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Inherited recessive epidermolysis bullosa simplex in monochorionic twins

Deon Raditya Hibbattino[1]*, Nurani Widianti[1], Zahrah Hikmah[1]
[1]Department of Child Health, Faculty of Medicine, Airlangga University, Dr. Soetomo General Academic Hospital, Surabaya, East Java, Indonesia; masedeon@gmail.com (D.R.H.).

Abstract: Epidermolysis bullosa (EB) is a rare disease characterized by skin disorders in the form of blister formation that is inherited in a recessive manner. The incidence of EB is estimated at approximately 1 per 50,000 births with a wide clinical spectrum. The main characteristics of EB are skin that is fragile and easily forms blisters, which often heal on their own but leave scar tissue. This study aims to describe the clinical presentation, diagnostic process, and conservative management of twins diagnosed with dystrophic epidermolysis bullosa. This study used a case report method from a journal that focused on two twins diagnosed with dystrophic epidermolysis bullosa. The primary focus of the study was on clinical presentation, diagnostic workup, and conservative treatment approaches. Blisters appear with varying degrees of severity and significantly affect the patient's quality of life. A history of blistering or peeling lesions without an obvious cause should be explored further. The diagnosis is made based on clinical and histopathological findings. Epidermolysis bullosa has a serious impact on the patient's quality of life, especially in severe cases such as twins with dystrophic EB. It is important to make an early diagnosis based on clinical presentation and histopathological examination to appropriately manage the condition and reduce further complications.

Keywords: *Blister, Epidermolysis bullosa, Identical twins, Skin biopsy.*

1. Introduction

Epidermolysis bullosa (EB) refers to a clinically and genetically heterogeneous group of rare disorders characterized by fragility of the skin and mucous membranes[1]. Hereditary EB refers to a kind of bullous skin disease characterized by the appearance of blisters or vesicles following the slightest trauma to the skin. EB may affect skin, mucosae, or both[2]. Epidemiological data is different around the world based on studies of EB incidence and prevalence. A research group mainly based in United States estimated the EB incidence between 1986-2002 and the EB prevalence on 2002 in the country to be 19.57 and 11.07 per 1,000,000 individuals, respectively[3].

The EB has complex classification due to mutations in the same gene could be inherited as the autosomal dominant or recessive pattern. The process is resulted in several distinct clinical phenotypes. There are currently 4 major types of EB disorders is known to consist of epidermolysis bullosa simplex (EBS), junctional epidermolysis bullosa, dystrophic epidermolysis bullosa, and Kindler syndrome[4]. EBS is the most common type of skin disorder. Blisters in EBS usually present immediately after birth or during the neonatal period. Characteristics of EBS comprise of keratinocyte disorder, intraepidermal blistering, and little to none systemic involvement. Skin lesions usually disappear without scarring and blistering disappeared as the patient got older[5]. Diagnosis of EB is based on clinical and laboratory findings. The family history is also an important finding as inheritance is directly connected with the consanguinity status of the parents[2]. The clinical presentation of inherited EB can be similar or varies each other according to the type of disease. A definite diagnosis can only be reached by examining skin biopsy using immunofluorescence or electron microscopy[5]. There is no definite cure for epidermolysis

* Correspondence: masedeon@gmail.com

bullosa in present time, therefore until a curative treatment becomes available, the palliative management of epidermolysis bullosa is to adhere on the principles of blister prevention, wound care, nutritional support, monitoring for complications, and psychosocial support[6].

A case report of twin children diagnosed with dystrophic epidermolysis bullosa is reported. The focus mainly explains about the clinical presentation, diagnostic workup, and conservative treatments.

2. Case Report

A neonatal boy, firstborn, twin siblings, from non-consanguineous parents was admitted to the emergency department of a tertiary hospital. The boy was developed worsened blisters on the little finger of left food in the last six day. The blisters were also found around both of hands and left thigh. The blisters in little finger of left food eventually ruptured spontaneously followed by with skin peeling and reddish to black discoloration. A similar event was experienced when he was one month old. Parents gave a history of blisters appearing in hands and feet which ruptured spontaneously. His twin sibling suffered same complaint of skin blistering seen on fingers, hand, and knees. Baby was delivered by C-section, cried immediately after birth, and single placenta. The parents reported that there had never been a similar incident in the other family member before.

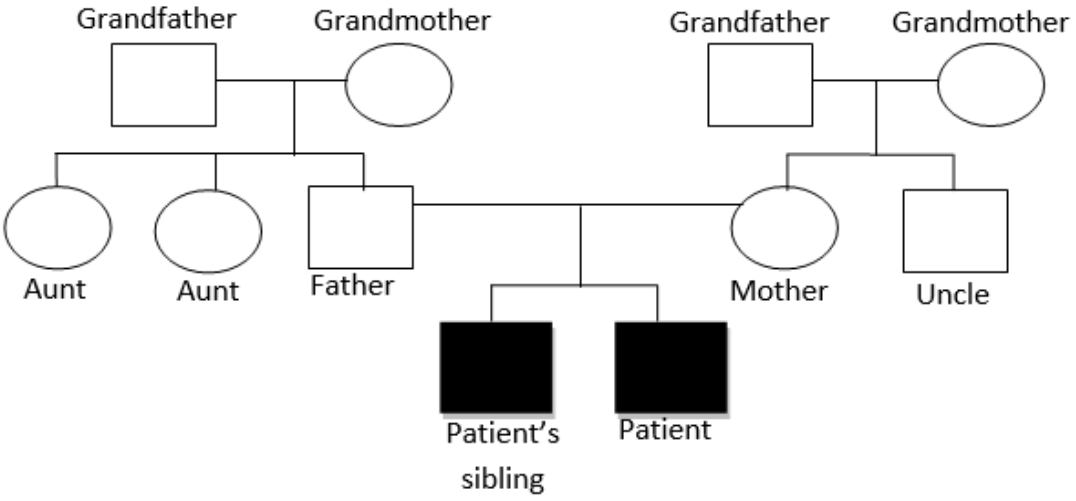

Figure 1.
Patient's family pedigree showing three generation of lineage. There was no other family member suffered from epidermolysis bullosa. A thorough genetical testing has not been performed yet.

On the further physical examination of the present case, there were multiple blisters and fresh skin lesion from several ruptured blisters. There was blackish lesion of ruptured blister and loss of nail in left foot little finger. Oral cavity, conjunctiva, cornea, scalp, and genitalia were normal. Systemic physical examination did not reveal abnormal results. Skin biopsy was performed which showed epidermolysis bullosa. Skin culture identified staphylococcus aureus.

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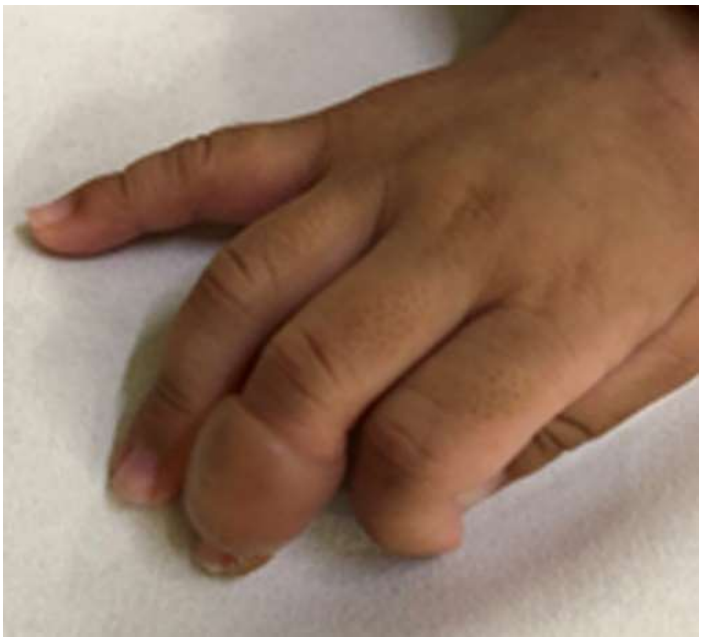

Figure 2.
A newly formed blister on the right hand.

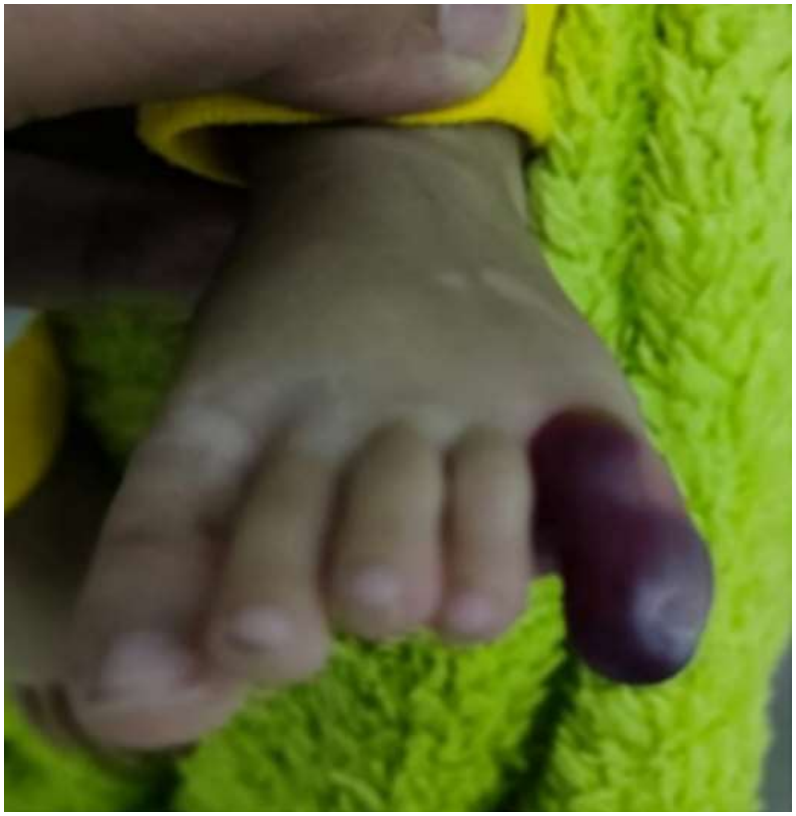

Figure 3.
Blister in left foot little finger that became black accompanied by loose nail. Several hypopigmentation scar can be seen in the dorsal region of left foot following blister healing.

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A diagnosis of epidermolysis bullosa simplex and localized secondary infection was made from clinical sign, histopathological examination, and skin culture. Antibiotic cloxacillin was given according to antibiotic sensitivity results. The boy's blisters were treated conservatively using soft foam pad and movement restriction to prevent new blisters formation due to skin rubbing. During the hospital stay, the lesion was improved. Most of blisters were healed with a hypopigmentation scar. Distinctive black lesion on left foot little finger shown granulation tissue and remaining crust without pus or complication in the surrounding area. The parents were explained about the boy's condition, also related to the similar occurrence in his twin siblings.

3. Discussion

Inherited epidermolysis bullosa (EB) is a genetically descended skin disorders of various group that present bullous lesion in skin and mucosal fragility, causing the patient susceptible to the development of blisters and/or erosions after minimal trauma or friction[5]. Inherited children with epidermolysis bullosa may have a complex and lifetime medical needs[7]. The etiology of EB is the mutations in any of 14 genes encoding proteins that maintain the integrity of the skin. There are hundreds of different possibility genetic mutations between 14 gene loci that leading to wide variability in phenotype and disease severity. These mutations result in either abnormal, absent, or significantly reduced concentration of a specific protein responsible of epidermis to dermis adhesion[6]. Consequently, genetic changes that alter the dynamics and function of these proteins result in failure of the structures that provide mechanical stability to the epidermis (such as the keratin, cytoskeleton, and desmosomes) and to the basement membrane area (such as hemidesmosomes, focal adhesions, anchoring filaments, and anchoring fibrils). Structure failure leading to the formation of blisters and spontaneously skin peeling[3].

The most prevalent symptoms in EB were formation of blisters. All types of EB have identical distinctive characteristic of recurrent blistering or skin erosion upon minor friction. In some patients, blistering of EBS starts in the neonatal period, but in milder cases, blistering can begin even in later years[8]. In this case, the first sign of blistering appeared at the age of one month old, and the symptoms were more severe than his twin siblings resulted in secondary infection. Inherited EB can be descended from the parents either as an autosomal dominant, autosomal recessive, or de novo inheritance playing important factors determining EB type and subtype[9]. Both twin siblings in this case experienced similar symptoms without any other family members with similar symptoms. Both parents are unaffected and act as carriers of EB. For any child of theirs to be born with EB, the child would have to inherit the disease-causing variant from both parents. There is a 25% chance of the disease occurring in children from carriers' parents.

There are 4 major types of inherited EB, differentiate not only genotypically and phenotypically but also by the site of structural disruption. Epidermolysis bullosa simplex (EBS) is characterized by a disorder of keratinocytes, intraepidermal blistering, and little systemic involvement. Nail dystrophy, alopecia, and mucosal lesions may occur in more severe forms of the disease. Skin lesions usually disappear without scarring. Blistering was diminished as the patient got older. Inheritance of EBS is typically autosomal dominant, although few cases of autosomal recessive inheritance have been reported[5,10,11]. The clinical manifestation in this case include frequent blisters formation since infant period. The blistering occurred often in the hand and foot which typical to friction or compression. The lesions were almost always healed spontaneously, with several lesion leaving hypopigmentation mark. Based on other studies blistering can persist throughout the childhood but tend to decrease as the child age. Nail defects, milia, and ulceration are common whereas dyspigmentation is not prominent factor[12,13]. Follow up during hospitalization found that skin defects was mild, no oral ulceration was found. Severe form of black lesion in the left foot little finger was caused by secondary infection and improved remarkably by antibiotic treatment.

The diagnosis of EB is mainly made by clinical symptoms. Skin biopsy and immunofluorescence is useful diagnostic tools to determine the separation of skin layer and identify the protein responsible for each condition. Immunological mapping by transmission electron microscopy (TEM) remains the gold

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standard method for differentiation between the various forms of EB. However, it is expensive and time-consuming to perform and to interpret, does not permit cleavage to be visualized as a whole, and is only available in specialized centers[2,14]. Genetic testing can determine the precise site and type of mutation, provide a definitive diagnosis of epidermolysis bullosa type and subtype, and the mode of inheritance. Furthermore, genetic testing can be useful for families with epidermolysis bullosa or at risk for having a child with epidermolysis bullosa. However, genetic testing is expensive and not widely available [6].

The management of EB patients is very important because a specific attention to the fragile skin is required in order to reduce pain, risk of trauma, ulceration and infection[1]. Currently, there is no cure for epidermolysis bullosa, and therefore until an effective treatment becomes available, the management of epidermolysis bullosa is based on the principles of blister prevention, wound care, nutritional support, monitoring for complications, and psychosocial support. The long-term therapy requires multidisciplinary approach involving pediatrician, dermatologist, surgeon, nutritionist, dentist, physiotherapist, nurse, psychologist, pain specialist, and geneticist according to the type of EB[4,15]. In the neonatal period, prevention of new blister formation is attempted by gentle handling of the infant, using loose-fitting clothing to avoid skin friction, padding bony prominences, and avoiding adhesive or direct rubbing of the skin. The skin should always be moist and the infant should be maintained in a cool, air-conditioned environments. As the infant gets older, prophylactic wrapping is often used to prevent new blisters[6]. Patients with EB may be hospitalized for a variety of reasons such as care in the newborn period, worsening of disease requiring more intensive skin care, operative procedures (including esophageal dilatations, placement of feeding gastrostomy tubes, and hand-release surgeries), or non-EB related conditions[16]. Special precautions need to be taken in the use of adhesive tapes, sphygmomanometer cuffs, tourniquets, and another medical equipment that might tear the skin[17]. Vaccination is not contraindicated for any type of EB. Particular concern needs to be addressed when providing vaccination using intracutaneous injection[18]. Lastly, the rarity of EB and the variable involvement of several organs and systems challenge the appropriate treatment of these patients. Parents should be advised about prevention of trauma, awareness of changing conditions, occurrences of new lesions, and possible complication[1,19].

4. Conclusion

Epidermolysis bullosa, specifically inherited recessively in twin siblings represent a rare case but impose significant early recognition and management to prevent complications, improve outcomes and patient's quality of life. Early detection is very important because its impact on the lives of patients and their family for a long term. Applied at early stage, efficiency of treatment may prevent associated complications and risks of the disease.

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Abbreviations:

EB: Epidermolysis Bullosa
EBS: Epidermolysis Bullosa Simplex
TEM: Transmission Electron Microscopy

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