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BUTTERFLY CHILDREN : A RARE CASE OF CONGENITAL EPIDERMOLYSIS BULLOSA

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ABSTRACT

Epidermolysis bullosa (EB) is an intractable skin condition characterized by the development of blistering of the skin and mucosa spontaneously or as a result of minimal trauma. These disorders represent heterogeneous phenotypes and are associated with a variable range of complications, from localized skin fragility to neonatal death. Its affects 1 out of every 50,000 live births and those born with it are often called 'Butterfly Children'.

INTRODUCTION

Epidermolysis bullosa (EB) constitutes a group of phenotypically diverse genodermatoses, which manifest with blistering and erosion of the skin and mucous membranes.[1] Recent advances in research on EB have led to the identification of mutations in 10 different genes, which account for the clinical heterogeneity in EB.[2] However, the term "epidermolysis" is not correct as epidermal disruption is not the primary change in two of the main categories of EB.[3,4] This complex and heterogeneous group is classified on the basis of the mode of inheritance, clinical, laboratory and epidemiological studies into three major forms: EB simplex (EBS), junctional EB (JEB), and dystrophic EB (DEB). We report a fullterm, low birth weight male neonate, who had extensive bullous lesions in the first week of life.

CASE REPORT

A fullterm male baby weighing 2600 gms born to a 26 years old primigravida through vaginal delivery presented with blistering of skin since birth. The neonate had normal extra uterine transition with normal APGAR scores. Parents of the babies were non-consanguinously married and there was no history of similar disorder among their families. Baby had blistering of the skin involving both the lower limbs and upper limbs predominantly on right lower limb involving the lateral and posterior aspect of foot arising most frequently over pressure points. Blistering was also seen on dorsum of penis and lower aspect of scrotal sac. Erythema & local rise of temperature was noted. Conjunctiva, cornea, nails, scalp and other mucous membrane were normal. Basic interventions such as intravenous cannulation and minimal trauma elicited fresh blisters. The bullae peeled off on third day of life with no subsequent scarring. Baby was treated conservatively; empirical antibiotic coverage was given to treat secondary bacterial infection. Good nursing care of skin was taken. Daily wound care, pain management and protective bandaging were done to protect from undue trauma inducing blister formation. Parents were explained of the condition of the baby and discharged on persistent request on 7th day of life. The neonate was discharged with topical emollients, skin protective measures and nutritional supplements. Though the skin biopsy could not be performed due to the financial constraints, clinically EB simplex was considered in view of non involvement of nails and no scarring.

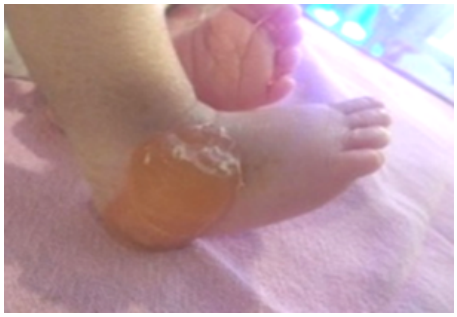

Fig1.

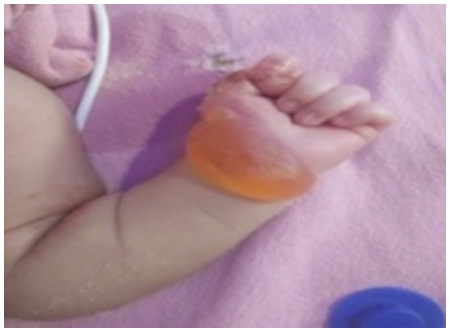

Fig2.

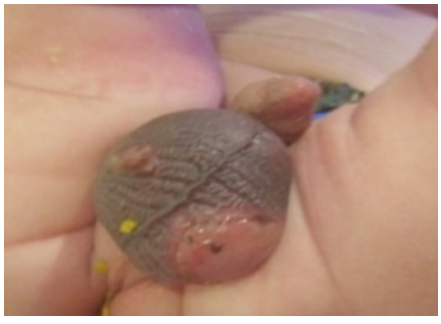

Fig3.

DISCUSSION

"Butterfly children"[5] is the term given to those baby born with this disease, as their skin is seen to be a delicate and fragile as that of a butterfly. Epidermolysis bullosa refers to a group of inherited disorders that involve the formation of blisters following trivial trauma. Incidence is not affected by race or ethnic group,[6] and the disease affects both sexes equally. Researchers have identified more than 10 genes implicated in the etiology of EB and have reported over 1000 mutations that can occur *de novo* or be inherited in either an autosomal dominant or an autosomal recessive manner.[1] 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.[7] The forms of EB are categorized into the following 3 subtypes: EB simplex, junctional EB, and dystrophic EB. EB simplex is the most common form (92%) and dystrophic EB has the second highest incidence (5%), followed by junctional EB (1%).[8] These 3 subtypes are differentiated according to the level at which the tissue separates and the blisters form, that is, depending on whether this happens above, within, or below the epidermal basement membrane.[9] The level of separation in EB simplex is intraepidermal and is at lamina densa in junctional EB. However, in dystrophic EB the separation is below the basement membrane.[10]

Kindler syndrome, which was added as the fourth major

epidermolysis bullosa type to the EB classification in 2008, describes a specific entity that is characterized by the presence of clinical phenotypic features unique among EB (most notably photosensitivity) and blistering that arises in multiple levels within and/or beneath the BMZ, rather than within a discrete plane, as occurs in all other EB types.[1]

In Epidermolysis bullosa simplex, cytolysis causes blisters in the basal or spinous layers of the epidermis, and keratinocytes often have abnormal density and organization of keratin filaments. In Junctional epidermolysis bullosa, the epidermis separates from the basal lamina, forming a blister cavity in the plane of the lamina lucida, where hemidesmosome structure and density are frequently diminished. In Dystrophic epidermolysis bullosa, the basal lamina remains attached to the epidermis, but the blister cavity forms beneath the lamina densa of dermoepidermal junction, and anchoring fibrils may appear abnormal, reduced in number, or altogether absent.

With the help of immnunohistochemistry, the major epidermolysis bullosa genes identified are those that encode keratins 5 and 14 in EBS.[11] In JEB the underlying defect lies in the hemidesmosomes which tend to be sparse and very small, especially in the more severe forms of the disease and the majority of mutations have been found in the *LAMB3* gene.[12] Immunofluorescence studies have also shown reduced staining of another hemidesmosome-anchoring filament component, BPAG2, or collagen 17 in the skin of patients with generalized atrophic benign EB (GABEB), suggested that mutations in the BPAG2 gene might underlie this condition.[13] DEB is caused by mutations in a single gene, COL7A1, encoding the anchoring fibril protein, the type 7 collagen. Quantitative electron microscopy and immune-electron microscopy have shown complete absence of anchoring fibrils in severe forms of dystrophic EB.[14]

Epidermolysis Bullosa Simplex(EBS), the mildest and most common type of EB, ischaracterized by the lysis of basal keratinocytes above thebasement membrane zone. The genes identified are those that encode keratins 5 and 14. Keratin 5 and 14 function in the adhesionof cells to the hemidesmosome through plectin, another EBS associated protein. ***In Weber--Cockayne type of EBS,*** blisters are rarely present at birth and usually begin with crawling. Blisters are usually confined to the hands and feet, but can occasionally occur anywhere if trauma is significant. Symptoms are worse in warm weather and worsen with sweating. A study has demonstrated reduced thermal stability of the keratin filaments. In ***Dowling--Meara type of EBS*** multiple grouped clumps of small blisters occur which are typical of the disease hence the name EB herpetiformis. Dowling-Meara (DM) EBS is most severe in the neonate and infant, and can be fatal in the neonatal period. ***Koebner type*** EBS is distinguished from EBS-Weber-Cockayne by its more widespread involvement, but misdiagnosis is common. In infancy, blistering commonly occurs on the occiput, back, and legs, while in childhood, hands and feet are mainly affected. Unlike other major EBS disorders, EBS with muscular dystrophy is characterized by an autosomal recessive mutation in the gene coding plectin.[15] EBS with mottled pigmentation has the presence of discrete pigmented macules 2--5 mm in diameter, which usually appear in infancy and persist throughout life.[16] Epidermolysis bullosa simplex (EBS) blisters typically heal with minimal to no scar and do not result in skin atrophy. Secondary infection is the primary complication.[17]

Currently, there is no definitive and curative treatment for EB. Hence, the mainstay of treatment is symptomatic, supportive and preventive. The key measures that need to be taken in neonates and children with EB are preventing trauma induced blisters by dressing with a soft, non-adhesive material soaked with emollients such as vaseline along with empirical antibiotics to prevent secondary infection. Optimum management of this disease can only be achieved by a multidisciplinary team, which should include the following specialists: dermatologist, surgeon, nutritionist, dentist, physiotherapist, nurse, psychologist, pain specialist, and geneticists.[18] The treatment plan must be individualized and optimal communication among team members is a vital factor in obtaining good results. Psychological support for parents and family members is vital, Genetic counseling is recommended for prospective parents who have a family history of any form of epidermolysis bullosa. During pregnancy, chorionic villus sampling to test the fetus. For couples at high risk of having a child with epidermolysis bullosa, the test can be done as early as 8 – 10 week of pregnancy.

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