Supplementary data. *Supplementary data associated with this article can be found, in the online version, at doi:10.1684/ejd.2020.3926.*
Table S1: Demographic features of study participants.
Table S2: Demographic features of study participants, grouped by hydroxychloroquine exposure.

Department of Dermatology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, and Hubei Engineering Research Center for Skin Repair and Theranostics, Wuhan, China
[a]These authors contributed equally to this work.
<2018xh0170@hust.edu.cn>
<tjhappy@126.com>

Jingjing WEN[a]
Huinan SUO[a]
Yamin ZHANG
Juan TAO

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Self-improving dominant dystrophic epidermolysis bullosa: phenotypic variability associated with *COL7A1* mutation p.Gly2037Glu

Dystrophic epidermolysis bullosa (DEB) is one of the four major types of inherited epidermolysis bullosa, the prototypic skin fragility disorder [1]. DEB is characterized by blister formation below the lamina densa of the cutaneous basement membrane zone (BMZ) and by mutations in the *COL7A1* gene, encoding type VII collagen (colVII). DEB is inherited as a dominant or recessive trait and several subtypes are distinguished based on clinical features. A peculiar subtype, self-improving DEB (previously referred to as "bullous dermolysis of the newborn"; OMIM #131705), is characterized by major improvement or complete resolution of skin fragility within the second year of life [1]. Self-improving DEB blisters are predominantly acral and heal with no or minimal scarring. Laboratory diagnostic features are granular colVII deposits within the epidermis, and specific cytoplasmic inclusions (stellate bodies) in keratinocytes [2, 3]. Self-improving DEB can be dominantly or recessively inherited [1].

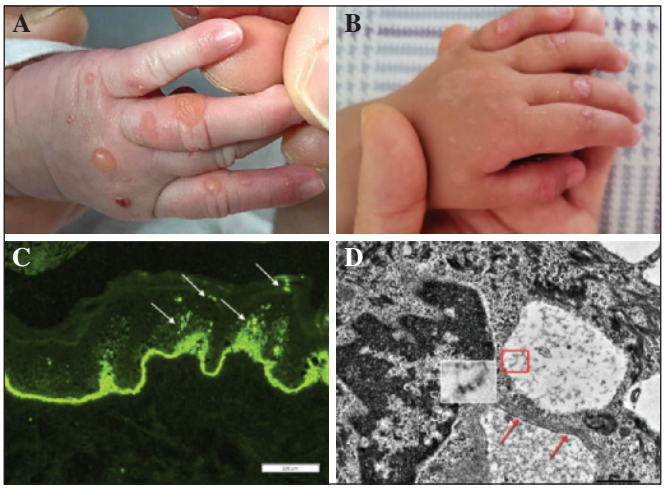

Figure 1. A) Clear blisters on the dorsum and fingers of the left hand at one month. **B**) Numerous milia and hypopigmented patches on the fingers and dorsum of the left hand at 17 months. **C**) Indirect immunofluorescence of a perilesional skin biopsy performed at three months of age showing granular labelling for type VII collagen scattered throughout the epidermis up to the horny layer (arrows), together with bright linear staining along the cutaneous basement membrane zone. **D**) Ultrastructural examination showing paranuclear inclusions bound by rough endoplasmic reticulum (arrows) within a suprabasal keratinocyte; these have a granular content with some elongated dense structures, in part, presenting a cross-banded pattern (insert). Bars: (**C**) 100 μm, (**D**) 500 nm.

We describe the clinical, immunopathological and ultrastructural features of a case of self-improving dominant DEB (SI-DDEB) due to the glycine substitution p.Gly2037Glu in colVII and discuss the phenotypic variability associated with this mutation.

A full-term female infant, the third child of healthy non-consanguineous Chinese parents, developed tense blisters on the extremities from the fifth day of life (*figure 1A*). The oral mucosa was also affected and subungual haemorrhages were present. Lesions healed with milia and minimal atrophic scarring. Muco-cutaneous fragility rapidly improved in the first months of life. Following informed consent, a skin biopsy and blood sample were taken at three months of age. Immunofluorescence mapping (IFM) showed colVII-positive granular deposits within the epidermis, and linear labelling at the BMZ (*figure 1C*). Ultrastructural examination demonstrated cleavage below the lamina densa and a few rudimentary anchoring fibrils. Rough endoplasmic reticulum (RER)-bound perinuclear inclusions were present mainly within suprabasal keratinocytes (*figure 1D*). These were partially filled with granular content and some elongated electron-dense structures, compatible with stellate bodies (*figure 1D*). Molecular testing performed in the patient and healthy parents revealed a *de novo* heterozy-

gous missense mutation, c.6110G>A (p.Gly2037Glu), in exon 73 of the *COL7A1* gene [4, 5]. In the child, who is now 18 months old, spontaneous blisters no longer develop, although milia are still present on extremities (*figure 1B*).
Our patient was diagnosed with SI-DDEB based on laboratory findings and clinical course. In self-improving DEB, colVII cytoplasmic inclusions are regularly observed by IFM and correspond to colVII retention within the RER [2, 3, 6]. Usually, staining for colVII is reduced to such an extent that it is absent at the BMZ. The epidermal inclusions resolve over time, with parallel increase in colVII expression [7, 8]. The concomitant reduction or cessation of skin fragility is thought to be secondary to normalization of colVII secretion from keratinocytes. However, persistence of intraepidermal colVII in the presence of normal BMZ labelling has been observed after resolution of skin fragility [8]. In our patient, the skin biopsy was performed at three months of age, when disease was already markedly attenuated. At that time, IFM for colVII showed granular labelling throughout the epidermis but also linear staining at the BMZ, and ultrastructural examination revealed cytoplasmic inclusions mainly localized within suprabasal keratinocytes, containing few elongated dense structures. We hypothesize that these features capture an intermediate phase in self-improving DEB pathology, corresponding to initial secretion of colVII concomitant with residual retention within keratinocytes.
The dominant colVII glycine substitution, p.Gly2037Glu, identified in our patient has been previously reported. The mutation causes colVII retention within HaCaT keratinocytes and is associated with granular labelling in the basal epidermis [4, 5]. In previous cases, the mutation p.Gly2037Glu resulted in a phenotype of intermediate DDEB; a 12-year-old female had acral and oral blisters together with albopapuloid lesions [4] and a two-year-old child continued to develop blisters on the trunk and lower extremities (*supplementary table 1*). In contrast, in our patient, oral involvement rapidly resolved in infancy and skin blisters were strictly localized to extremities and ceased by the second year of life. However, our relatively short follow-up does not allow to formally exclude that some skin fragility signs recur in the future, a limitation shared by other self-improving DEB cases reported in the literature [6]. In conclusion, comparison of our patient with the other cases carrying the missense p.Gly2037Glu mutation shows that the same mutation may result in a variable phenotype, possibly due to individual genetic backgrounds and environmental factors.

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Table S1: Clinical, immunopathological and ultrastructural findings in dystrophic epidermolysis bullosa (DEB) patients carrying the dominant missense mutation, p.Gly2037Glu, in the COL7A1 gene.

[1] Dermatology Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
[2] Institute of Dermatology, Catholic University and Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[3] Molecular Genetics Laboratory, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
[4] Pathology Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
[5] Genetics and Rare Diseases Research Division, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
<andrea.diociaiuti@opbg.net>

Andrea DIOCIAIUTI[1]
Cristina GUERRIERO[2]
Claudia CESARIO[3]
Sabrina ROSSI[4]
Roberta ROTUNNO[1]
Giovanna ZAMBRUNO[5]
May EL HACHEM[1]

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Herpes zoster following COVID-19: a report of three cases

Milan, its metropolitan area and two close cities, Bergamo and Brescia, in the region of Lombardy, have been severely affected by a dramatic outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease caused by this virus, named coronavirus disease 2019 (COVID-19), is associated with numerous, different cutaneous manifestations, including erythematous exanthems, erythematous-papulo-vesicular eruptions, urticaria, papular acrodermatitis, pseudo-chilblains and other acral ischaemic lesions [1]. Herpes zoster (HZ) is a manifestation of the reactivation of latent varicella zoster virus (VZV) infection and has been very rarely described in patients with