Novel Variant c.7795-1G>A of COL7A1 Gene in a 12-month-old Female Child with Recessive Dystrophic Epidermolysis Bullosa

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Title: Novel Variant c.7795-1G>A of COL7A1 Gene in a 12-month-old Female Child with Recessive Dystrophic Epidermolysis Bullosa**Type of article:** Case Report**Authors**: Francesca CAROPPO[1,2], Fortunato CASSALIA[1], Anna BELLONI FORTINA[1,2]**Affiliations**:

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Corresponding Author: Francesca Caroppo, MD Unit of Dermatology, Department of Medicine University of Padova, Italy Via Vincenzo Gallucci 4, 35121, Padova, Italy e-mail:*francesca.caroppo@outlook.it***Keywords**: Dystrophic Epidermolysis Bullosa, DEB, Epidermolysis Bullosa, EB, Congenital diseases, genetic diseases, mutation, rare skin diseases**Word count**: 664**Tables**: None**Figure**: 2**References**: 9**Patient Consent** Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.**Conflicts of interest**: None**Acknowledgements**: None**Author Contributions**: All authors contributed to designing and conducting the work, drafting, and revising the manuscript and approved the final version for submission.

ABSTRACT:

Dystrophic Epidermolysis Bullosa is a subtype of Epidermolysis Bullosa. The group of Epidermolysis Bullosa diseases includes several rare genetic disorders characterized by skin fragility and blistering and mutations in several genes, such as KRT5, KRT14, PLEC, TGM5, COL17A1, ITGB4, COL7A1. Recessive Dystrophic Epidermolysis Bullosa is the most severe form, and it is a very rare disease, with an incidence of approximately 1/51,000 live births. We report a case of novel variant c.7795-1G>A of COL7A1 Gene in a 12-month-old female child with Recessive Dystrophic Epidermolysis Bullosa, reporting clinical characteristics and signs**.**

BACKGROUND: We report a case of a novel c.7795-1G>A variant of the COL7A1 gene in a 12-month-old female child with recessive dystrophic epidermolysis bullosa (RDEB) syndrome. Dystrophic Epidermolysis Bullosa (DEB)[1] is a subtype of Epidermolysis Bullosa (EB)[2]. EB refers to a group of rare genetic skin diseases characterized by skin fragility and blistering. According to data from the National Epidermolysis Bullosa Registry, the estimated prevalence of epidermolysis bullosa in the United States is approximately 11.1 cases per one million live births. The incidence is reported to be approximately 1 in every 51,000 live births[3]. There are different classifications and subtypes of epidermolysis bullosa, each with different clinical features and mutations. The main genes associated with EB subtypes are KRT5, KRT14, PLEC, TGM5, LAMA3, LAMB3, LAMC2, COL17A1, ITGB4, COL7A1 and FERMT1[4]. The patients who suffer from it have extremely fragile skin that blisters and forms open sores in response to minor trauma or friction. The severity of symptoms can vary widely, ranging from mild blisters to life-threatening complications[5].

Recessive DEB (RDEB) is the most severe form, and it is a very rare disease[6]. The incidence of Recessive Dystrophic Epidermolysis Bullosa (RDEB) is reported ranging from 0.2 to 6.65 per million births[7]. RDEB follows an autosomal recessive inheritance pattern, which means that an affected individual inherits two copies of the mutated gene, one from each parent who usually carries the condition. Both males and females can be affected. RDEB is caused by mutations in the COL7A1 gene, which codes for type VII collagen. Mutations in the COL7A1 gene result in a deficiency or absence of functional type VII collagen, which leads to the characteristic blistering and fragile skin in RDEB. The main clinical feature of RDEB is the formation of blisters and erosions on the skin and mucous membranes. These blisters can occur anywhere on the body and in addition to the skin, the oral cavity and gastrointestinal tract can be involved. Blisters are often painful and slow to heal, causing scarring and the development of contractures, which can limit joint mobility. Other complications may include dental abnormalities, nail dystrophy and corneal erosions. Diagnosis of EBD usually involves a combination of clinical examination, evaluation of family history, skin biopsy and genetic testing. The clinical evaluation includes a thorough examination of the skin and mucous membranes to identify characteristic features such as blisters, scars, and nail dystrophy. A family history of blistering disorders may also suggest a potential genetic cause.**CASE REPORT:**We report a case of a 12-month-old female child referred to our Pediatric Dermatology Regional Center for the recurrent onset of blisters and large boils localized mainly on the upper and lower limbs (Figure 1 and Figure 2). No similar cases in the family were reported in her medical history. Suspecting a genetic bullous disease, such as EB, a skin biopsy and genetic testing were performed. Skin biopsy and genetic testing reported the diagnosis of RDEB. Genetic analysis revealed a novel mutation, the c.7795-1G>A variant of the COL7A1 gene, to date, the c.7795-1G>A variant was never described before in patients with RDEB syndrome[6] and is absent in the general population (gnomAD). The patient is currently undergoing regular dermatological follow-up where she is periodically re-evaluated and medicated if necessary. The chronic nature of the condition, pain and physical limitations can lead to emotional distress, social isolation, and depression.**CONCLUSION:**The management of DEB focuses on symptom reduction, wound care, pain management, nutritional support, and infection prevention. A multidisciplinary approach involving dermatologists, geneticists, wound care specialists, nutritionists and other health professionals is essential. Specialized dressings and creams are used to protect fragile skin and promote healing. nutritional support ensures adequate nutrition and measures are taken to prevent infection. At present, there is no cure for EBD, but future treatment prospects for DEB are promising, including gene therapy or protein replacement therapy[8,9]. In all patients with suspected EB, clinicians should recommend genetic examination to achieve the correct diagnosis and to identify the specific syndrome among the heterogeneous group of EB.**Figure 1Figure 2REFERENCES:**

1. Yadav, R. S., Jayswal, A., Shrestha, S. et al. (2018). Dystrophic Epidermolysis Bullosa. *JNMA; journal of the Nepal Medical Association* , *56* (213), 879–882.
2. Bardhan, A., Bruckner-Tuderman, L., Chapple, I. L. C et al (2020). Epidermolysis bullosa. *Nature reviews. Disease primers* , *6* (1), 78.
3. Mariath, L. M., Kiszewski, A. E., Frantz, J. A., Siebert, M., Matte, U., & Schuler-Faccini, L. (2021). Gene panel for the diagnosis of epidermolysis bullosa: proposal for a viable and efficient approach. *Anais brasileiros de dermatologia* , *96* (2), 155–162.
4. Fine J. D. (2016). Epidemiology of Inherited Epidermolysis Bullosa Based on Incidence and Prevalence Estimates From the National Epidermolysis Bullosa Registry. *JAMA dermatology* , *152* (11), 1231–1238.
5. Bruckner-Tuderman L. (2010). Dystrophic epidermolysis bullosa: pathogenesis and clinical features. *Dermatologic clinics* , *28* (1), 107–114.
6. Petrof, G., Papanikolaou, M., Martinez, A. E., Mellerio, J. E., McGrath, J. A., Bardhan, A., Harper, N., Heagerty, A., Ogboli, M., Chiswell, C., & Moss, C. (2022). The epidemiology of epidermolysis bullosa in England and Wales: data from the national epidermolysis bullosa database. *The British journal of dermatology* , *186* (5), 843–848.
7. Eichstadt, S., Tang, J. Y., Solis, D. C. et al. (2019). From Clinical Phenotype to Genotypic Modelling: Incidence and Prevalence of Recessive Dystrophic Epidermolysis Bullosa (RDEB). *Clinical, cosmetic and investigational dermatology* , *12* , 933–942.

8. Tang, J. Y., Marinkovich, M. P., Lucas, E., Gorell, E., Chiou, A., Lu, Y., Gillon, J., Patel, D., & Rudin, D. (2021). A systematic literature review of the disease burden in patients with recessive dystrophic epidermolysis bullosa. *Orphanet journal of rare diseases* , *16* (1), 175.
9. Hon, K. L., Chu, S., & Leung, A. K. C. (2022). Epidermolysis Bullosa: Pediatric Perspectives. *Current pediatric reviews* , *18* (3), 182–190.