blistering skin eruption, which had developed in adolescence. In the past, the patient was treated with topical, intralesional, and oral corticosteroids for presumptive atopic dermatitis, lichen planus, and dermatitis herpetiformis. Her symptoms temporarily resolved with the use of oral corticosteroids. The patient denied a family history of bullous disease in her parents or siblings. On physical examination, scattered, eroded papules and vesicles were observed on the back, buttocks, and abdomen with no involvement of the eyes, mouth, or genitalia (Fig 1, *A-C*). Two punch biopsies of an intact vesicle on the lower back submitted to hematoxylin-eosin (H&E) staining and perilesional direct immunofluorescence (DIF) demonstrated subepidermal bullae with subtle dermal fibrosis and minimal perivascular inflammation with a negative DIF (Fig 2, *A*). A repeat perilesional punch biopsy for DIF of the lower abdomen was negative. Serum tissue transglutaminase antibody and indirect immunofluorescence with human salt-split skin and monkey esophagus were negative. Serum enzyme-linked immunosorbent assays for BP180 and BP230 were negative. The patient had an upper endoscopy and colonoscopy with no findings suggestive of celiac disease. A complete metabolic panel was notable for transaminitis (aspartate transaminase, 120 IU/L; alanine aminotransferase, 239 IU/L) with negative hepatitis A, B, and C serology. Twenty-four–hour urine porphyrins were within the normal limits. Both serum anti-mitochondrial antibody and smooth-muscle antibody were negative. The antinuclear antibody titer was 1:80. There was no evidence of iron overload, and the ceruloplasmin level was within the normal limits.

Subsequent genetic testing for epidermolysis bullosa using a next-generation sequencing-based panel (Prevention Genetics Epidermolysis Bullosa Panel V19.01) included covered the following genes: *COL17A1, COL7A1, DSP, DST, FERMT1, ITGA3, ITGA6, ITGB4, JUP, KRT10, KRT14, KRT5, LAMA3, LAMB3, LAMC2, PKP1, PLEC,* and *TGM5*. The result of genetic testing demonstrated a heterozygous mutation in the *COL7A1* gene, where the guanine at position 6,216 in exon 74 had been substituted with

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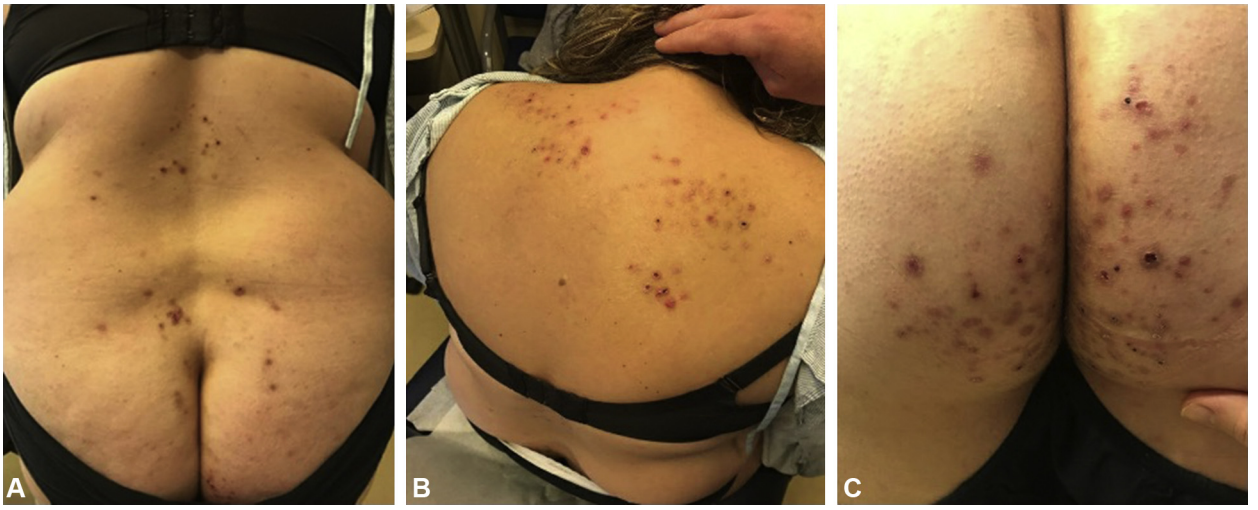

Fig 1. Clinical presentation. Scattered pink-to-red atrophic papules and eroded vesicles on the (**A**, **B**) back and (**C**) buttocks.

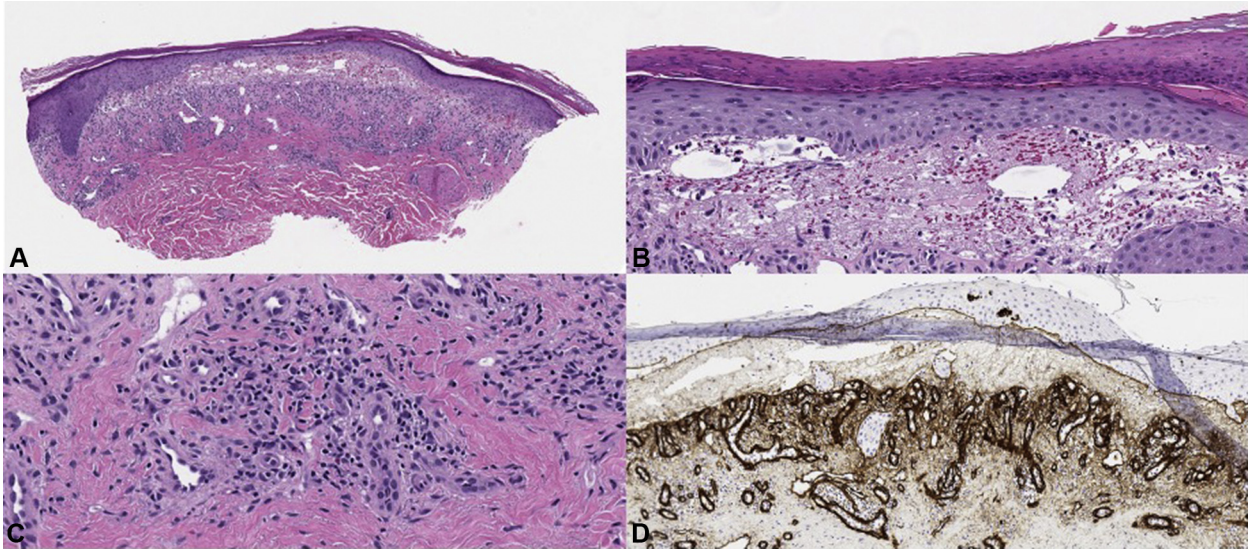

Fig 2. Histology. **A**, Acanthosis and hyperkeratosis with a subepidermal blister. **B**, hemorrhage and fibrin within the blister cavity and a perivascular inflammatory infiltrate within the dermis, composed primarily of lymphocytes and histiocytes. **C**, Subtle dermal fibrosis and vascular ectasia. **D,** Immunohistochemistry highlighting collagen IV in blister roof. (**A**, **B**, and **C**, Hematoxylin-eosin stain; original magnifications: **A**, ×10; **B**, ×20; **C**, ×40; **D**, ×20.)

an adenine (c.6216+1G>A), a sequence variant so far never reported in the literature.

DISCUSSION

Collagen VII is an important constituent of anchoring fibrils.[1] The single nucleotide polymorphism disrupts the consensus of the GT donor splice site; thus, the intron 74 is included in the protein product, albeit this has yet to be confirmed by a functional study. The patient's vesicles occur at sites of trauma, with reported involvement of the scalp, neck, back, buttocks, genitalia, and thighs with associated pruritus. The severity of her toenail dystrophy in childhood led to toenail removal, given significant discomfort while wearing shoes.

Given the patient's history, as well as the clinical and genetic findings, the patient may have a rare subtype of DEB, which is referred to as pruriginosa subtype. Since the diagnosis, the patient has been counseled regarding the disease and the risk of her children inheriting the mutation. She has also been recommended to apply non-adherent dressings to

her wounds and receive regular skin examinations due to an increased risk of developing skin cancer, particularly squamous cell carcinoma.

Conflicts of interest

None disclosed.

REFERENCES

1. Pfendner E, Lucky A. Dystrophic epidermolysis bullosa. 2006 [Updated 2018]. [Internet]. *GeneReviews®*. Seattle (WA): University of Washington, Seattle; 1993-2020. Accessed April 1, 2021. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1304/
2. Vahidnezhad H, Youssefian L, Zeinali S, et al. Dystrophic epidermolysis bullosa: COL7A1 mutation landscape in a multi-ethnic cohort of 152 extended families with high degree of customary consanguineous marriages. *J Invest Dermatol*. 2017;137(3):660-669.
3. Fine JD, Johnson LB, Weinder M, Li KP, Suchindran C. Epidermolysis bullosa and the risk of life-threatening cancers: The National EB Registry experience, 1986-2006. *J Am Acad Dermatol*. 2009;60(2):203-211.
4. McGarth JA, Schofield OM, Mayou BJ, McKee PH, Eady RA. Epidermolysis bullosa complicated by squamous cell carcinoma: report of 10 cases. *J Cutan Pathol*. 1992;19(2):116-123.
5. Montaudié J, Chiaverini C, Sbidian E, Charlesworth A, Lacour JP. Inherited epidermolysis bullosa and squamous cell carcinoma: a systematic review of 117 cases. *Orphanet J Rare Dis*. 2016;11(1):117.
6. Ryynänen J, Sollberg S, Parente MG, Chung LC, Christiano AM, Uitto J. Type VII collagen gene expression by cultured human cells and in fetal skin: Abundant mRNA and protein levels in epidermal keratinocytes. *J Clin Invest*. 1992;89(1):163-168.