A Case Report of an Infant with Autosomal Recessive Dystrophic Epidermolysis Bullosa: COL7A1 Gene Mutations at C2005T and G7922A

INTRODUCTION

A male infant was born by spontaneous delivery on February 7, 2020, with a gestational age of 40 weeks and a birth weight of 4.1 kg. After birth, the infant presented with appearance of skin loss on the bilateral lower limbs, feet, left wrist, face, and lips. Large areas of skin defects, erosion, and exudation were noted on the extensor side of the bilateral lower limbs and feet, and some skin loss with a small amount of exudation was observed on the left wrist, face, and lips, which was accompanied by dorsal hyperextension of the right foot and oral mucosal ulceration (Figure 1).

Because the parents refused invasive examinations (skin biopsy, i.e., transmission electron microscopy and immunofluorescence examination (1)) and the child was hospitalized in a period during which the strictest prevention and control measures for novel coronavirus pneumonia were enacted, the hospital canceled the invasive examinations; therefore, skin biopsy was not performed.

The infant's parents were healthy and nonconsanguineous. They reported that neither of them had skin defects at birth. They also denied nail dystrophy or complete absence of the nail and a history of recurrent oral herpes or ulcers, and no other family members had such symptoms. The mother had multiple scheduled prenatal examinations during the pregnancy, and the sick infant delivered via natural birth was her first child. She did not have a history of previous miscarriage and underwent a thyroid function test and ultrasound B-mode examinations, which did not show obvious abnormalities. Ultrasound B-mode examination in the second trimester suggested bilateral renal sinus separation and excessive dorsiflexion of both feet of the fetus. A nuchal translucency (NT) scan, a noninvasive prenatal DNA test, and an oral glucose tolerance test (OGTT) showed no significant abnormalities.

Ultrasound B-mode findings indicated that the infant had congenital dysplasia, suggesting that he may have a genetic disease. In a subsequent genetic test, compound heterozygous variations of c.C2005T (the nucleotide at position 2005 in the coding region was mutated from C to T) and c.G7922A (the nucleotide at position 7922 in the coding region was mutated from G to A) were detected in the child's collagen type VII alpha 1 chain (*COL7A1*) gene, and the mutations were from the child's parents' genes (Table 1). The *COL7A1* gene is a well-established causative gene for autosomal recessive dystrophic epidermolysis bullosa. Based on these results, *COL7A1* gene mutations may have been the cause of the disease in the child; thus, the child was definitively diagnosed with autosomal recessive dystrophic epidermolysis bullosa.

CASE REPORT

After admission, the child received aggressive nutritional support. For treatment, cefmetazole was given for anti-infection, aseptic dressings were applied on the body surface with skin defects, iodophor disinfection was carried out, recombinant human epidermal growth factor gel and chlortetracycline eye ointment were applied externally, petrolatum was used to cover the skin defects, sterile gauze was used to wrap the lesions, and the dressings were changed

Table 1. Subsequent genetic test results

Gene	Exon	Nucleotide change	Amino acid change	Genotype	Source of variation
COL7A1	15	C.C2005T	p.R669X	Heterozygous	Mother
COL7A1	106	C.G7922A	p.G2641E	Heterozygous	Father

Acta Dermatovenerol Croat
2021;29(3):164-166

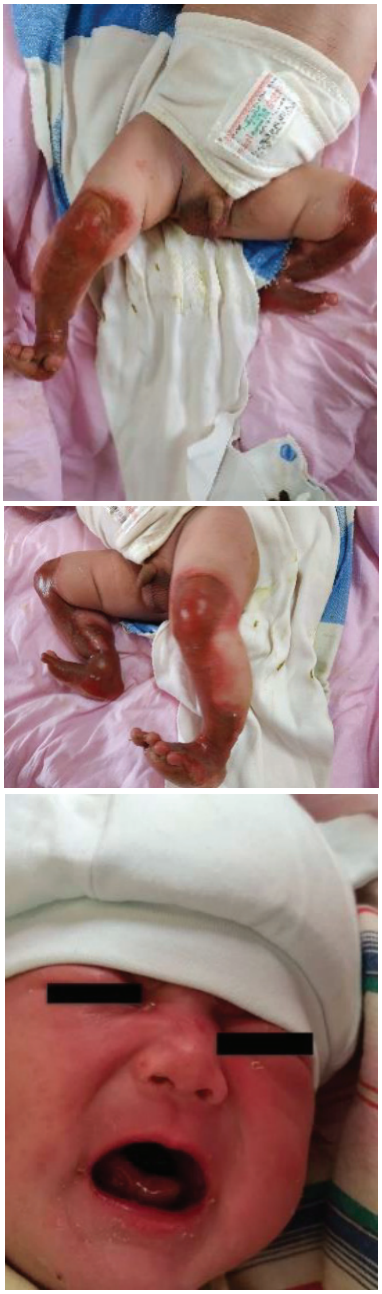

Figure 1. After birth, the patient had hyperextension of the right lower limb, skin damage with a small amount of exudation on the bilateral lower limbs, and oral mucosal damage.

daily or every other day. The wounds were kept dry, prolonged compression was avoided, and secondary bacterial infection was actively prevented and treated symptomatically as necessary. At discharge, the child's vital signs were stable, some epidermal defects were visible on the extensor side of the bilateral lower limbs, feet, and left wrist as well as on the face and lips with reduced exudation, and fresh epidermal coverage was observed (Figure 2).

DISCUSSION

Congenital epidermolysis bullosa must be differentiated from other diseases such as staphylococcal scalded skin syndrome (SSSS), neonatal impetigo, congenital bullous ichthyosiform erythroderma, congenital syphilis, and neonatal herpes simplex. Among these diseases, SSSS is a severe acute generalized exfoliative pustulosis that occurs in neonates and is characterized by the development of flaccid scalded bullae and large areas of skin exfoliation due to generalized erythema throughout the body (2). SSSS mostly occurs with sudden onset 1-5 weeks after birth. Initially, erythema occurs around the mouth or eyelids and then rapidly spreads to the trunk and proximal extremities or even to the entire body, which usually heals after 7-14 days. SSSS is a blistering and desquamative skin disease caused by the exfoliative toxins of staphylococcus aureus. It is a toxin-mediated condition (3), so the blisters and erosions are usually sterile. In this case, the child had three consecutive negative common bacterial culture test results during hospitalization, enabling exclusion of SSSS. Neonatal impetigo, congenital bullous ichthyosiform erythroderma, congenital syphilis, and neonatal herpes simplex all have associated specific pathogenic infections or are accompanied by other typical clinical manifestations,

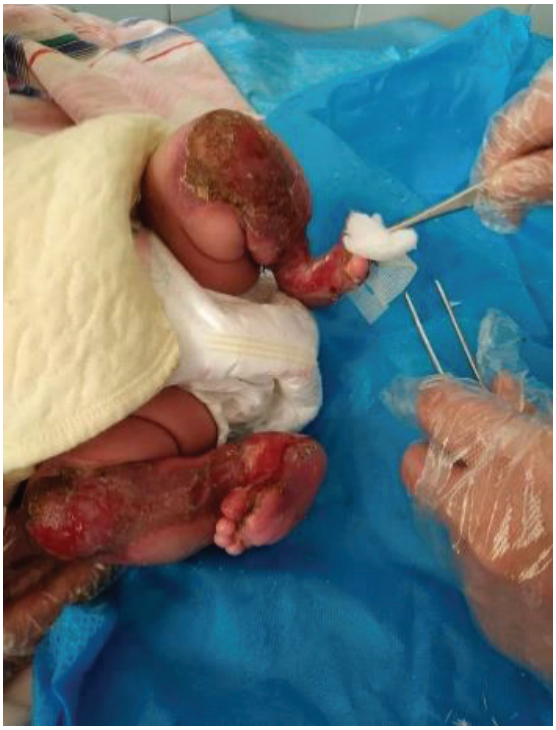

Figure 2. When the child was discharged one week after birth, partial epidermal defects were visible on the extensor side of the bilateral lower limbs and feet, but the amount of exudation had decreased, and fresh epidermal coverage was observed.

but in this case the child had no obvious infection manifestations except for specific skin lesions, allowing exclusion of the above diseases.

Autosomal recessive dystrophic epidermolysis bullosa was first reported in 1966 by Bart et al. (4) and was confirmed to be caused by mutations in *COL7A1* by Chrlstiano et al. in 1996 (5,6). The disease takes the form of dystrophic epidermolysis bullosa (7), and patients have congenital local skin defects, mucocutaneous blisters, and nail abnormalities (8). This disease is mostly sporadic, but familial predisposition has also been reported.

In this case, the defective skin had begun to heal without complications at discharge. Based on our experience, nutritional support and infection prevention should be prioritized. The child was isolated from other patients during hospitalization, his blankets and clothes were autoclaved, and strict aseptic practices were carried out (9). Dressings were changed as needed by a designated person, and secretions were managed in a timely manner. The wounds were protected, and the child was carefully monitored and supported to improve his immunity and protect the function of his organs.

This case once again demonstrates the crucial importance of prenatal diagnosis, genetic counseling, and genetic testing, which are effective measures to prevent the birth of children with genetic diseases, and early intervention can minimize the pain of the family.

References:

1. Fine JD, Eady RA, Bauer EA, Bauer JW, Bruckner-Tuderman L, Heagerty A, *et al*. The classification of inherited epidermolysis bullosa (EB): report of the third ınternational consensus meeting on diagnosis and classification of EB. J Am Acad Dermatol. 2008;58:931-50.
2. Mishra AK, Yadav P, Mishra A. A Systemic Review on Staphylococcal Scalded Skin Syndrome (SSSS): A Rare and Critical Disease of Neonates. Open Microbiol J. 2016;10:150-9.
3. Yamasaki O, Yamaguchi T, Sugai M, Chapuis-Cellier C, Arnaud F, Vandenesch F, et al. Clinical manifestations of staphylococcal scalded-skin syndrome depend on serotypes of exfoliative toxins. J Clin Microbiol. 2005;43:1890-3.
4. Bart BJ, Gorlin RJ, Anderson VE, Lynch FW. Congenital localized absence of skin and associated abnormalities resembling epidermolysis bullosa: A new syndrome. Arch Dermatol. 1966;93:296-303.
5. Christiano AM, Bart BJ, Epstein EH, Uitto J. Genetic Basis of Bart's Syndrome: A glycine Substitution Mutation in the Type VII Collagen Gene. Journal of Investigative Dermatology.1996;106:,1340-2.
6. Zelickson B, Matsumura K, Kist D, Epstein EH, Bart BJ. Bart's Syndrome: Ultrastructure and Genetic Linkage. Arch Dermatol. 1995;131:663-8.
7. Fine JD, Eady RA, Bauer EA, Briggaman RA, Bruckner-Tuderman L, Christiano A, et al. Revised classification system for inherited epidermolysis bullosa. Journal of the American Academy of Dermatology. 2014;42:1051-66.
8. Fine JD. Epidemiology of Inherited Epidermolysis Bullosa Based on Incidence and Prevalence Estimates From the National Epidermolysis Bullosa Registry. JAMA Dermatology. 2016;152:1231.
9. Goldschneider KR, Good J, Harrop E, Liossi C, Lynch-Jordan A, Martinez AE, et al. Pain care for patients with epidermolysis bullosa: best care practice guidelines. BMC Med. 2014;12:178.

Jing Liu, Lin Wang

Huaibei People's Hospital (The Huaibei Clinical College of Xuzhou Medical University), Huaibei City, China

Corresponding author:

Jing Liu, MD

Huaibei People's Hospital (The Huaibei Clinical College of Xuzhou Medical University), Huaibei City, China

judialiu@outlook.com

Received: November 5, 2020

Accepted: September 1, 2021