

## **A rare case of Epidermolysis bullosa in a fifty day old male child with one affected sibling- A Case Report**

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**Abstract:** Epidermolysis bullosa (EB) is a rare, inherited group of disorders due to defects in the skin structures that clinically manifests with extensive, intractable and recurrent blistering of the skin, occurring either spontaneously or due to minor trauma or friction. There are three major types of EB, namely: simplex (EBS), junctional (JEB) and dystrophic (DEB), with a prevalence of 8.22 per 1 million births [1, 2]. A fifty day old male child was brought with complaints of fever since 4 days and recurrent blisters over the body since birth. The lesions were first noted at third day of life over the buttocks and right elbow, which initially appeared as blisters that ruptured in 2-3 days resulting in ulceration, the ulcers healed spontaneously with crusting, leaving behind a hypo pigmented scar. Born to second degree consanguineous parents, his older sibling also had multiple, similar lesions over the trunk and lower limbs, along with nail dystrophy. Skin biopsy for histopathological examination revealed presence of bullous cavities in the dermo epidermal junction without any inflammatory cells, thus confirming the diagnosis, the child was given supportive and symptomatic treatment with intravenous anti biotics, along with wound care. In conclusion we report cases of EB in a fifty day old male baby who presented with history of recurrent blisters and ulceration over the body since birth, born to a 2oconsanguineous parents, with history of similar complaints in the older, female sibling.

**Keywords:** Blisters, Epidermolysis bullosa, Herlitz and non Hermits junctional epidermolysis bullosa, GABEB or Hinter Wolf type.

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### **INTRODUCTION**

Epidermolysis bullosa is a rare, inherited group of disorders due to defects in the skin structures that clinically manifests with extensive, intractable and recurrent blistering of the skin, occurring either spontaneously or due to minor trauma or friction. There are three major types of EB, namely: simplex (EBS), junctional (JEB) and dystrophic (DEB). While simplex is the most prevalent phenotype, dystrophic epidermolysis bullosa is rare and more severe form with high mortality. Reported prevalence of EB varies from 8.22 cases per 1 million live births as per various EB registries [1, 2]. The severity may range from localised skin infection to life threatening septicaemia.

### **CASE REPORT**

A 50 day old male child was brought to the paediatric outpatient department with complaints of fever since 4 days and recurrent blisters over the body since third day of life. The child was born at 36 weeks of

gestation to a third gravida, by elective caesarean section. His birth weight was 2.5 Kgs, which was appropriate for gestational age; he was born to second degree consanguineous parents, with history of similar complaints in the older, female sibling. The lesions were first noted at third day of life over the buttocks and right elbow, which initially appeared as blisters that ruptured in 2-3 days resulting in ulceration, the ulcers healed spontaneously with crusting, leaving behind a hypo pigmented scar. Since then the lesions have been appearing on and off extensively over the face, trunk, wrist and lower limbs. There was no history of injury or trauma. On examination the child was febrile, temperature 101o F, mild tachycardia, with a normal respiratory rate, head to toe examination did not reveal any facial dysmorphism. At present the child had lesions over his cheek, lower limbs, and buttocks (as shown in figure 1A, 1B). Hair and nails, appeared normal. No mucosal involvement was seen. Systemic examination was inconclusive.

**Fig1A: Fresh lesions over the buttocks and lower limbs (black arrow) with hypo pigmented scar from previous blister (white arrow) in the index child.**



**Fig 1B: crusted blister over the cheek in the index child.**

The index patient's older sibling was also examined, who had multiple granulated lesions over the trunk and lower limbs (as shown in figure 2A, 2B) along with nail dystrophy. (as shown in figure 3).



**Fig 2A: Lesions over the trunk in the female sibling (black arrow).**

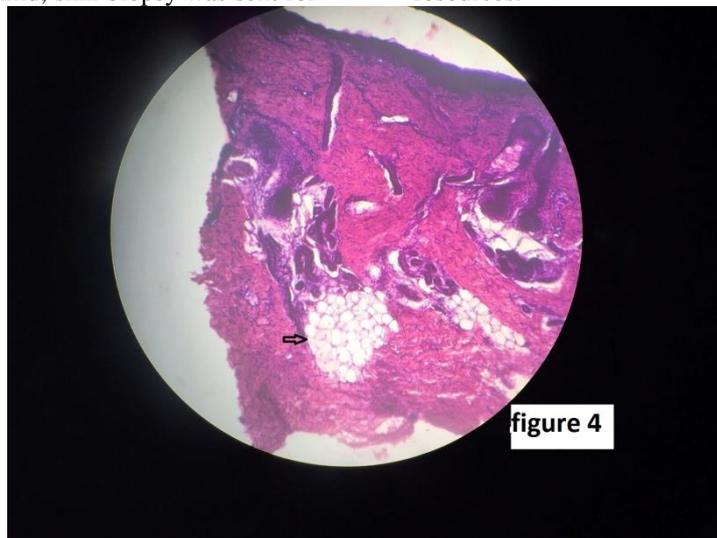
**Fig 2B: crusted erosions over the lower limb in the female sibling (black arrow).**



**Fig 3: Dystrophic nail changes (black arrow)**

Routine investigations showed a white blood cell count of 20,000/mm<sup>3</sup> (with neutrophils 72%, lymphocytes 22%, monocytes 1%); haemoglobin 15 gm./dl; platelet 250,000/mm<sup>3</sup>; C - reactive protein >6 IU/ml, but no organism was isolated from blood culture. Serum electrolytes were within normal range. Keeping epidermolysis bullosa in mind, skin biopsy was sent for

histopathological examination which revealed presence of bullous cavities in the dermo epidermal junction without any inflammatory cells, (as shown in figure 4) thus confirming the diagnosis. Direct immunofluorescence test, electron microscopy and gene mutation studies could not be done due to limited resources.



**Fig 4: Skin histopathology showing irregular bullous cavity at the dermo-epidermal junction (black arrow).**

The child was given supportive and symptomatic treatment with intravenous antibiotics, along with wound care, using non-adherent wet dressing with petroleum impregnated gauzes. Genetic counselling was given to the parents.

#### **DISCUSSION**

Epidermolysis bullosa is a rare, heterogeneous group of genetic disorder due to defects in the skin

anchoring structures that clinically manifests with extensive and recurrent blistering of the skin, occurring either spontaneously or due to minor trauma or friction. The name 'epidermolysis bullosa hereditaria' was coined by Koebner in 1886 [3].

The most accurate epidemiological data are derived from the National EB registry project from USA and also from Scotland [1, 2]. According to it, the

incidence and prevalence of EB are estimated to be 19.60 per million live births and 8.22 per million populations, respectively. The incidence and prevalence rates of EB simplex are 10.75 and 4.65, of junctional EB are 2.04 and 0.44 and dystrophic EB dominant type 2.86 and 0.99 and recessive dystrophic EB 2.04 and 0.92, respectively. Currently, more than 1000 mutations, encompassing more than 10 distinct structural genes expressed within the cutaneous Basement Membrane Zone (BMZ) have now been documented for epidermolysis bullosa. [4]

Characterization into major groups was first done by Pearson in 1962[5].Based on the level of dermoepidermal separation at the BMZ, three major groups have been identified - simplex, junctional and dystrophic [1, 5]. The level of separation in EB simplex is intra epidermal, in junctional EB it is at lamina densa and in dystrophic EB it is below the basement membrane [6, 7]. Autosomal dominant as well as autosomal recessive forms of EB exist within each of the three major types. The mode of inheritance is mostly autosomal dominant in EB simplex and autosomal recessive in junctional EB [6].The most recent classification of EB has been proposed by the third international consensus meeting held in Vienna in 2007 [1]. In these classifications, attempts were made to eliminate eponyms, streamline it, and add a fourth group to the major EB types, the mixed or Kindler Syndrome. The patients are then separated by major and minor EB subtypes

The three major clinical subtypes of junctional epidermolysis bullosa include Herlitz JEB (letalis),Non-Herlitz JEB (mitis) and generalized atrophic benign epidermolysis bullosa (GABEB or Hinter Wolf type).

Wide range of genetic abnormalities occurs in various types of EB. K5 or K14 gene mutations result in bullous formation by disrupting the basal cells in dominant EB simplex as well as some forms of recessive EB simplex. While, type XVII collagen, lamin in 5 and  $\alpha 6$ ,  $\beta 4$  integrin in gene mutations are seen in junctional EB and dystrophic variant is linked with type VII collagen gene abnormalities [7]. Onset is usually soon after birth, presenting with spontaneous blistering of the skin, apart from the cutaneous lesions, mucosal involvement may also be seen involving oral, nasopharyngeal, ocular, and genitourinary, GI, and respiratory mucosa. Dental anomalies, alopecia, onychodystrophy are also common manifestation, some patients may present with multi organ system involvement or with metastatic squamous cell carcinoma [8] which is commonly associated with recessive Herlitz form of JEB, EB in association with muscular dystrophies and pyloric stenosis [7, 9] have also been reported. Diagnosis is usually made by history, physical examination and skin biopsy for

histopathology which helps in differentiating it from other conditions. While definitive diagnosis for the type of EB is made with transmission electron microscopy (TEM), immuno fluorescence antigen mapping (IF), and EB related monoclonal antibody testing as well as mutational analysis. In order to make a correct diagnosis, it is most important that the skin biopsy should be performed properly, as described by Intong and Murell.

Prenatal and pre implantation diagnosis can also be performed. Dunnill *et al.*; [10] was first to perform a successful prenatal diagnosis using intragenic and flanking COL7A1 markers in a pregnancy at risk for recessive DEB. Recently, chorionic villi immuno fluorescence examination has successfully been used for prenatal diagnosis of inherited epidermolysis bullosa with pyloric atresia.

In spite of extensive research no definitive treatment is available, avoidance of provoking factors, good nursing care, maintenance of oral and dental hygiene is commonly advised. Amitriptylline has been used for pain management, physiotherapy or surgical release for contractures, along with skin grafting is the mainstay of treatment in DEB. Drugs like steroids, minocycline, vitamin E, cyclosporine, and phenytoin and retinoid have been tried in the past with no proven efficacy. Gene therapy is the ultimate goal which is likely to become a reality in the near future. Michele De Luca reported the first-ever successful gene therapy for EB. [11]

## CONCLUSION

We report rare cases of EB in a fifty day old male baby who presented with history of recurrent blisters and ulceration over the body since third day of life, born to 2<sup>o</sup> consanguineous parents, with history of similar complaints in the older, female sibling, based on the history and skin histopathology diagnosis of junctional type of EB was made.

## ABBREVIATIONS:

**EB**-Epidermolysis bullosa

**EBS**-Epidermolysis Bullosa simplex

**JEB**-Junctional Epidermolysis Bullosa

**DEB**-Dystrophic Epidermolysis Bullosa

**GABEB**-Generalized atrophic benign epidermolysis bullosa

**BMZ**-Basement membrane zone

## DECLARATION OF CONFLICTING INTERESTS:

No conflicting interests with regard to this case and this case was solely managed in, Owaisi Hospital and Research Centre, Deccan College of Medical sciences.

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