



Case Report

Localised Epidermolysis Bullosa Simplex in Mono-Zygotic Twins

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ABSTRACT

Epidermolysis bullosa simplex is a rare blistering disorder without any curable treatments, mainly inherited in an Autosomal Dominant fashion. It is even rarer in twins. It is characterised by cutaneous fragility and blister formation after minimal trauma. It typically presents with localised, mild, acral blistering and normal life expectancy. Its localised presentation, confined to the palms and soles and association with punctate callosities, may lead to misdiagnosis of Palmoplantar warts. We report two cases of localised EBS occurring in mono-zygotic twins with no family history.

Keywords: Epidermolysis bullosa, Epidermolysis bullosa simplex, Mechanobullous disorders, Punctate callosities, Twins

INTRODUCTION

Epidermolysis bullosa (EB) is a rare genodermatosis, characterised by mucocutaneous fragility and blister formation after minor friction or trauma.^[1,2] EB is classified based on the level of split and is divided into four types, that is EB Simplex (EBS), Junctional EB (JEB), Dystrophic EB (DEB) and mixed EB (Kindler syndrome).^[3] EBS is the most common type of EB, accounting for 75–85% of cases of EB in the Western world.^[4] EBS is usually caused by pathogenic variants in the keratin genes (*KRT5* and *KRT14*) with resultant formation of a cleavage plane at the level of the basal keratinocytes. Localised EBS (formerly known as Weber–Cockayne EBS), usually associated with little or no extracutaneous involvement, is the mildest and most common form of EBS.^[5] In this report, we describe two cases of Localised EBS occurring in mono-zygotic twins with no family history.

CASE REPORT

Two 16-year-old monozygotic twin females presented with recurrent painful blisters on their hands and feet, starting at 3–4 years of age. The blisters initially contained clear fluid, later becoming cloudy or red-black before rupturing and forming black scabs that eventually healed, leaving white patches. Over time, thickened, raised lesions developed on the soles. The blisters worsened in hot weather, and both patients experienced excessive sweating in the palms and soles. No family history of similar conditions was noted, though the parents were consanguineous.

On examination, both patients had tense bullae with cloudy fluid, brownish crusts on their feet and soles and hypopigmented macules on the palms and hands. Hyperkeratotic calluses with

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Figure 1: Clinical presentation of Patient 1. (a) Hypopigmented macules on the hands (blue arrow). (b) Tense bullae with cloudy fluid and overlying brownish crusts on the feet (blue arrow). Nail changes, including onychodystrophy and subungual hyperkeratosis (red arrow). (c) Hyperkeratotic calluses with brown crusts on the soles (blue arrow).

brown crusts were also seen on the soles. Nail changes included onychodystrophy and subungual hyperkeratosis. General examination was normal, with no mucosal or hair involvement [Figures 1 and 2].

Laboratory tests, including complete blood count and liver/renal function, were normal. Histopathology revealed a suprabasal cleft in the epidermis without inflammation [Figure 3]. Direct immunofluorescence was negative. Due to high costs, electron microscopy and genetic testing were not performed.

The patients were counselled about the chronic nature of the condition and lack of curative treatments. Topical fusidic acid cream was prescribed for lesions, and protective footwear was recommended. Parental consent for anonymised photographs was obtained for publication.

DISCUSSION

It is acknowledged that hereditary elements and genetic mutations can contribute to the predisposition to EB group of disorders. The defining characteristics of EB encompass



Figure 2: Clinical presentation of Patient 2. (a) Hypopigmented macules on the palms (blue arrow). (b) Tense bullae with clear fluid over the finger dorsa (blue arrow). Nail changes, including onychodystrophy (red arrow). (c) Hyperkeratotic calluses with brown crusts on the soles (blue arrow).

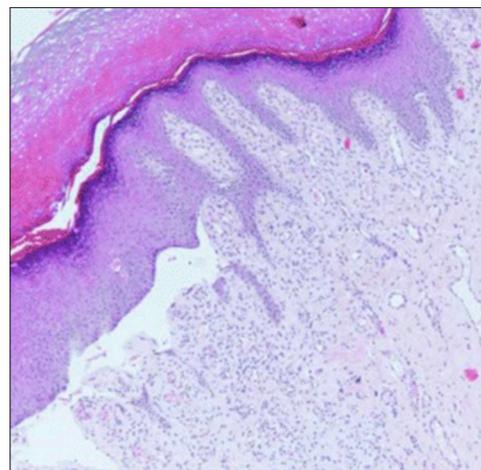


Figure 3: Histopathology: Suprabasal cleft in the epidermis, without inflammation (Haematoxylin and eosin stain, 10x).

mucocutaneous blisters resulting from tissue injury which leads to erosion and ulceration, typically resulting from frictional trauma. The EB group of disorders is classified based on the level of split and is divided into four types – EBS,

JEB, DEB and mixed EB (Kindler syndrome). According to epidemiological data, EBS emerges as the predominant form of EB, constituting over 70% of all EB cases. According to the most recent classification, there are 14 EBS subtypes. The three primary subtypes include Localised EBS (Weber–Cockayne), intermediate (generalised intermediate/Koebner) and severe (Dowling-Meara).^[2,3] Common features frequently observed in EBS include symptoms that manifest early in life (during early childhood), and blistering symptoms are often provoked by elevated air temperatures. In our case report, these symptoms were aggravated by hyperhidrosis. In EBS, occurrences of mucosal symptoms and nail damage are infrequent. It is inherited in an autosomal dominant manner in most cases. In some cases, it can be inherited in an autosomal recessive manner. Electron microscopy is the gold standard diagnostic method for EB. It provides a more precise assessment of blistering levels compared to biopsy and immunofluorescence examinations. In addition, electron microscopy offers the capability to visualise cells and subcellular structures that conventional (ultrastructural) microscopes cannot access. In this instance, direct immunofluorescence is utilised to eliminate potential differential diagnoses of EB. The findings from the direct immunofluorescence analysis showed that no presence of immunoglobulin G and C3 deposits in the basement membrane zone, thus excluding the diagnosis of bullous pemphigoid and EB acquisita. Another supplementary examination for determining the type of EB is genetic testing. Research indicates various genetic mutation causes for each EB type. Most common mutation in EBS is the *KRT5* gene, which codes for Keratin, type II cytoskeletal 5 protein.^[2] A novel *de novo* c.2T>C (p.M1T) variant in *KLHL24* was identified by Xu *et al.* (2021) and linked to EBS in twin boys, emphasising the importance of early genetic diagnosis for effective management.^[6] Most EB therapy is carried out in a supportive manner. Treatments, including wound care, infection control, adequate nutrition and genetic counselling, are available, alongside the potential for novel therapeutic approaches like gene therapy in the near future.^[5,7,8]

EBS occurring in twins without a family history of EBS is an exceedingly uncommon occurrence, hence the report due to its rarity.

CONCLUSION

EBS is a genetically driven disorder characterised by mucocutaneous blistering, with EBS accounting for over 70% of EB cases. Diagnostic precision is achieved through electron microscopy and genetic testing. The occurrence of EBS in twins without a family history is exceedingly rare, emphasizing the importance of early genetic diagnosis. While current treatment focuses on supportive care, advancements in gene therapy hold promise for future management.

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