

Junctional Epidermolysis Bullosa (Non-Herlitz Type)

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ABSTRACT

Junctional epidermolysis bullosa (JEB) is a recessively inherited skin blistering disease and is caused due to abnormalities in proteins that hold layers of the skin. Herlitz JEB is the severe form and non-Herlitz JEB is the milder form. This report describes a case of congenitally affected male child aged 5 years, with skin blistering. He has mitten-like hands and soft skin blistering on hands, legs and knees. Symptoms almost disappeared at the age of 3 years but reappeared with increased severity after 6 months. Histopathological examination showed epidermal detachment with intact basal cell layer and sparse infiltrate of lymphocytes with few eosinophils in the dermis. There was no blistering on the moist lining of the mouth and digestive tract. Localized symptoms with less lethality and histopathological examination indicated the presence of non-Herlitz type of JEB. This is the first report which confirms the presence of non-Herlitz junctional epidermolysis bullosa in Pakistan.

Key Words: *Consanguineous marriage. Autosomal recessive. Non-Herlitz junctional epidermolysis bullosa (JEB). Skin blister. Male child. Pakistan.*

INTRODUCTION

Junctional epidermolysis bullosa (JEB) is caused by gene mutations resulting into underproduction of hemidesmosomes that anchor the epidermis to the basement layer, leading to blistering of skin. JEB is an autosomal recessive disorder with a frequency of 1 in 30,000 people.¹ There are two types of JEB. In the more severe form, Herlitz JEB blistering is over large areas of the body also affecting the mucosal lining of the mouth and digestive tract. Granulation tissue in the airway may lead to breathing problems. Granulation tissue bleeds easily and abundantly, making affected infants exposed to serious infections and loss of necessary proteins, minerals, and fluids. Complications may include fusion of the fingers and toes, abnormalities of the fingernails and toenails, and joint aberrations. Due to severity of symptoms, patients usually die within the first year of life.² In the milder form, non-Herlitz JEB blistering may be limited to the particular areas like feet, hands, elbows, knees, and often appears and improves after the newborn period. Other features may include irregular tooth enamel, malformed fingernails and toenails and

alopecia. Most affected children do not have granulation tissue formation, so breathing problems and other severe complications are unusual and patients survive with normal lifespan.³

In the absence of any published report, non-Herlitz JEB had been considered to be absent from Pakistan. Revealing of this case may guide to find more cases of non-Herlitz JEB.

CASE REPORT

A male baby, aged 5 years, presented with complaints of blistering of skin on hands, legs and feet since birth. After one hour of birth, the child had faced shedding of skin on little area of face and within 2 - 3 hours, the skin shed off from parts of legs and hands. Interestingly, the child became almost normal at the age of 3 years. The hands became normal by healing of wounds. But after 6 months, symptoms started again and fusion of the fingers and toes, and abnormalities of the fingernails and toenails appeared. At the age of 5 years, the child had blistering of skin on hands, feet and legs with increased severity. Small patches of denuded skin were found on perioral region. The affected parts were raw, rich red in color and completely devoid of skin. An abrupt transition to normal skin at the boundaries of lesions was clearly notable. The baby's cry was sufficiently loud and he sucked well during feeding. This excluded any problem in pharynx and larynx. No disease symptom was observed in rest of aerodigestive tract or respiratory system. Fingers of hands and toes of feet had become fused (pseudosyndactyly) as a result of blistering. Fingernails and toenails had disintegrated (Figures 1a and 1b). Absence of skin from hands, feet and some parts of legs, including knee, could be observed (Figure 1). Tooth decay was in progress. Disease

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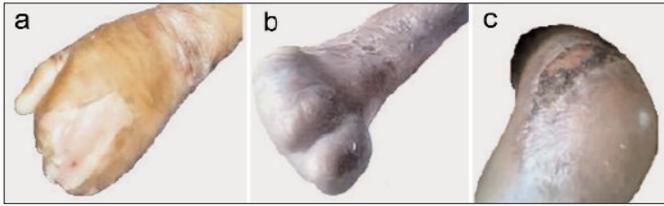


Figure 1: Peripheral body parts of 5 years old boy showing features of non-Herlitz JEB. (a) Fusion of fingers, absence of nails and blistering on hand. (b) Fusion of toes and absence of nails. (c) Partial skin blistering on knee.

distribution concentrated on extremities of body. The parents of affected child were first cousins and belonged to Arain caste. Parents and siblings of the child had no symptom of JEB. Skin was biopsied and submitted for histopathological examination.

Epidermal detachment (with intact basal cell layer) at the level of the lamina lucida of the basement membrane zone and sparse infiltrate of lymphocytes with few eosinophils in the dermis were observed in histopathological examination.

The patient was treated with antibiotic, antifungal and antiallergic combination. Skin ointment with a combination of three antibiotics (Bacitracin, Polymyxin, Neomycin) and a local anesthetic (Lignocaine) was advised to be applied thrice a day. An antifungal ointment was recommended to be applied on wet body parts after taking bath. Anti-histamine syrup was suggested as antiallergic to reduce irritation on skin. A multivitamin syrup (A, C, D and B-complex) was also included in prescription to strengthen the immunity of the patient against infections. The mother was instructed to prevent the baby from trauma to avoid blistering. There was modest improvement in the lesions. Bimonthly examination of patient was advised. Family was asked to refrain from consanguineous marriages.

DISCUSSION

Junctional epidermolysis bullosa (JEB) is a dermatological condition characterized by fragility and blistering of skin. JEB is caused by mutations in genes including *LAMA3*, *LAMB3*, *LAMC2* and *COL17A1*.⁴ Mutations in these genes have been found to contribute to defects in the development of hemidesmosomes or anchoring filaments. Defects in proteins of these genes allow the separation of tissue and blister formation whenever skin faces friction or trauma to an area. In many instances, blistering can occur spontaneously.⁵

Rate of consanguineous marriages is high in Pakistan, which increases the chances of autosomal recessive diseases. Due to lack of awareness, many people do not consult qualified physicians for congenital diseases. This may be a possible reason for absence of any report on non-Herlitz epidermolysis bullosa from Pakistan. This report indicates possibility of occurrence of more cases of non-Herlitz epidermolysis bullosa in Pakistan. Also

there is no genetic test available in Pakistan to detect carrier status for JEB. As warmer climates can exacerbate blistering and Pakistan has warmer climate during the most parts of year, patients of EB may face more harshness of symptoms. In this case, symptoms were present congenitally which were improved at the age of 3 years and patient became almost normal. But after 6 months, the symptoms appeared again and severity of symptoms increased with time. There may be involvement of any environmental factor in increase of this severity. Pseudosyndactyly was present in the patient which was feature of non-Herlitz JEB (3-5%).⁶

Disease symptoms and histopathological examination lead to the diagnosis of non-Herlitz junctional epidermolysis bullosa. Localized blistering, absence of granulation tissue, non-involvement of respiratory and gastrointestinal tracts, absence of blistering on mucous membranes, help to differentiate it from the Herlitz type of JEB. Due to skin blistering, frequency of infection increases; consequently, the patient has to use topical applications containing antibiotics. Affected children usually do not develop granulation tissue, so breathing problems and other severe complications are unusual and patients survive with normal lifespan. Some complications such as sepsis, dehydration, electrolyte imbalances, respiratory failure etc. may lead to death, if left untreated. *LAMA3*, *LAMB3*, and *LAMC2* genes encode the subunit polypeptides of laminin 5; and mutations in these genes have been found to be disease causing in patients with both types of JEB. Mutations in *COL17A1* gene are involved in the non-Herlitz type of JEB.⁷ Some research on Herlitz type of JEB in Pakistani patients has been published;⁸⁻¹⁰ R635X in exon 14 of *LAMB3* gene has been found to be a recurrent Pakistani mutation, which has also been observed frequently in various ethnic groups² (Europeans, Caucasians, Americans, Chileans, Middle Easterners etc.) where it accounts for 40% of all Herlitz JEB mutated alleles.¹⁰ There is no report of non-Herlitz type of junctional EB from Pakistani patients to date. This report reveals the existence of non-Herlitz type of JEB for the first time in Pakistan. This may pave the way to further research on Pakistani patients with a strong potential of any novel variant.

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