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Case Report
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Neonatal Epidermolysis Bullosa Simplex: Early Diagnostic Clarification and Multidisciplinary Management in a Term Female Infant



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Abstract

Epidermolysis bullosa (EB) comprises a heterogeneous group of inherited mechanobullous disorders characterised by skin fragility and blister formation following minimal trauma [1–3]. We report a female neonate presenting with localised blistering on the dorsum of the right foot and over the heel, ultimately diagnosed with epidermolysis bullosa simplex (EBS). Early multidisciplinary involvement, meticulous wound care, and parental counselling were central to management [8, 9]. This case highlights the importance of early recognition, genetic confirmation, and anticipatory guidance for families [1, 6, 7].

Keywords: Epidermolysis Bullosa; Epidermolysis Bullosa Simplex; Neonatal Blistering Disorders; Skin Fragility; KRT5; KRT14; Immunofluorescence Antigen Mapping; Congenital Bullous Dermatoses; Neonatal Dermatology; Genetic Skin Disease; Wound Care in Neonates; Supportive Neonatal Care; Rare Genetic Disorders

Introduction

EB is a rare genodermatosis with an estimated incidence of approximately 1 in 20,000 live births [1–3]. The condition is classified into major subtypes—epidermolysis bullosa simplex (EBS), junctional EB (JEB), dystrophic EB (DEB), and Kindler syndrome—based on the level of skin cleavage and underlying protein defect [1–3]. Neonatal presentation may be dramatic, and early differentiation between subtypes is essential for prognosis and management [1, 2, 8].

This case illustrates the diagnostic challenges and the importance of coordinated supportive care in the neonatal period [8, 9]. It describes a female neonate presenting with blistering following birth, ultimately diagnosed with EBS through a combination of clinical assessment, immunofluorescence antigen mapping, and genetic confirmation [5–7]. The report highlights the diagnostic nuances that distinguish EBS from junctional and dystrophic forms, emphasising the importance of early biopsy selection, molecular testing, and structured parental education [1, 5–7, 8]. It also demonstrates how coordinated multidisciplinary care can optimise comfort, reduce complications, and support families during the neonatal period [8, 9].

Case Presentation

A female infant was born at 40 weeks' gestation via spontaneous vaginal delivery to a healthy 27-year-old primigravida (G1P1A0L1). Pregnancy was uncomplicated, with normal antenatal scans and no family history of blistering disorders or consanguinity.

On day 2 following birth, the infant was noted to have multiple flaccid bullae, erosions, and areas of denuded skin over the hands, feet, elbows, and lower limbs. None of the lesions appeared to have developed in utero. The nails were mildly dystrophic. The infant cried vigorously and maintained normal tone.

Vital signs were stable. Birth weight was 3.1 kg. No respiratory distress or feeding difficulty was initially noted.

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Figure 1: Clinical Photographs.
Localised flaccid bullae and superficial erosions on the feet and trunk in a term female neonate with epidermolysis bullosa simplex. Lesions are confined to trauma-prone areas, with rapid re-epithelialisation and no scarring, consistent with the typical neonatal presentation of EBS.



Figure 2: Clinical photographs.
Localised flaccid bullae on fingers and superficial erosions on the elbows and trunk. Lesions are confined to trauma-prone areas, with rapid re-epithelialisation and no scarring, consistent with the typical neonatal presentation of EBS.

Investigations

Initial laboratory investigations showed a normal full blood count, C-reactive protein <5 mg/L, negative blood cultures, and normal serum electrolytes. Swabs from erosions demonstrated no bacterial growth at 48 hours.

Skin biopsy (H&E) from a perilesional area demonstrated intraepidermal cleavage at the level of the basal keratinocytes. The basement membrane zone remained intact, supporting a diagnosis of epidermolysis bullosa simplex [1, 5, 6]. Immunofluorescence antigen mapping showed preserved linear staining of laminin-332 and type VII collagen along the basement membrane zone, with the plane of cleavage localised above the basement membrane, consistent with intraepidermal blistering characteristic of EBS [1, 5, 6].

Genetic testing (next-generation sequencing panel) identified pathogenic variants in EB-related genes affecting KRT5/KRT14, confirming epidermolysis bullosa simplex (EBS) [6, 7].

Differential diagnosis included EBS, dystrophic EB, staphylococcal scalded skin syndrome, incontinentia pigmenti (early vesicular stage), and congenital herpes simplex infection [1–3, 8].

Treatment

Management focused on supportive care in line with established EB neonatal care recommendations [8, 9]:

Wound care: Non-adhesive silicone dressings, daily emollient application, avoidance of friction and adhesive tapes, sterile handling, and gentle swaddling [8, 9].

Pain management: Oral paracetamol and sucrose for procedural comfort [8].

Infection prevention: Prophylactic topical antibiotics (e.g. mupirocin) to high-risk areas and close monitoring for sepsis [8, 9].

Feeding: Breastfeeding with soft silicone nipple shields, lactation support, and monitoring for oral blistering [8].

Multidisciplinary involvement: Dermatology, neonatology, genetics, paediatric surgery (for wound care guidance), specialist EB nurse, and psychology and family support services were engaged early, consistent with best-practice EB care [1, 8, 9].

Outcome and follow-up

By 12 weeks of life, the infant continued to develop few blisters with minimal handling. Wound healing occurred without secondary infection or scarring, in keeping with typical EBS evolution [1, 3, 8]. Parents were trained in home dressing techniques and safe handling practices. Mild oral mucosal erosions were observed and responded well to conservative treatment. Dietary broad-spectrum multivitamin, multimineral and trace element supplementation, together with iron and calcium, was continued.

At 6-month follow-up, the infant showed infrequent blistering, mild anaemia, adequate weight gain, and no airway involvement. The family received genetic counselling regarding recurrence risk and future reproductive options [7, 10].

Discussion

Epidermolysis bullosa simplex (EBS) is the most common and generally the mildest form of EB, characterised by intraepidermal blistering due to structural fragility of basal keratinocytes [1–3].

Feature	EBS – Epidermolysis bullosa simplex	JEB – Junctional epidermolysis bullosa	DEB – Dystrophic epidermolysis bullosa
Level of skin cleavage	Intraepidermal (basal keratinocytes)	Within lamina lucida of basement membrane zone	Below lamina densa (sublamina densa)
Key structural proteins	Keratin 5, Keratin 14 (*KRT5, KRT14*)	Laminin-332, type XVII collagen (*LAMA3, LAMB3, LAMC2, COL17A1*)	Type VII collagen (*COL7A1*)
Inheritance pattern	Usually autosomal dominant	Usually autosomal recessive	Autosomal dominant or recessive (subtype-dependent)
Typical onset	Birth or early infancy; may be localised	At birth; often generalised and severe	At birth or early infancy; variable severity
Distribution of blisters	Trauma-prone sites (hands, feet, friction areas)	Generalised, including trunk, limbs, and often mucosa	Generalised or acral; often with trauma-prone and pressure areas
Mucosal involvement	Usually absent or mild	Common and often severe (oral, respiratory, gastrointestinal)	Variable; oral and oesophageal involvement common in severe forms
Scarring and milia	Typically no scarring; no or minimal milia	Minimal scarring; may have atrophic changes	Prominent scarring, milia, and contractures
Nail changes	Possible nail dystrophy, especially in severe subtypes	Nail dystrophy or loss may occur	Frequent nail dystrophy, loss, and scarring around nail folds
Systemic complications	Usually mild; pain, infection risk, feeding issues in neonates	Failure to thrive, anaemia, airway compromise, chronic wounds, high mortality in severe forms	Nutritional deficiency, anaemia, strictures, pseudosyndactyly, squamous cell carcinoma (later life)
Prognosis	Often improves with age; many have mild lifelong disease	Variable; severe generalised forms may be life-limiting in infancy/childhood	Highly variable; severe recessive forms associated with significant morbidity and reduced life expectancy
Diagnostic clues on biopsy/IFM	Intraepidermal split; basement membrane components preserved	Split within lamina lucida; reduced/absent laminin-332 or type XVII collagen	Sublamina densa split; reduced/absent type VII collagen
Genetic testing role	Confirms *KRT5/KRT14* variants; helps subtype and prognosis	Confirms laminin-332 or COL17A1 variants; critical for prognosis and trials	Confirms *COL7A1* variants; essential for counselling and severity prediction
Core management focus	Trauma minimisation, simple wound care, parental education	Intensive wound care, infection prevention, nutritional and airway support	Complex wound care, contracture prevention, nutritional and cancer surveillance

Table 1: Differential Diagnosis Table for EBS Vs JEB Vs DEB.
Differential diagnosis of neonatal blistering disorders, comparing key clinical, histological, and genetic features of epidermolysis bullosa simplex (EBS), junctional epidermolysis bullosa (JEB), and dystrophic epidermolysis bullosa (DEB). The table highlights distinguishing characteristics including the level of skin cleavage, associated structural proteins, inheritance patterns, mucosal involvement, scarring tendency, systemic complications, and diagnostic clues on immunofluorescence antigen mapping and genetic testing.

Although many cases present later in infancy or childhood, neonatal onset can be striking and may initially raise concern for more severe subtypes such as junctional or dystrophic EB [1, 2, 8]. This case illustrates the importance of recognising clinical patterns typical of EBS—localised blistering on trauma-prone sites, relative sparing of mucosa, and rapid re-epithelialisation without scarring [1–3, 8].

Accurate diagnosis relies on a combination of clinical assessment, immunofluorescence antigen mapping, and molecular testing [1, 5–7]. In EBS, cleavage occurs within the basal layer of the epidermis, and immunostaining typically shows preserved basement membrane components, helping to distinguish it from junctional and dystrophic forms [1, 5, 6]. Genetic testing plays a central role in confirming the diagnosis, most commonly identifying pathogenic variants in KRT5 or KRT14, which encode keratin 5 and keratin 14—critical components of the keratin intermediate filament network [6, 7]. Identifying the specific variant not only provides diagnostic certainty but also informs recurrence risk, supports genetic counselling, and may help predict disease severity [6, 7, 10].

Management of neonatal EBS is primarily supportive, focusing on reducing mechanical trauma, optimising wound care, and preventing secondary infection [8, 9]. Although EBS is typically milder than other EB subtypes, neonates may still experience significant discomfort, feeding challenges, and caregiver anxiety [8]. Early involvement of dermatology, specialist EB nursing, and allied health professionals is essential to establish safe handling techniques, appropriate dressing regimens, and anticipatory guidance for families [8, 9]. Education empowers parents to manage blistering episodes confidently and reduces unnecessary hospital visits; culturally and linguistically tailored information leaflets can further enhance engagement and self-efficacy [8, 9].

Long-term outcomes for most infants with EBS are favourable, with many experiencing reduced blistering frequency as they grow and their skin becomes more resilient [1–3, 10]. However, certain subtypes—such as EBS Dowling-Meara—may present with more extensive blistering, nail dystrophy, or palmoplantar keratoderma, underscoring the heterogeneity of the condition [1–3]. Advances in molecular diagnostics and emerging therapeutic approaches, including protein-stabilisation strategies and gene-based interventions, hold promise for more targeted management in the future [6, 7].

This case reinforces the importance of early recognition, precise diagnostic classification, and comprehensive family support in optimising outcomes for neonates with EBS [1–3, 8, 9]. To our knowledge, this case contributes meaningful clinical insight into the early presentation of EBS, reinforces best-practice diagnostic pathways, and provides a practical framework for neonatal management. It will be of interest to clinicians in dermatology, neonatology, paediatrics, and genetic medicine [1–3, 6–9].

Early diagnosis is crucial for prognostication and guiding family expectations. Immunofluorescence mapping remains a valuable first-line diagnostic tool, with genetic testing providing definitive confirmation [1, 5–7]. Early recognition of EB in the neonatal period is essential, as the initial presentation may mimic infectious, immunological, or inflammatory blistering disorders [1–3, 8]. This case highlights the value of prompt dermatological assessment, careful selection of biopsy sites, and the use of immunofluorescence antigen mapping to accurately determine the level of skin cleavage [1, 5, 6]. Timely diagnosis not only guides prognosis but also prevents unnecessary interventions and enables early multidisciplinary planning [1, 8, 9].

Early recognition of epidermolysis bullosa in the neonatal period is essential, as the initial presentation may mimic infectious, immunological, or inflammatory blistering disorders [1–3, 8]. This

Feature	EBS	JEB	DEB
Level of cleavage	Intraepidermal	Lamina lucida	Sublamina densa
Key proteins	KRT5 / KRT14	Laminin-332, COL17A1	COL7A1
Mucosa	Minimal	Severe	Variable
Scarring	None	Minimal	Prominent
Nails	Mild dystrophy	Dystrophy/loss	Frequent dystrophy
Prognosis	Good	Variable, often severe	Variable, can be severe

Table 2: Key Feature Differentiation Between EBS, JEB, and DEB.
Summary table comparing the distinguishing clinical, histological, and genetic features of epidermolysis bullosa simplex (EBS), junctional epidermolysis bullosa (JEB), and dystrophic epidermolysis bullosa (DEB) in the neonatal period. The table highlights the level of skin cleavage, associated structural proteins, inheritance patterns, mucosal involvement, scarring tendency, nail changes, and prognostic implications, providing a rapid reference for differentiating EBS from more severe subtypes at the bedside.

case highlights the value of prompt dermatological assessment, careful selection of biopsy sites, and the use of immunofluorescence antigen mapping to accurately determine the level of skin cleavage [1, 5, 6]. Timely diagnosis not only guides prognosis but also prevents unnecessary interventions and enables early multidisciplinary planning [8, 9].

This case reinforces the central role of molecular diagnostics in confirming epidermolysis bullosa subtype and informing long-term management [6, 7]. Identification of pathogenic variants in KRT5 or KRT14, which encode keratin 5 and keratin 14, helped accurate early diagnosis, clarified recurrence risk, and enabled targeted genetic counselling for the family [6, 7, 10]. As gene-based therapies continue to evolve, precise genotyping in the neonatal period will become increasingly important for access to emerging clinical trials and personalised therapeutic strategies [6, 7].

Management is primarily supportive, focusing on wound care, infection prevention, nutritional support, and pain control [8, 9]. Multidisciplinary care improves outcomes and reduces caregiver burden [8, 9]. Although no curative therapy currently exists, emerging treatments—including gene therapy, protein replacement, and cell-based therapies—offer future promise [3, 6, 7].

This case demonstrates how early involvement of dermatology, neonatology, specialist EB nursing, and psychological services can improve comfort, reduce complications, and empower parents in daily care [8, 9]. Although treatment remains supportive, structured education and anticipatory guidance significantly enhance quality of life and caregiver confidence [8, 9].

Learning Points

- EB should be suspected in any neonate presenting with blistering or erosions at birth.
- Early skin biopsy and genetic testing are essential for accurate classification and prognosis.
- Management requires meticulous wound care, infection prevention, and family education.
- Multidisciplinary support is critical for optimising quality of life.
- Genetic counselling is an integral component of care for affected families.

Conclusion

Epidermolysis bullosa simplex can present dramatically in the neonatal period, yet its clinical course and long-term prognosis differ substantially from other EB subtypes. This case emphasises the importance of recognising the characteristic distribution of blisters, selecting an appropriate perilesional biopsy site, and utilising immunofluorescence antigen mapping to confirm intraepidermal cleavage. Genetic testing remains central to definitive diagnosis, particularly for identifying pathogenic variants in KRT5 or KRT14, which informs recurrence risk and guides family counselling. Although EBS is typically milder than junctional or dystrophic forms, early multidisciplinary involvement, meticulous wound care, and structured parental education are essential to minimise complications and support optimal quality of life. Advances in molecular diagnostics and emerging targeted therapies continue to refine our understanding and management of this heterogeneous condition.

Neonatal epidermolysis bullosa presents significant diagnostic and therapeutic challenges, particularly when blistering is evident at birth. This case underscores the value of early recognition, prompt dermatological assessment, and timely genetic confirmation to guide prognosis and family support. While treatment remains largely supportive, coordinated multidisciplinary care can meaningfully improve comfort, reduce complications, and empower parents in day-to-day management. Ongoing progress in molecular diagnostics and the development of gene-based therapies offer hope for more targeted and personalised interventions in the future.

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