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Localized variant of junctional epidermolysis bullosa with R795X mutation

Stefano Bighetti,[1] Luca Bettolini,[1] Sara Rovaris,[1] Antonio Novelli,[2] Paolo Incardona,[3] Piergiacomo Calzavara-Pinton,[1] Simone Caravello,[4] Vincenzo Maione[1]

[1]Dermatology Department, University of Brescia, ASST Spedali Civili di Brescia; [2]Laboratory of Medical Genetics, Translational Cytogenomics Research Unit, Bambino Gesù Children's Hospital, Rome; [3]Pathology Department, University of Brescia, ASST Spedali Civili di Brescia; [4]Dermatology Department, Ospedale di Circolo e Fondazione Macchi, ASST Sette Laghi, Varese, Italy

Correspondence: Stefano Bighetti, Dermatology Department, University of Brescia, ASST Spedali Civili di Brescia, Piazzale Spedali Civili, 1, 25123 Brescia, Italy.
Tel.: + 39 0303995301
E-mail: s.bighetti@unibs.it

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Abstract

Epidermolysis bullosa (EB) refers to a group of inherited disorders characterized by skin and mucous membrane fragility. This report presents the case of a 61-year-old Italian male with a localized variant of junctional epidermolysis bullosa (JEB) linked to the R795X mutation in the *COL17A1* gene. The patient presented with bullous lesions, erosions, scars, and pigmentary changes on the pretibial areas and dystrophic nails. Genetic analysis confirmed the presence of the *COL17A1* variant p.Arg795Ter (R795X) mutation, establishing a rare, localized variant of JEB. This case underscores the criticality of early and accurate diagnosis in the management of rare genetic disorders, as misdiagnosis can lead to ineffective treatments.

Introduction

Epidermolysis bullosa (EB) encompasses a group of inherited disorders characterized by the fragility of skin and mucous membranes. Among these, the localized variant of junctional epidermolysis bullosa (JEB) is notably rare and varies significantly in severity depending on the genetic mutation involved.[1,2]

Case Report

A 61-year-old Italian male presented with bullous lesions, erosions, scars, and pigmentary changes on the pretibial areas of both legs, accompanied by dystrophic nails on his hands and feet (Figure 1a-c). The patient reported the onset of these lesions after childhood, with subsequent appearance after traumas. The parents were not consanguineous, and the family's individuals had no similar manifestations. In the following years, dental enamel had no alterations besides the locations affected by trauma. Androgenetic alopecia has developed over the years. The patient had been followed in other centers for acquired epidermolysis bullosa without any clinical benefit from systemic or local immunosuppressive treatments.

To exclude an immunologic disease, a serological assessment for bullous disease had been performed, yielding negative results. Histological examination revealed a dermo-epidermal detachment, with a positive collagen IV stain at the base of the bulla, indicating a deeper level of skin involvement (Figure 2a-c). A detailed genetic analysis identified a mutation in the *COL17A1* gene, specifically *COL17A1*, variant p.Arg795Ter, known as nonsense mutation R795X (Figure 2c), confirming the diagnosis of JEB, a localized variant.

Discussion

Other authors reported the same mutation.[3,4] In a study on 6 patients, a limited variant of EB was reported due to the residual presence of the product of the *COL17A1* gene.[3] The presence of enamel alterations or alopecia varied significantly.[3,4] This data is interesting; however, it may not be solely attributable to the identified mutation and could be related to other unknown factors.

Four out of the 6 examined people had direct familial connections with each other.[3] Our case, along with the others that have been described, suggests an Italian founder variant as the primary cause for patients with a similar condition.

Due to its rarity and diagnostic delay, as in our case, this condition can represent a diagnostic and therapeutic challenge to clinicians, often misinterpreted and resulting in ineffective treatments. Furthermore, another significant problem is access to facilities that perform such diagnosis through next-generation procedures. Similar symptoms in family members could aid in diagnosis. However, it is crucial to rule out other similar conditions like EB simplex, localized/acral, or pruriginosa variant of dystrophic EB. Other diseases, such as EB acquisita, lichen planus, porphyria cutanea tarda, and pretibial bullous pemphigoid, must be considered in the absence of family history.

Conclusions

In this report, we describe a novel case of a localized variant of JEB associated with the R795X mutation in the *COL17A1* gene, which is predominantly observed in Italian populations. This case highlights the importance of early and precise diagnosis in managing such rare genetic disorders. Early identification of JEB can significantly enhance therapeutic interventions and potentially improve the quality of life for affected individuals.

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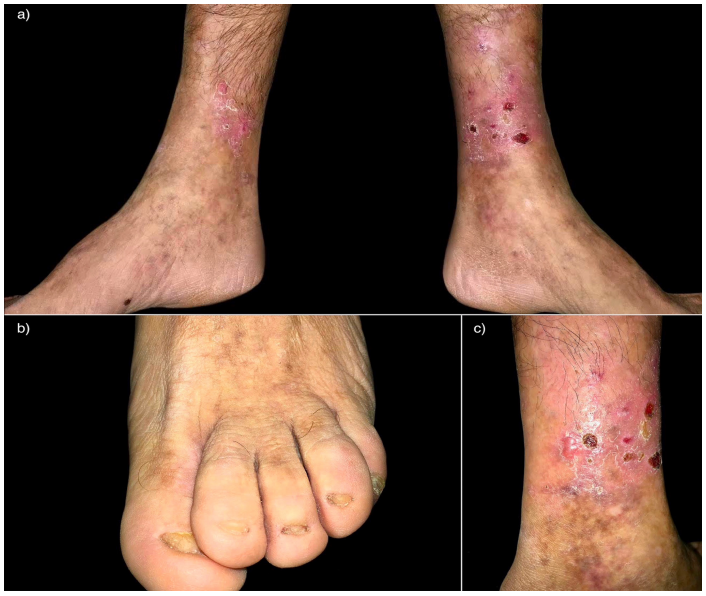

Figure 1. a) Pretibial bullous lesions on the legs, showing blisters and erosive areas; **b, c)** detailed view of scars, bullous blisters, pigmentary alterations in the left pretibial region, and nail dystrophy of the left foot.

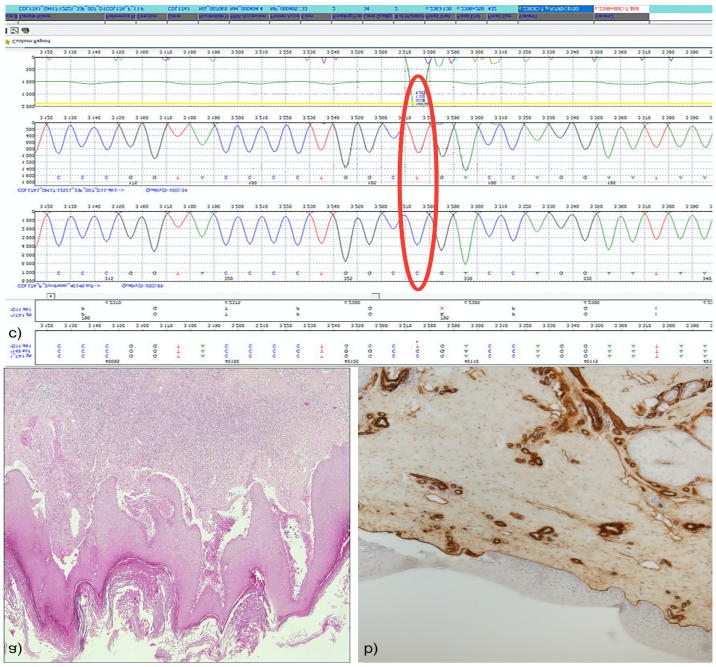

Figure 2. a) Histopathology displaying subepidermal blister with granulocytic infiltrate (H&E, original magnification ×40); **b)** immunohistochemistry demonstrating positive staining for collagen IV deposits at the base of the blister (original magnification ×200); **c)** genetic analysis report confirming a mutation in the *COL17A1* gene (p.Arg795Ter).