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Junctional Epidermolysis Bullosa: A Case Report

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Introduction

Epidermolysis bullosa (EB) is a heterogenous group of diseases of the skin and mucous membranes which share the common feature of the formation of blisters and erosions in response to minor mechanical trauma. These disorders often have been referred to as mechanobullous diseases. Diagnosis is based on clinical symptomatology, histopathology, electron microscopy and genetic studies.[1]However in a resource limited setting, the diagnosis is mainly clinical. Age of onset, symptomatology and prognosis of various subtypes are varied.[2]Most cases of EB are inherited.[3,4] A comprehensive classification based on clinical presentation, genetic pattern of inheritance and electron microscopic features was proposed in 1991 by the subcommittee of the National EB Registry.[5] EB is classified into major 3 groups by the level at which separation occurs: EB simplex (EBS), is characterized by intraepidermal blistering, is usually inherited in an autosomal dominant manner with complete penetrance. Junctional EB (JEB), an autosomal recessive disease, demonstrate cleavage within the lamina lucida. Dystrophic EB (DEB) is characterized by separation of the sublamina densa and may be inherited as an autosomal dominant or recessive disease. The incidence of EB estimated by a National EB Registry report is 50 EB cases per 1 million of live births; of these cases, approximately 92% are EBS, 5% DEB, 1% JEB and 2% unclassified.[3]We describe a patient with JEB (which has an incidence of 1%) who was managed accordingly.

Case Report

This male neonate of 1st degree consanguineous parents ,of 38th wks gestation, weighing 2.8 kg, was born at home by vaginal delivery without complication. At birth blisters were evident on the lower back, buttocks, left knee joint with adjoining area, lower part of leg with dorsum of the foot, left elbow joint including dorsum of the hand. New blisters developed gradually. There was family history of blistering disease of sibs who died early infancy. The blisters became widespread and prominent in areas of friction and trauma. At 3rd day of age, the newborn was transferred to the Noakhali Medical College Hospital with lethargy, reluctance to feed and skin blisters and erosion in areas of pressure and trauma with relative sparing of the face. Most of the fingernails were dystrophic. No dysmorphic features were noted on clinical examination.

On admission physical examination revealed, axillary temp of 100^{0}F, Ht/R of 160 beats/m, respiratory rate of 60/m. Breath sounds were clear, and heart examination was normal. In addition to skin lesions, 1 blister was found in the oral cavity.

Laboratory investigations showed: white blood cell count 18,000/mm^3 (with neutrophils 78%, lymphocytes 19%, monocytes 3%) ; hemoglobin 16.5 gm/dl; platelet 240,000/mm^3 ; c-reactive protein>6 IU/ml. Staphylococcus were found in subsequent wound and blood culture.

Skin biopsy was performed when he was 9 days old. Histopathology revealed sub-epidermal blistering without inflammatory cells. The roof of the blister consisted of full-thickness epidermis. The picture was compatible with JEB (Fig-5). Direct immuno-fluorescence of lesional skin was negative for IgG, IgA, IgM and C_3.

Hospital management included topically applied antibiotic with non-adherent wet dressing (with petroleum impregnated gauzes). Intravenously administered antibiotics and saline were given during a period of toxicity. Vit-c was given intravenously as an adjuvant therapy.Patient recovered over 10 days.

The patient was discharged after hospitalizetion for 18 days. The wounds were covered with non-adherent wet dressing (white petroleum impregnated gauzes). He was not on regular follow up and the baby was died at 36th day of age which was known over phone.

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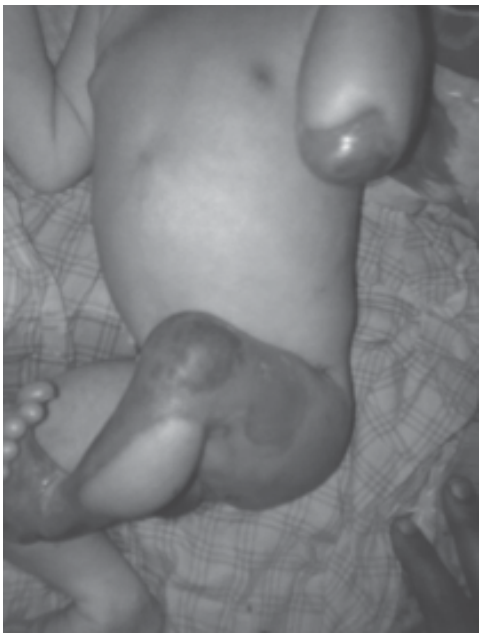

Fig-1: *Ruptured blisters and erosions in the areas of friction and trauma*

Fig.- 2*: Blister in oral mucosa*

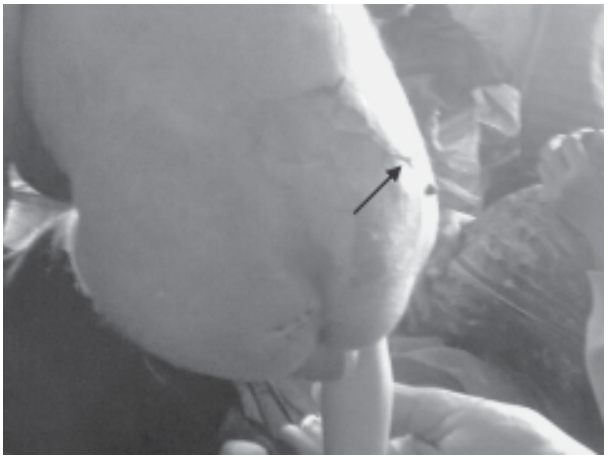

Fig.-3: *Ruptured blisters and erosions on the lower back and buttocks*

Fig.- 4: *Dystrophic nails*

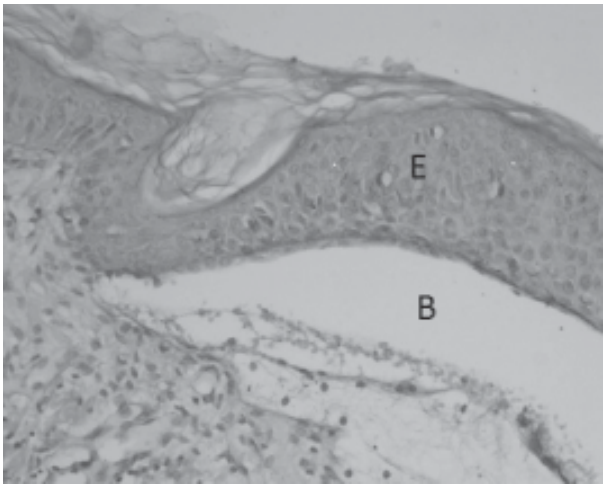

Fig.- 5: *Histopathology shows subepidermal blistering without inflammatory cells.The roof of the blister consisted of full-thickness epidermis.*

Discussions

A neonate presenting with blisters opens a broad spectrum of differential diagnosis which include infectious diseases such as bullous impetigo, staphylococcal scalded skin syndrome, or toxic epidermal necrolysis, and immunologic diseases such as pemphigus or bullous pemphigoid, and hereditary diseases such as EB. Differential diagnosis based on clinical symptomtology, histopathology, direct immunofluorescence and bacterial culture. The initial presentation of this case included a few blisters with erosions on the skin after birth which differ from staphylococcal scalded skin syndrome where blisters appear in flexural and periorificeal area but in our case blisters appeared in areas of trauma and friction.

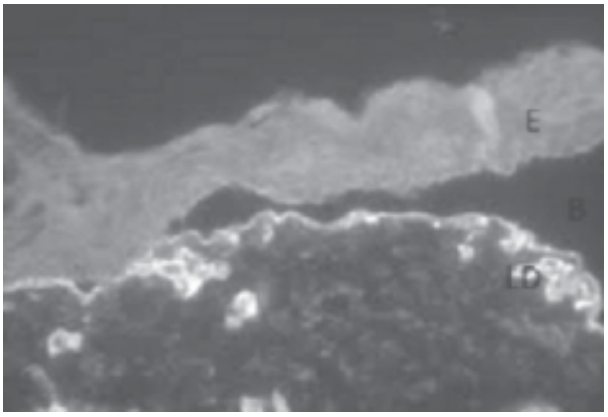

Fig.-6: *Direct immunofluorescence mapping with fluorescence antisera against type IV collagen (localized on the lamina densa) shows a positive linear immunofluorescence (arrow) at the base of the blister. This allocation of collagen IV in the blister indicates a junctional cleavage. E=epidermis , B=blister,* LD=lamina densa.

EB can be differentiated from immunologic bullous dermatoses through clinical,histologic and immunofluorescent methods.In immunologic bullous dermatoses bullae appear predominantly on the flexural aspects of extremities,in the axillae, and on the groin and central abdomen.In EB,the histologic picture is subepidermal bulla without inflammatory cells,while the direct immunofluorescence of both lesional non-lesional skin is negative for IgA,IgG,IgM and C3.[6]Histopathology is generally not very helpful in delineating a specific subtype of EB,since all subtypes appear as subepidermal split on light microscopy.[6] Ultrastructurally,EBS shows an intraepidermal separation at the level of basal cells;JEB and DEB show subepidermal split through the lamina lucida,or beneath the lamina densa,respectively.[7] The level of tissue separation can be rapidly and reliably detected using immunofluoroscence mapping.[8]Based on immunofluoroscence staining,this method relates the level of cleavage to specific markers for structural proteins,which are strongly expressd in both normal skin and skin from EB patients.In JEB anti-BP180(anti-collagen type XVII) antibody will be located on the roof of the blister,whereas collagen type IV antibodies stain the floor.[5] In this patient , immunofluoroscence mapping with antisera against collagen type IV showed a positive linear Immunofluoroscence at the base of the blister.This allocation of collagen type IV in the blister indicated a junctional cleavage.

There are more than 25 subtypes of EB,and they often become manifest at birth or during the 1st year of life.[3] The more severe the involvement,the earlier the blisters will occur,usually from mild trauma such as that encountered when a baby crawls or lifts objects or during teething.[9] Each type of EB has several variants based on inheritance,prognosis and clinical features.EBS is usually with little or no extracutaneous involvement,while the more severe junctional and dystrophic forms of EB may produce significant multiorgan involvement.[10] EBS, mostly an autosomal dominant disorder,comprises 92% of EB.There is an intraepidermal cleavage at the lower portion,owing to cytolytic alterations of basal keratinocytes with defects in cytokeratins 5(KRT5 gene) and 14(KRT14 gene).[11] JEB is an autosomal recessive disorder characterized by cleavage at the lamina lucida. JEB mutations have been described in the 3 genes (LAMA3, LAMB3, LAMC2) that encode the anchoring filament protein, laminin 5,and the 2 transmembrane components of the hemidesmosome, collagen type XVII and integrin á6â4.[11] DEB include autosomal recessive and dominant forms. The mechanism of the disorder is a mutation in the gene encoding collagen type VII, leading to defective anchoring fibrils and causing sublamina densa separation.[12,13] Skin biopsies are required for appropriate diagnosis and classification in affected patients.[4]

The management of EB patients are primarily preventive and supportive, consisting of prevention of trauma, careful wound care, nutritional support and infection control. Surgical procedures are indicated when deformities are caused by the blistering and scarring.[14] EB are genetic disorders, no drug is capable of correcting the molecular defect.[15] Gene therapy is, potentially, a future therapy. Clinical physicians should provide genetic counseling for families at risk for EB.

It right be concluded from this case report that efforts should always be given to reach a definitive and early diagnosis of EB. Clinical pictures could help to distinguish lethal from non-lethal type of Epidermolysis Buttosa.

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