Single Case

Dominance of Methicillin-Resistant *Staphylococcus aureus* in a Japanese Infant with Recessive Dystrophic Epidermolysis Bullosa

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Keywords

Microbiome · Recessive dystrophic epidermolysis bullosa · *Staphylococcus aureus* · MRSA · Atopic dermatitis

Abstract

A male infant had the very fragile skin and easily formed bullas by rubbing and scratching from his birth. He was diagnosed with severe recessive dystrophic epidermolysis bullosa (RDEB) due to the lack of type VII collagen by performing an immunofluorescence mapping method from a skin biopsy specimen of the patient's bulla. We analyzed the skin microbiome using next-generation sequencer. The species from the patient's skin revealed the dominance of *Staphylococcus aureus* (*S. aureus*) similar to the reports from Austria and Chile severe RDEB patients, and these results are same as the pattern isolated from the skin of atopic dermatitis (AD) patients with flares. The interaction of microbiome and skin microenvironment may be similar between RDEB and AD worldwide.

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Introduction

The mutation of *COL7A1* gene encoding type VII collagen results in dystrophic epidermolysis bullosa (DEB). Severe recessive DEB (RDEB) is the classic form, and RDEB infants are typically born with widespread bulla and erosion and often caused by rubbing and scratching

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Fig. 1. **a** RDEB infant is stripping his skin on the whole body, especially rubbed lesion. **b** RDEB infant's toes are fused by recurrence of inflammation. **c** The microbiome in top 10 data in the RDEB patient at 3 years shows the most occupied species to be *S. aureus*, same as severe AD. RDEB, recessive dystrophic epidermolysis bullosa; AD, atopic dermatitis.

during birth. Severe atopic dermatitis (AD) patients also show scratching behavior causing erosion. In AD, the increasing dominant species of skin bacteria is *Staphylococcus aureus* (*S. aureus*), accompanied by a decrease in filaggrin and natural moisturizing factor. RDEB and AD show similarity in skin condition, and previous studies reported *S. aureus* as dominant species. The growth of *S. aureus* is known as a cause of exacerbation in AD patients; therefore, we considered that it is important to understand the distribution of superficial skin bacteria in patients with RDEB in Japan as a possible link to skin exacerbation. We here report a case of severe Japanese RDEB infant showing *S. aureus* predominance in skin microbiome analysis without erosion and bulla.

Case Report

A male infant delivered naturally presented with bulla and erosion on the whole body including the mouth at the time of his birth (Fig. 1a). The infant had nonconsanguineous parents with no family history of DEB. The bulla and erosion were managed using a soft fitting gauze with petrolatum ointment; he sometimes received intravenous antibiotics for frequent remission and exacerbation of the infection. His toes fused gradually owing to repeated inflammatory changes (Fig. 1b). We performed skin biopsy of the bulla, and immunofluorescence mapping revealed an absence of type VII collagen. Based on these findings, we made a diagnosis of severe RDEB. The mutation in the *COL7A1* gene was not checked by the hope of parents. The infant grew to the age of two with repeated occurrence of bulla, erosion, and scars accompanied by secondary skin infection. Methicillin-resistant *Staphylococcus aureus* was always detected at any skin whether erosion or not since 37 days after birth. We analyzed his skin microbiome using a wet swab from intact skin of the arm without bulla and erosion after obtaining informed consent from his parents. We performed 16SrRNA analysis using the

next-generation sequencer and identified 371 species in the investigated 2,200 species. *S. aureus* comprised approximately 33% of all bacterial species (Fig. 1c).

Discussion

RDEB is an incurable disease caused by mutation in the gene encoding type VII collagen [1], leading to repeated development of bulla and erosion due to the weak connection of the epidermis. Skin microbiome plays an important role in this condition and in the protection from pathogens. We analyzed the skin microbiome of a patient with recessive RDEB using the next-generation sequencer. The disrupted microbiome diversity with an increase in the *S. aureus* population has been reported in severe AD [2], and the dominant species were similar to those in our patient. The epidermis is damaged by the toxins including toxic shock syndrome toxin-1, staphylococcal enterotoxins AE, exfoliative toxins, and leukocidin derived from *S. aureus*, and apoptosis of keratinocytes accelerated by staphylococcal α -toxin has been found to induce profound keratinocyte cytotoxicity [3]. The microbiome of RDEB patients revealed an abundance of *Staphylococcus* species, regardless of the presence of wound, in studies conducted in Austria, the Netherlands, and Chile [4, 5].

Staphylococcus species were more detected in Austria than in Chile, regardless of the area in the body and the presence of wound. To the best of our knowledge, this is the first report in Asia, and *S. aureus* may occupy a large part in Japan. The interaction of microbiome and skin microenvironment may be similar between RDEB and AD worldwide because of the skin erosion or wound. The current research may suggest the importance of amelioration of skin condition for suppression of the increased *S. aureus* in patients with RDEB. Further investigation will be required for the mechanism and significance in the increase of *S. aureus* in RDEB patients.

Statement of Ethics

The research was conducted in accordance with the Declaration of Helsinki. The parents of the patient provided written informed consent to publish this case report, including publication of images. The paper is exempt from ethical committee approval because of the single case study.

Conflict of Interest Statement

The authors have declared that no competing interests exist.

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Author Contributions

Hiroyuki Goto and Makoto Kondo treated the patient. Makoto Kondo, koji Habe, and Keiichi Yamanaka wrote the manuscript. Shota Takashima and Ken Natsuga investigated the presence of type VII collagen. Makoto Kondo investigated microbiome of patient's skin.

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