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Case Report

Palliative Care in Epidermolysis Bullosa: Beyond Skin

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Abstract

Generalized severe junctional epidermolysis bullosa (JEB) is the rarest and most severe form of epidermolysis bullosa (EB), often leading to a 90% mortality rate within the first year of life. This case report describes a 35-week premature male infant diagnosed with JEB, and highlights the critical role of pediatric palliative care teams (PPCT) in managing complex clinical challenges. Initially treated for suspected bullous impetigo, JEB was confirmed through genetic testing at one month old. Patient presented with severe symptoms, including extensive mucocutaneous lesions, impaired wound healing, sepsis, anemia, protein loss, and failure to thrive. Despite pharmacological interventions, including albumin infusions, red blood cell transfusions, oral iron supplementation, IgG and plasma infusions, and rounds of antibiotics, the patient's condition deteriorated overtime. Following the JEB diagnosis, invasive procedures were withheld to prioritize comfort. Pain management was maintained with continuous morphine infusion and oral gabapentin until venous access was lost. Afterwards an oral-only analgesic regimen with morphine and transmucosal fentanyl provided relief, as transdermal or subcutaneous analgesia was not feasible due to extensive skin involvement. Patient died at two months old, one month after admission, and 48 hours after starting sedoanalgesia. This case underscores the importance of early PPCT involvement for symptomatic management and holistic support, highlighting the need for timely genetic diagnosis to guide care decisions. Despite significant challenges, the palliative approach effectively met the needs of the patient and family, emphasizing the value of compassionate care in the management of terminal conditions such as JEB.

***Keywords:** Epidermolysis Bullosa, Junctional; Palliative Care; Wound Healing; Referral and Consultation; Morbidity*

Introduction

Inherited epidermolysis bullosa (EB) encompasses a diverse group of genodermatosis characterized by mucocutaneous blisters occurring spontaneously or after minimal trauma. [1]

Generalized severe junctional epidermolysis bullosa (JEB) is the rarest (<0.08 cases/million live births) and severest type of EB, [2] with a 90% mortality rate in the first year of life. [1] This condition has multisystemic involvement with loss of proteins, fluids and iron, resulting in impaired wound healing, anemia, gastro-intestinal and respiratory morbidity, failure to thrive and sepsis. [2]

This case highlights the impact of early referral of these children to pediatric palliative care teams (PPCT) given multiple clinical challenges and complex care burden.

Case Presentation

A 35-week premature male infant, 32 days old, was transferred to a tertiary hospital with a clinical diagnosis of EB. The pregnancy and spontaneous vaginal delivery were uneventful. At 72 hours of age, he was admitted to the neonatal intensive care unit with suspected bullous impetigo. Due to atypical presentation, EB was suspected and genetic EB NGS panel was performed.

At admission he was on iv vancomycin for Staphylococcus epidermidis sepsis. Mucocutaneous lesions affected around 40% of the body surface, including the oropharyngeal mucosa, causing a hoarse cry. His analgesic regimen consisted of scheduled iv acetaminophen (15mg/kg, qid) and rescue iv morphine (0.03mg/kg/dose) before wound treatment. Non-nutritive suction and minimal manipulation were employed to minimize discomfort and trauma. He received mixed breastfeeding and formula feeding to mitigate defecation-related skin damage. Due to uncontrolled pain, he rotated to scheduled iv morphine (0,1 mg/kg/dose qid) and was transferred to a positive pressure room for sepsis prevention and temperature control.

On day 4, laboratory findings showed increased C-reactive protein (20,5 mg/dL), hypoalbuminemia (1,4 g/dL), hypogammaglobulinemia (IgG <1,08 g/L) and anemia (8,7 g/dL). Despite pharmacological interventions, including albumin infusions (daily for 3 days and then every 72h), 3 red blood cells transfusions, oral iron supplementation, IgG and plasma infusions (due to factor XI, anti-thrombin and fibrinogen deficit) there was clinical deterioration.

Skin lesions progressed, becoming more exudative and hemorrhagic, associated with feeding difficulties, prompting an adjustment in morphine (0,2 mg/kg/dose qid) and initiation of parenteral nutrition.

Two weeks later, continuous infusion of morphine (0,02 mg/kg/h) with rescue boluses (0,1 mg/kg, PRN) and oral gabapentin (5 mg/kg/dose 3id) were initiated for pain management. Alongside, iv gentamicin (7,5 mg/kg/day) was started to promote skin healing. The child underwent complex skin treatments, particularly impressive given the extensive wounds covering almost 90% of the body surface, figure 1 and 2. Pain-related wound care required multiple rescue doses of morphine. These were very stressful moments for parents and the healthcare team, as they realized the seriousness and the rapid clinical deterioration. Multiple rounds of antibiotics were completed to address bacterial superinfection and mitigate the elevated risk of sepsis.

Genetic diagnosis of Generalized severe junctional EB - one of the worst prognosis variants of EB, (c.283C>T p. (Arg95*) homozygote in LAMC2 gene) - was confirmed. A family conference was scheduled with PPCT for decision-making and advance care planning. Given the prognosis, both parents and PPCT focused on prioritizing comfort care and pain management. The decision to withhold invasive procedures in case of further deterioration was established. Parents' psychological, social and spiritual support were reinforced, and a memory-making plan was encouraged.

Three days after genetic diagnosis, the second central line access was lost. An oral-only analgesic regimen with morphine (with progressively increasing doses) supplemented with transmucosal fentanyl (10 mcg/kg/dose during dressing changes and every 4h PRN) was adopted. Due to his condition, transdermal or subcutaneous analgesia was not feasible. Other palliative measures included furosemide and fluid restriction for edema, dimetindene for pruritus, and off -label use of cannabidiol (2.5 mg/kg/dose, bid) for pain relief, though without response. Nutritional supply was kept with continuous nasogastric tube (NGT) feeding with a mixture of elemental supplement and oral rehydration solution.

Clinical deterioration and significant muscle stiffness prompted a shift to prioritizing end-of-life care. Deprescribing ineffective or inadequate medications (cannabidiol, iron, albumin supplements, furosemide, antibiotics) was started. Wound treatments were only made when needed and enteral feeding was also stopped. In last 48 hours, enteral (by NGT) sedoanalgesia with morphine (maximum 0.5 mg/kg/dose) and midazolam (0.4 mg/kg/dose) with very frequent boluses, were satisfactory to achieve apparent comfort.

He died at two months old, one month after admission and about 48h after sedoanalgesia was started. Parents were always present throughout his admission and were given all the support by the PPCT.

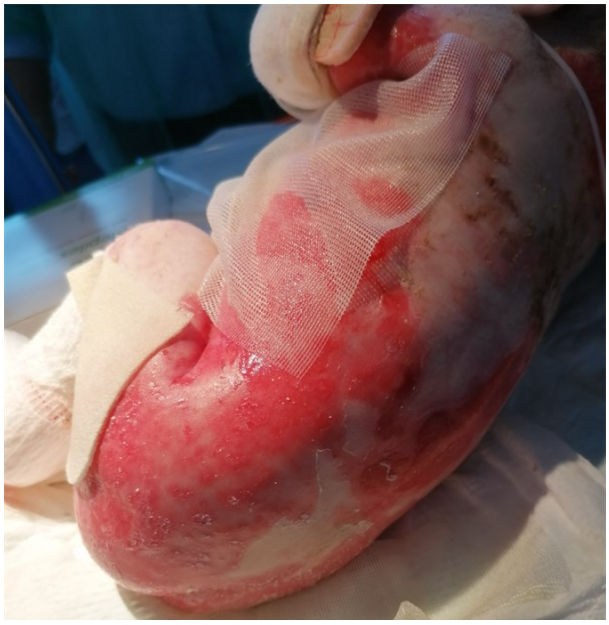

Figure 1. *Extensive ulcerative exudative lesion occupying most of the trunk.*

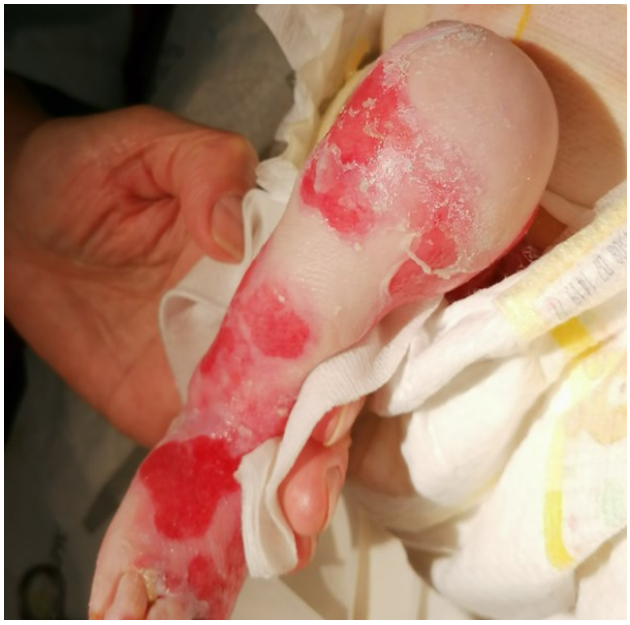

Figure 2. *Deep ulcerated lesions on the feet and legs.*

Discussion

This case presented significant challenges for several reasons:

1) The multisystemic impact and extent of skin damage;
2) Severe pain management;
3) Difficulty in maintaining venous access;
4) The struggle in managing parents and medical team's expectations, especially before diagnosing one of the most severe types of EB. The complexity of this case underscores the importance of timely referral to PPCT, not only to optimize symptomatic control but also for a holistic approach and support in the decision-making process, even before the definitive diagnosis is known.

Treatment initially focused on wound healing and symptomatic control. Albumin, plasma and IgG infusions aimed to restore losses from protein-losing enteropathy and exudative wounds. Despite blood cell transfusions, anemia persisted, which is one of the most frequent complications of this condition. [3] Although adequate weight gain is associated with longer survival, assessing it became impractical due to increased dressings. [1]

Parenteral nutrition emerged as the preferred choice due to elevated metabolic demands, malabsorption issues and oral feeding difficulties. Although enteral route, with a NGT, remains controversial [3], after losing venous access and before end-of-life period, it was the reasonable solution for nutrition, hydration and pharmacological support.

The use of the enteral route as the primary method for symptomatic control is sparsely documented in the literature. [4,5] However, reported cases, including our own, highlight the effectiveness of the enteral route in managing pain and symptoms, underlining the role of non-invasive but suitable approaches. Although subcutaneous medications are described in the literature, the large extension of wounds in our case made their use impractical. [5]

Genetic diagnosis helped to facilitate the adjustment of goals of care, focusing the importance of PPCT involvement with the patient and the family. Reflection and continuous assessment of the benefits and burdens of each intervention were crucial to better management of such a difficult case. It was vital that the wound management strategy, encompassing the regularity of dressing adjustments, was aligned with comfort care priority.

In the last days of life, sedoanalgesia and psychological support became paramount. Early, transparent communication (even before definitive diagnosis) about the clinical course enabled parents to understand the disease's nature, adjust expectations and better accept the serious prognosis.

Despite significant challenges and very demanding care burdens for both health professionals and parents, the palliative approach lead by dedicated professionals proved crucial in meeting the family's needs, who valued the effective pain relief, as well as bereavement construction process.

Conclusion

EB encompasses diverse clinical manifestations, prognoses and outcomes, highlighting the critical role of genetic diagnosis in directing the therapeutic approach and preventing futile measures. While significant, it should not delay the early integration of palliative care into the multidisciplinary team. This case exemplifies its crucial importance, particularly in managing the complexities of patient care, notably in addressing pain and wound care, as well as providing psychosocial support.

Conflict of Interest

The authors declare that they have no competing interests.

Acknowledgement

None.

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