CASE REPORT
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Epidermolysis bullosa simplex: A case report

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ABSTRACT

Epidermolysis bullosa (EB) is a rare inherited disorder of the skin characterized by blistering of the skin with variable severity ranging from localized to generalized involvement of the body; sometimes severely incapacitating the life of the patient. Treatment of EB is challenging and till date there is no cure. Epidermolysis bullosa simplex (EBS) is the most common and usually autosomal dominantly inherited disease, where blisters present usually at birth. Here blisters are intraepidermal, hence heal with no scar. A three years old boy of non-consanguineous marriage with family history of bullous disease presented with superficial blisters and erosions at the pressure sites was diagnosed as EBS.

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INTRODUCTION

Epidermolysis bullosa (EB) is a heterogeneous group of hereditary disorders characterized by extreme fragility of the skin and mucous membranes, which gives rise to the formation of blisters and ulcers following minor trauma. Most often affected areas of the body are sites subject to frequent pressure or friction, these conditions are also called mechanobullous disorders. The incidence of this disorder is approximately 1 in 17000 live births with an estimated 500000 cases worldwide. More than 10 genes are implicated in the etiology of EB and over 1000 mutations can be occur red de novo or be inherited in either an autosomal dominant or an autosomal recessive manner.[1] Depending on the level of tissue separation and blister formation, EB can be divided into 3 subtypes: (i) Epidermolysis bullosa simplex where separation occurs above the basement membrane; (ii) Junctional epidermolysis bullosa- where separation occurs at the level of basement membrane zone; and (iii) Dystrophic epidermolysis bullosa- where separation occurs below the level of basement membrane zone. There is also an acquired form (EB acquisita) that develops during the fourth or fifth decade of life and is caused by the production of immunoglobulin (Ig) G autoantibodies to collagen VII within the dermis.

The Case

A 3 years old boy presented to us with the complaints of blisters at the site of minor trauma since birth. The blisters were flaccid, appeared at the site of frequent friction e.g., elbow, knees, legs (Figure 1).

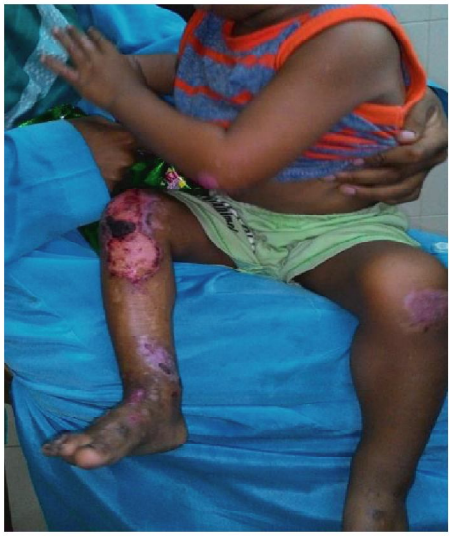

Figure 1. Denuded areas over the pressure areas of the patient

They ruptured spontaneously and healed with some pigmentary changes in the skin. The blistering of the skin increased during summer and reduced in frequency during winter.

On examination, there were multiple bilaterally symmetrical denuded areas with hemorrhagic crusts over both knees, dorsum of the foot, elbows, dorsum of hands. His oral cavity, conjunctiva, cornea, nails, scalp and genitalia were normal. Systemic examination findings were normal.

His mother's antenatal period was uneventful and he was delivered by normal vaginal delivery. There was no consanguinity of marriage of his parents. His father had similar history of blisters during his childhood, which had improved with age leaving some scars over the skin (Figure 2).

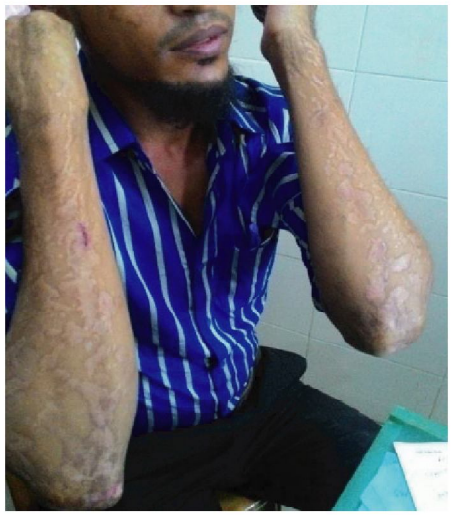

Figure 2. Scars over the extensor surfaces of both forearms of patient's Father

To exclude other bullous diseases of this age, e.g., chronic bullous disease of childhood, childhood bullous pemphigoid, a skin biopsy was taken from the lesion area for histopathology and perilesional normal skin for direct immunofluorescence (DIF). Histopathology revealed intra epidermal bullae with no immunoflurescence deposition in DIF – these findings coincide with EB simplex.

As there is no specific treatment of EB simplex, the parents were advised to wear the boy full sleeve shirts and trousers and soft shoes to avoid friction, use of soft toys, regular dressing of the wound areas, daily bathing and moisturizing the skin, and adequate nutritional support.

DISCUSSION

Epidermolysis bullosa can be divided into inherited and acquired forms. Inherited EB occurs due to mutation of several genes coding for structural proteins involved in constitution of hemidesmosomes of dermoepidermal junction, e.g., proteins K5/K14 in simplex type; laminin5

and 4 integrins in junctional type and COL7A1 in dystrophic. EB can be both autosomal dominant or autosomal recessive or de novo and bullae usually presents at birth. Acquired EB is known as epidermolysis bullosa aquicita and bullae appears in elderly age.[2]

EB simplex encompasses all subtypes of EB having blisters confined to the epidermis; Junctional EB includes all subtypes of EB in which blisters develop within the lamina lucida of the skin basement membrane zone (BMZ). Dystrophic EB includes all EB subtypes in which blistering occurs within the upper most dermis, just beneath the lamina densa of the skin BMZ.[3] In relation to age and different EB types and subtypes, there is marked variation in skin and mucous membrane lesions and multiorgan involvement. These cutaneous and extracutaneous manifestations and complications in several subtypes lead to a significant morbidity and even to premature death. Till date, no cure is still available for EB. In the absence of a specific therapy, patient management is currently centered on skin care measures, early recognition and symptomatic treatment of complications.[4]

As clinical features and routine histologic features overlap among different subtypes of EB, accurate diagnosis depends on genetic mutation mapping, electron microscopy study, or immunofluorescent mapping.[5] Unfortunately latter three are not available in our country. So we have to confirm our diagnosis by taking complete history, histology of the skin and direct immunofluorescent (DIF) study. This DIF study will help to differentiate EB from other bullous diseases of the skin e.g. chronic bullous disease of childhood. In EB there will be no deposition of immunoglobulins in DIF.

Different subtypes of EB simplex are caused by defects in genes encoding transglutaminase 5, plakophilin, desmoplakin, plakoglobin, keratin 5 and 14, plectin, exophilin 5 and bullous pemphigoid antigen 1.[5,6] Prenatal diagnosis can be done by fetal skin biopsy, fetal DNA analysis from amniotic fluid and chorionic villus cell sampling, 3 dimensional ultrasound and analysis of fetal DNA taken from a maternal blood sample.[1] The disadvantage of diagnosing EB prenatally is that nothing can be done to prevent progression of the disease. Most cases of EB simplex are inherited in an autosomal dominant pattern. Autosomal recessive EB simplex, lethal acantholytic EB simplex, plakophilin deficiency, EB simplex with muscular dystrophy, and EB simplex with pyloric atresia are transmitted in an autosomal recessive pattern.[1]

EB simplex generalized intermediate, previously known as EBS Koebner, inherited as autosomal dominant trait and the child is affected at birth or shortly thereafter, with improvement within first few months. The disease recurs as the child begins to crawl. There is seasonal variation also with worsening of condition during summer and improvement during winter.[5] Mucous membranes and nails are not involved. This is milder than other forms of EB and there is no internal organ involvement. All these findings coincide with our patient. EB simplex generalized severe, previously known as Dowling-Meara, is also inherited as autosomal dominant trait. In this subtype oral mucosa is involved, nail dystrophy, hyperkeratosis of palms and soles may occur. EB simplex localized, also known as Weber-Cockayne, has autosomal dominant inheritance, presents as recurrent bullous eruption of the hands and feet in infancy or at times later in life. There may be associated hyperhidrosis and blisters exacerbate during hot weather. In EB simplex with muscular dystrophy, there is minimal skin involvement but laryngeal involvement can be severe enough for the

requirement of a tracheostomy. Progressive muscular dystrophy usually starts any time from the first year onwards.[7]

As there is no definite cure for EB, the objective of treatment is to alleviate symptoms and provide supportive measures. A multidisciplinary team consisting of dermatologist, nutritionist, dentist, physiotherapist, nurse, psychologist, pain specialist is required for optimum management of the disease.[7] Protein and micronutrient needs are increased in EB patients due to accelerated skin turn-over, blood and protein losses through skin wounds, recurrent infections and chronic inflammation. Micronutrient deficiencies (iron, zinc, selenium, vitamins, etc.) can lead to severe complications. Insufficient fluid and fiber intake frequently causes constipation, which can induce painful defecation (anal fissures).[4] The child should be duly vaccinated as there is no contraindication to vaccination.[8]

A mild antiseptic cleanser (e.g. chlorhexidine 0.1% or polyhexanide, sodium hypochlorite 5–10 ml in 5 L of water, acetic acid 0.25%) should be used for extended and/or critically colonized/ infected lesions. An emollient/oil-based cleanser should be chosen for xerotic skin and hyperkeratotic or crusted lesions. Intact blisters should be lanced at their lowest point with a fresh hypodermic needle or sterilized sewing needle or scalpel blade to limit tissue damage. A soft piece of gauze can be used to gently compress the blister for complete emptying and the roof should be left on the blister as de-roofing can lead to additional pain. A soft bristle toothbrush previously soaked in hot water should be used to maintain oral hygiene.[7]

Frequent skin infections may worsen EB course. Topical agents which do not have systemic formulation (e.g. fusidic acid, mupirocin) are preferred and should be used for short period to avoid resistances. Pruritus is frequently chronic, severe and unresponsive to conventional treatments. Short courses of topical mild potency steroids, sedating antihistamines, gabapentin or pregabalin, anti-inflammatory agents (e.g. cyclosporine, thalidomide or topical tacrolimus) can be used for pruritus. Non adherent dressings are preferred for regular wound care.[4]

In EB simplex wounds heal without any scarring. Use of full sleeve dress, trouser, shoes to prevent friction induced trauma and avoidance of hard toys are advised to prevent blister formation. In junctional and dystrophic EB where wounds heal with scarring, more extensive skin care is required. Some innovative therapeutic strategies like protein therapy, gene therapy, and bone marrow transplantation are being used to correct gene mutation in severe forms of EB.[9, 10] Psychological support is vital for both parents and family members. The chance of development of skin cancer from chronic wounds is more or less absent in EB simplex but higher in junctional and dystrophic EB.

CONCLUSION

Epdermolysis bullosa simplex is one of the inherited bullous diseases of childhood. Early diagnosis and treatment of the complications can reduce patients' sufferings. Except for certain lethal variants, e.g., recessive dystrophic EB, EB simplex is milder with minimal affection of life expectancy.

Conflict of Interest: Nothing reported.

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