Improvement in Quality of Life of a Pediatric Patient with Inherited Dystrophic Epidermolysis Bullosa Following Oral Lesions Treatment

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Abstract

Inherited Dystrophic Epidermolysis Bullous (DEB) is a rare disease, a subtype of Epidermolysis Bullous (EB) due to mutations in collagen VII, COL7A1. The clinical features of DEB were mucocutaneous blisters, hemorrhagic bullous, and secondary erosions due to minor mechanical trauma. Oral manifestations of DEB can affect the patient's Quality of Life (QoL). The objective of this case report is to describe the oral manifestation of DEB and its management to improve the QoL in a pediatric patient. A 12-year-old girl was referred to Oral Medicine Clinic with a chief complaint of pain throughout the oral mucosa. Based on the OHIP-14 assessment, the patient's QoL was categorized as poor with a score of 46. Extraoral examination revealed clear fluid-filled hemorrhagic bullous lesions and multiple erosive lesions over mostvof the body. Intraoral examination revealed hemorrhagic bullae on the left side of the buccal mucosa and erosive lesions on the mucobuccal folds. Hyperkeratotic lesions were found on the dorsum of the tongue that could not be scraped off. Diagnosis of DEB was established based on histopathology from the left-thigh skin which showed acantholysis with blister formation in the subepidermal layer. The patient was given systemic and topical corticosteroids, antiseptic mouthwash, and multivitamins. Oral lesions were improved after 5 weeks of treatment. Improvement of oral mucosal lesions appeared to be a particularly successful management intervention in improving the QoL for a pediatric patient with DEB.

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Introduction

Inherited Epidermolysis Bullosa (EB) is a rare genetic disorder that clinically belongs to heterogeneous genodermatosis and is characterized by fragility of the skin epithelial tissue and mucous membranes and the formation of mucocutaneous blisters or secondary erosions as well as ulceration resulting from minimal mechanical trauma (*mechanobullous dermatoses*).[1,2,3,4,5] Terminology of Epidermolysis Bullosa (EB) was first proposed by Korbner in 1886.[6] However, the first medically reported case of EB was in 1871 by Ferdinand von Hebra.[7]

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Epidemiological data and the prevalence of EB vary greatly for each country. Based on the data from National Epidermolysis Bullosa Registry (NEBR), the incidence of EB in the USA involved 3,271 patients between 1986 and 2002. In Indonesia, the incidence of EB was not yet available. However, in 2021 the Indonesian DEBRA Foundation collected data on EB and found that there were 62 patients with EB in Indonesia (unpublished data).[8,9]

Variations in the pathophysiology of EB depend on the specific defect in epithelial/subepithelial connective tissue, with varying degrees of blistering severity, an increased risk of the defect leading to the formation of potentially debilitating scar tissue, and premature death.8 However, no literature proves that EB had a predilection based on gender, race, or specific geographic location. 9 Several studies concluded that clinical manifestations of EB could also be found in the eyes, oral mucosa, teeth, esophagus, intestinal tract, genitourinary and musculoskeletal

systems.[1,2,10,11]

In general, EB had a significant influence on many aspects of the patient's and family's daily life including the patient's Quality of Life (QoL).[12] Based on the complexity of DEB, collaboration from all relevant parties was needed in a comprehensive set of management thus the efforts to cure DEB could be carried out properly and the patient's QoL could be improved. This case report aimed to describe the findings of oral manifestations accompanied by the comprehensive management provided to improve the QoL of a pediatric patient with DEB.

Case Report

A 12-year-old girl came to the Oral Medicine Clinic, RSUP. Dr. Hasan Sadikin with a chief complaint of pain in the entire oral mucosa which often bleeds, causing the patient to have difficulty swallowing. In addition to the oral cavity, lesions were also found almost all over the body. The history shows that the lesions appeared when she was born (12 years ago) but the patient's family ignored her condition.

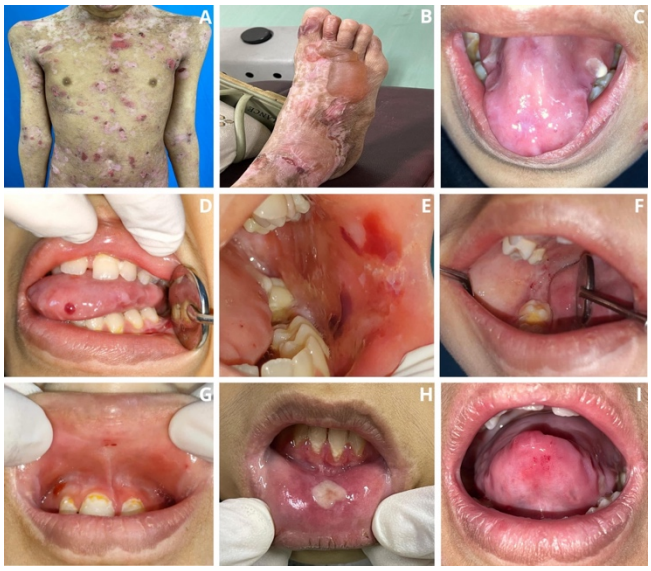

Figure 1. Oral manifestations in a 12-year-old-girl with Inherited Dystrophic Epidemolisis Bullosa (DEB). (A & B). Blood-filled blisters over most of the body were accompanied by fluid-filled bullae with erosive lesions and hemorrhagic found on the leg. (C & D). The anterior right and left dorsum of the tongue revealed superficial ulcerated lesions with a white, irregular, and hyperkeratotic layer that could not be scraped off. (E & F). Erosive, multiple, irregular red lesions, rupture of blood vessels, and well-defined borders revealed on the buccal mucosa extending to the mucobuccal fold area. (G.) On the upper labial mucosa revealed multiple erythematous macules with ruptured blood vessels in the anterior gingiva. (H). On the lower labial mucosa, there was a shallow white ulcer with clear boundaries. (I). Erythematous, multiple, shallow macules measuring < 5-7 mm on the ventral tongue.

Extraoral examination (Figure 1) revealed the presence of fluid and blood-filled blisters over most of the body, multiple confluent erosive lesions of irregular shape 2x1 cm in size, with erythematous macules and hemorrhagic crusts (Fig. 1A). Fluid-filled blisters were revealed with erosive lesions and hemorrhagic crusts in the leg area (Fig. 1B). Intraoral examination revealed clinical signs of the dorsum of dextra and sinistra anterior were ulcerated, shallow, white base, irregular, painful and there were hyperkeratotic lesions that could not be scraped off (Figs. 1C & 1D). On the buccal mucosa revealed hemorrhagic bullae on the left side and erosive lesions on both sides of the mucobuccal fold, multiple, irregular red painful lesions accompanied by blood vessel rupture that was not prominent, well-demarcated (Figs. 1E & 1F). The upper labial mucosa revealed erythematous lesions, multiple with blood vessel rupture in the anterior gingiva (Fig.1G). On the lower labial mucosa, there was a shallow white ulcer with clear boundaries and painful (Fig. 1H). On the ventral dorsum, there were erythematous lesions, shallow, measuring < 5 – 7 mm (Fig. 1I).

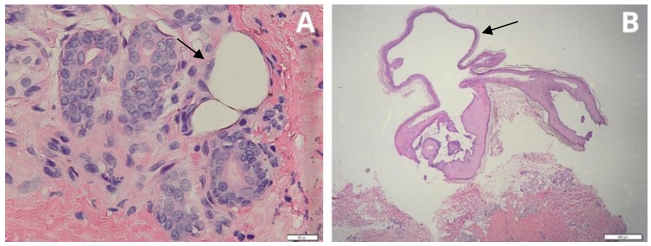

Figure 2. Histopatological of Dystrophic Epidemolisis Bullosa (DEB) with 400x dan 100x magnification. (A). The formation of blisters. (B). The occurrence of a vesicobullous reaction.

Based on the history taking and clinical examination, the patient was provisionally diagnosed with Epidermolysis Bullosa (EB). A biopsy examination was performed by taking the

erosive lesion on the left thigh. The results of the biopsy (Figure 2) showed that the keratinized stratified squamous epithelium layer had a vesiculobullous reaction with the formation of a subepidermal blister. In the stromal dermis layer, the fibro-collagenous connective tissue of plasma cells was found with dilated blood vessels. The pharmacological therapy given by the Dermatovenereology Clinic was hydroxyzine 25 mg, hydrocolloid, hydrogel, NaCL 0.9%, and vaseline album. The therapy given by the Oral Medicine Department in the early stages was topical corticosteroid and chlorhexidine digluconate 0.12% mouthwash for the oral cavity. The patient was given vitamin B12 50 mcg and folic acid 1 mg for 7 days as adjuvant therapy. The patient's family was also educated to always maintain oral hygiene and also avoid hard and spicy food. The goal of therapy in this case was to prevent the formation of blisters and complications. Topical steroids were used to speed up the healing process whereas antiseptic mouthwash was prescribed to help protect the oral mucosal surfaces against secondary infection. At this stage, QoL was assessed using the OHIP-14 questionnaire and found that the patient's QoL was poor with a score of 46.

A week later, the patient's complaints of oral mucosal pain were reduced. Intra-oral examination still revealed any erosive, spreading, multiple red lesions in the left buccal mucosa to the mucobuccal fold, however, the rupture of blood vessels had decreased. Pharmacological and non-pharmacological therapies were continued from the Oral Medicine Department including triamcinolone acetonide 0.1%, vitamin B12, folic acid, and 0.1% povidone-iodine mouthrinse, as well as instruction to maintain good oral health.

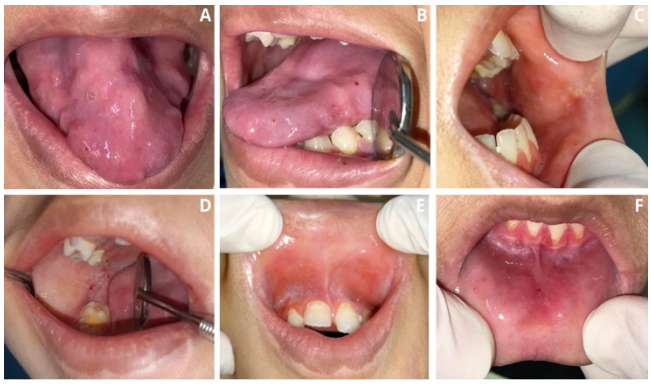

Figure 3. Clinical improvement of the oral mucosa lesions after 5 weeks of treatment.

Clinical improvement was seen at the second and third visit (5 weeks after treatment (Figure 3). The patient's complaints in the oral cavity showed a very significant improvement. Intraoral examination revealed that the erosive lesions, erythema, and ruptured blood vessels were healed, however, there were some new lesions on the tongue dorsum. The patient's family was instructed to keep the patient using povidone-iodine mouthwash, and information was also given on the possibility of a recurrence of his oral lesions so that the patient was still educated to always maintain oral hygiene. No side effects were found in patients during the treatment.

The patient's QoL was assessed and found that the patient's OHIP-14 was decreased with a score of 34. Based on the comparison of the patient's QoL score before and after therapies, it could be concluded that the patient's QoL was improved being better. The QoL assessment scores for the patient based on OHIP-14 are as follows (Table 1).

No	Domain	Situation	Score	
			Before Therapy	After Therapy
1	Functional limitations	Difficulty speaking or pronouncing words The sense of taste worsens	2 3	1 2
2	Physical pain	Oral pain Eating discomfort	4 4	3 3
3	Psychological Discomfort	Feeling awkward/anxious Feeling tense	3 3	2 2
4	Physical disability	Unsatisfactory diet Meal's interruption	4 3	3 2
5	Psychological Disabilities	Difficult to relax Feeling embarrassed	3 4	2 3
6	Social disability	Feeling irritable Difficulty doing work activities	3 4	3 3
7	Handicap	Feeling dissatisfaction with life Totally unable to function	3 3	3 2
	Total		**46**	**34**

Table 1. Patient's QoL based on OHIP-14 before and after therapy.
Responses were made on a 5-point scale: 0 = never, I = almost never, 2 = sometimes, 3 = quite often, 4 = very often.

Discussion

DEB is the 2nd most common of EB subtype after Epidermolysis Bullosa Simplex (EBS). DEB occurred due to a genetic abnormality of collagen VII, namely COL7A1, as a major component of anchoring fibrils (AF) that ensures the adhesion of the stratified epithelium to the underlying mesenchyme.[1,2] Loss of

structural function of COL7A1 leads to lifelong blistering and impaired wound healing, leading to chronic wounds characterized by increased inflammation and progressive scarring, which in turn can progress to systemic disease and even lead to skin cancer.[13] DEB is a hereditary disease comprised of dominant (DDEB) and recessive (RDEB) subtypes where generally the clinical manifestations of RDEB were more severe than DDEB.[1,3,14] In the USA, the prevalence of RDEB in 2002 was 1.35 while DDEB was 1.49 in every 1,000,000 people.[15]

Genetic mutations that occur in DEB resulted in changes of the structure and function of anchoring fibrils (AF) as an important polymer of collagen VII that binds the basement membrane of the epidermis to the dermis thereby producing damaged proteins. AF plays an important role in tissue cohesion as well as integrity of the skin and mucosa.[1,16,17] The patient in this Case Report had a genetic mutation of collagen VII, namely COL7A1 which was characterized by clinical manifestations of damaged attachment between the epidermis and dermis layers. Based on the history, there was patient's family who had experienced with DEB disease previously, therefore it could be concluded that the patient in this case suffered inherited dissease. The diagnosis with recessive type of DEB was established based on the clinical examination and histopathology taken from the left-thigh skin which showed acantholysis and vesiculosic reaction with blister formation in the subepidermal layer. Bullae and blisters on almost of the entire body with scar tissue and milia, as well as nail dystrophy.

Oral manifestation of DEB was varied in the terms of severity and frequency depending on the subtype of DEB.[5,6,18] In DEB patients, oral mucosal blisters or gingival erosions, dental caries, and prematurity were the oral manifestations most commonly reported.[3,18] In this patient, the oral manifestations that occurred were the appearance of blisters almost all over the oral mucosa and the presence of erosive lesions. Refers to the OHIP-14 questionnaire, these conditions caused the patient's QoL at the first visit to be categorized as poor.

Poor oral hygiene was the main problem and most often found in patients with DEB due to the appearance of blisters, lesions, and difficulty in opening the mouth.[5,8,10,16] Recurrent lesions and blisters since childhood could be an obstacle to maintaining good oral hygiene. Good oral hygiene could prevent other worse oral manifestations of DEB. To prevent worse oral hygiene and secondary infection, the patient was given chlorhexidine digluconate 0.12% mouthwash which has a cationic antiseptic to prevent secondary infection, a non-specific bacteriostatic activity that was able to bind the proteins and phospholipids of the bacterial cell wall structure which could inhibit and interfere the bacterial growth.[19,20]

Generally, the therapy of DEB was focused on the form of support from various parties. In this case, the therapy efforts were involving various health professionals such as Dermatologists and Venereologists, Oral Medicine, Pediatric orthopedics, Pediatric nutritionists, and Nurses. The further challenge is how to prevent the severity of DEB as early as possible by providing awareness to parents and patients themselves, as well as by appropriate treatment.[21] Currently, researchers from various countries are focusing their attention on the proper application of gene and cell therapy, infusion of protein recombinant, injection of intradermal allogeneic fibroblasts, and stem cell transplantation. The other things that could not be ruled out are efforts to improve faster wound healing and a better patient's QoL.[18]

Conclusions

DEB is a rare genetic disease characterized by blisters and erosive lesions on the skin that also manifest in the oral mucosa. Improvement of oral mucosal lesions appeared to be a particularly successful management intervention in improving the QoL for a pediatric patient with DEB.

Acknowledgements

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Declaration of Interest

The authors have no conflicts of interest to declare. The family of the patient has

approved and written informed consent for the publication of this report.

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