CASE REPORT

A CASE REPORT OF DOMINANT DYSTROPHIC EPIDERMOLYSIS BULLOSA IN SIBLINGS: A RARE GENETIC DISORDER WITH A THERAPEUTIC CHALLENGE

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INTRODUCTION: Dominant dystrophic Epidermolysis Bullosa (EB) is a subtype of dystrophic type of Epidermolysis Bullosa. Dystrophic EB are caused by mutations in a single gene, COL7A1, which encodes the anchoring fibril protein, type VII collagen. Immunofluorescence staining of the skin of patients using antitype VII collagen antibodies showed that the normal bright linear staining is absent in severe generalized recessive dystrophic EB, but present in dominant dystrophic EB.^[1-3] The main feature of dominant dystrophic EB is that the skin is generally less fragile than in severe generalized recessive dystrophic EB. Blisters usually follow sharp knocks or glancing blows rather than mild friction, Blisters mainly occur in skin overlying bony prominences, such as the knees, ankles and dorsa of the hands or feet. The most consistent findings are localized scarring with milia formation and dystrophic nails. Nail dystrophy is probably the most important diagnostic feature of the disease, especially in adults, because many patients have only limited scarring, which becomes less noticeable with age.

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Case 1: A 14years old boy (brother) came to skin OPD and presented with history of hemorrhagic bullous lesions over the body parts exposed to trauma since infancy and these lesions were leaving depigmented atrophic scars after rupturing. He was the youngest of four siblings and two among them, as well as his parents, were asymptomatic; only his elder sister had similar lesions. On examination multiple hemorrhagic bullae were present over trauma prone sites like elbow, shin of tibia, scapular region etc.

Scars healed with milia formation. Teeth were maloccluded and toe nails showed dystrophy with vestigial nail spurs in some. Oral mucosa had mild erosions with dysphagia for solid food occasionally. Scalp showed patchy cicatricial alopecia. Patient had never experienced any pruritus or any other symptoms over these lesions

Case 2: A 25years old female (sister) presented with some hemorrhagic bullous lesions over the exposed body parts since 1year of age which ruptured leaving depigmented atrophic scars. From last 2-3 years severity and number of lesions had reduced. Scalp showed subtotal cicatricial alopecia. Toe nails were dystrophic and malformed, especially of great toe. Milia formation was noted in scars. No complaints of dysphagia and deafness present.

Both patients were born out of non-consanguineous marriages and had no lesions at birth. Mode of inheritance pointed towards an autosomal dominant pattern. None of them had allopapuloid lesions. Nails, teeth mucosa were involved in both cases with significant degree.

Systemic examination findings and baseline biochemical parameters were normal. Histopathological examination of lesional skin from each patient had a similar picture with

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demonstrable hyperkeratosis, acanthosis with subepidermal bullae along with inflammatory infiltrates in the dermis.

Direct immunofluorescence test, electron microscopy and gene mutation studies could not be done due to limited resources.

DISCUSSION: It was first described as 'Erblichen pemphigus' by von Hebra in 1870.^[4] Epidermolysis bullosa (EB) comprises a group of genetically determined skin fragility disorders characterized by blistering of the skin and mucosae following mild mechanical trauma. The alternative term therefore is mechanobullous diseases.^[5] The name epidermolysis bullosa, as originally used by Koebner^[6] in 1886. The ultra-structural level of tissue cleavage (blister formation) in the skin is distinctive in the three major groups of EB: EB simplex, junctional EB and dystrophic EB.

The dystrophic forms of EB are characterized by skin fragility, blistering, scarring, nail changes and milia formation. Unlike junctional EB, there are both autosomal recessive and autosomal dominant subtypes. In contrast to EB simplex or junctional EB, in which several genes are now recognized in the pathogenesis of these disorders, both autosomal dominant and recessive forms of dystrophic EB are caused by mutations in a single gene, COL7A1, which encodes the anchoring fibril protein, type VII collagen. Sub-dividing the majority of cases of dominant dystrophic EB into the mutually exclusive Cockayne–Touraine or Pasini variants.

In 1928, Pasini described a single family whose EB was distinguished by the presence of numerous white papules that he called 'albopapuloid' lesions. Ultra structurally; the level of blistering or tissue cleavage in all dystrophic forms of EB is immediately below the lamina densa of the epidermal basement membrane, at a site normally occupied by anchoring fibrils. Dominant dystrophic forms of EB have been shown exclusively to be associated with glycine substitutions within the triple helical collagenous domain of the type VII molecule, characterized by a Gly-X-Y repeating amino-acid sequence.^[7,8]

This mutation is the most common COL7A1 mutation in dominant dystrophic EB throughout the world. Clinically, it is often impossible to distinguish this form of dominant dystrophic EB from the localized recessive dystrophic forms, making genetic counseling impossible in the absence of a positive family history or accurate molecular diagnosis. Management includes palliative treatment, avoidance of trauma, antibiotics with good nursing care.

In our case we gave precaution from trauma, palliative treatment and nutritional support given with autologous skin grafts on non-healing lesions.

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