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Case report

Herlitz epidermolysis bullosa in the paediatric patient: Anaesthetic implications[☆]



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ABSTRACT

Epidermolysis bullosa is a group of inherited disorders characterized by blistering of the skin and mucous membranes as a result of friction or minor trauma. Clinical, genetic and histopathological criteria are involved in its diagnosis, distinguishing between simple (SEB), junctional (JEB) and dystrophic (DEB) forms. Among them, the junctional forms, especially de Herlitz JEB type and the one associated with pyloric atresia, pose a major challenge to the anaesthetist, given the high comorbidity.

We report the case of a newborn diagnosed with Herlitz epidermolysis bullosa, taken to nasosejale transanastomotic tube placement due to congenital intestinal obstruction.

We focused on the main features in the anaesthetic management of these patients considering the preparation of the monitoring and surgical equipment to prevent skin damage by friction and the difficulties establishing venous accesses and airway management.

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Epidermolisis bullosa de Herlitz en el paciente pediátrico: implicaciones anestésicas

RESUMEN

La epidermolisis bullosa (EB) constituye una serie heterogénea de trastornos genéticos cuyo rasgo común es la facilidad para la formación de ampollas en la piel y mucosas ante el masaje mínimo roce o traumatismo. En su diagnóstico intervienen criterios clínicos, genéticos e histopatológicos, distinguiéndose entre formas simples (EBS), junctionales (EBJ) y distroficadas (EBD). De entre ellas, las formas junctionales, especialmente la EBJ tipo Herlitz y la asociada a atresia pilórica, suponen un reto en el manejo por parte del anestesiólogo dada su importante comorbilidad asociada.¹

Palabras clave:

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Se presenta el caso de un neonato diagnosticado de epidermolisis bullosa tipo Herlitz, propuesto para colocación de sonda nasoyeyunal transanastomosis por una obstrucción intestinal congénita. Se repasan las principales particularidades en el manejo anestésico de estos pacientes, en relación con la preparación de la monitorización y equipamiento quirúrgico con el fin de evitar lesiones cutáneas por fricción, y las dificultades en la canalización de accesos venosos y manejo de la vía aérea.

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Introduction

The term epidermolysis bullosa (EB) was coined by Koebner in 1886 and describes a group of dermatological, genetically determined mechanical blistering diseases with varying course and severity ranging from minor disability to death within a few weeks after birth.²

There are at least 23 pheno- and genotypically different diseases under EB, but histopathologically there are three major distinct groups: *epidermolytic or simplex* (EBS), *junctional* (JEB) and *dermolytic or dystrophic* (DEB). *Junctional* forms (JEB) have in common intraepidermal blisters inside the basement membrane. Of these, the lethal Herlitz-type generalized JEB is due to the congenital absence of the laminin-5 protein. Exuberant degranulation tissue plaques appear since birth, affecting the mucosa, larynx, digestive tract and urinary tract. Sometimes it is associated with pyloric atresia and prognosis is very poor, with death occurring within the first two years of life in more than 80% of cases due to overinfection, anaemia or visceral complications.³

There are very few references on the anaesthetic considerations required for the management of a patient with the Herlitz type of JEB. Adequate control of the airway and maintenance of skin integrity avoiding rubbing, friction and minor injuries are essential.⁴⁻⁷ The case presented illustrates the perioperative management of a newborn diagnosed with Herlitz JEB associated with pyloric atresia, taken to surgery for the placement of a naso-jejunal tube for enteral feeding.

Case description

A pre-term (36 weeks) male newborn was brought from the delivery room to the Neonatal Intensive Care Unit (NICU) and placed under isolation due to septic risk. The baby was delivered by C-section and had an Apgar score at birth of 9/10; weight was 2.70 g, length 47 cm, and head circumference 31.5 cm. Family history included a healthy 32-year-old mother born in Romania, G2 (3-year-old male, delivered normally at term) and a healthy 36-year-old father.

On physical examination, multiple disseminated blister-type lesions were found throughout the body surface, mainly in the occipital and cervical regions, both feet, and knees. In the chest, the lesions were squamous in appearance. Nikolsky's sign, consisting of epidermal detachment under light finger rubbing, leaving behind a reddish, moist and painful area, was positive. A skin biopsy was performed and reported as dermo-epidermal detachment with a high number of eosinophils. The electron microscopy ultrastructural study

supported the diagnosis of Herlitz JEB. Associated congenital bowel obstruction was suspected (pyloric atresia vs. duodenal atresia) with abdominal radiological evidence of absence of air in the gastro-intestinal-rectal portion, and abdominal ultrasound showing obstruction at the level of the gastric outlet.

After transfer to the NICU, umbilical access was selected given the difficulty in establishing a peripheral venous access. A continuous infusion of fentanyl and morphine hydrochloride was used for analgesia during dressing changes for the skin lesions using Furacin and Linitul. There was a cardiorespiratory arrest episode associated with high-dose hypnotics, requiring a slightly difficult orotracheal intubation (OTI) due to the frailty of the skin surface and a moderate degree of subglottic stenosis in the airway.

The patient was assessed by the Paediatric Surgery Service for congenital bowel obstruction, and the decision was made to place a trans-anastomotic naso-jejunal tube. Laboratory test results were haemoglobin, 15.9 g/dL; platelets, 288,000 unit/mm³; prothrombin time, 94%; blood sugar, 102; urea, 56; creatinine, 1.08; sodium ion, 144; potassium ion, 3.8; calcium ion, 2.20; bilirubin, 5.01. The remaining parameters were within the normal ranges.

The surgical and anaesthesia instruments and equipment were set up meticulously in the operation room in order to avoid skin lesions from friction: the operating table was covered with a special cotton mattress, the blood pressure and ischaemia cuffs were lined with a special film, and the number of measurements was restricted; cables, lines and electrodes were protected with Tubilast; the material for airway management was lubricated and padded; and Linitul and Mepilex-Lite dressings were used during surgery and as fixation material.

The 2-day-old patient arrived at the operating room already intubated (cuffless 2.5 mm internal diameter orotracheal tube) under sedation and analgesia, and connected to mechanical ventilation. A central venous line was placed (right femoral access) for medication administration. A dose of 0.02 mg/kg of atropine was used for premedication. Maintenance anaesthesia consisted of sevoflurane, MAC 1.1-1.2; atracurium 0.5 mg/kg and two boluses of 0.1 mg/kg; fentanyl 5.6 and 3 µg; dexamethasone, 0.25 mg/kg bolus; and saline glucose solution perfusion at a rate of 10 mL/h. The surgical intervention proceeded normally, lasting 2 h. At the end, the patient was transferred to the Neonatal ICU.

Discussion

EB or *epidermolysis bullosa* is a paediatric disease uncommonly seen in clinical practice (20 cases per one million inhabitants)

but with many variants depending on the different subtypes of dermal histological lesions. Among them, junctional forms (JEB), particularly Herlitz type and the form associated with pyloric atresia, have been recognized as a challenge for the anaesthetist due to their poor prognosis and associated comorbidity. There is no specific or definitive treatment at present for EB, other than education, preventive and support measures, wound and infection management, nutritional support, and prevention and management of haematological, haemodynamic, metabolic and nutritional disorders. It has been suggested that the use of high-dose steroids might be useful in Herlitz and dystrophic forms during the blister formation period.

The most frequent interventions required in these patients are dressing changes under anaesthesia, grafting, correction of deformities, gastrostomies, tracheostomies and central venous line placement.⁸

The anaesthetic management of EB starts with the pre-anaesthesia assessment, performed ideally in advance in order to allow for adequate preparation in technical and equipment terms.⁹

Airway assessment is critical during the preoperative visit, and is influenced by the frailty of the skin and mucosal surfaces since it will require careful manipulation of the face, the oral mucosa and the gums in order to check for potential lesions in those areas. EB patients usually have limited mouth opening or *microstomia*. *Ankyloglossia* may be pronounced, to the point that the patient may not be able to move the tongue. Finally, there is a greater proportion of glottic stenosis in JEB, as was the case in our patient, with granulation tissue accumulation in the paratracheal and intranasal regions. All these factors may create the conditions for a difficult intubation.^{10,11}

Confirming and correcting anaemia, hypoalbuminemia and electrolyte imbalances are required before surgery. It is also recommended to ask for a renal function test before surgery.

An important part of the preoperative workup consists of assessing potential venous accesses, which may also be compromised due to the patient's skin condition. The superficial venous network is usually deficient, rendering the implantation of a peripheral access impossible and creating the need, as in this case, of central venous catheterization. There are usually no lesions in the cervical region and jugular access may be feasible. However, in our case, the presence of blisters in that area led us to select the femoral approach.

There are no additional recommendations for premedication; in general terms, avoid intramuscular injections, give atropine to the patient, prescribe an antacid due to the high risk of aspiration in EB, and prescribe also antihistamine in case the patient has findings of pruritus.^{5,7}

As far as physical measures are concerned, it is important to bear in mind that friction, rather than direct pressure, is what leads to blister formation and erosion: hence the importance of preparing the operating room and the surgical materials very carefully. In general, all surfaces that come into contact with the patient must be padded or lubricated. It is advisable to place a special cotton mattress on the operating table to achieve this end. All blood pressure, ischaemia and other cuffs must be lined with a transparent film where they come into contact with the skin, and the number of

measurements must be restricted to only those that are absolutely necessary during surgery. Airway management material (goggles, facial masks, laryngoscopes, EKG monitoring) must be properly lubricated and padded. It is important to avoid the use of adhesive material as much as possible in the operating room.¹²⁻¹⁵

In our case, we used *Mepilex Lite*[®] dressings with *Safetac*[®] technology for fixation purposes. These materials are not adhesive and can be removed safely without injuring the patient.¹⁶ *Safetac*[®] is an exclusive soft silicone technology for dressings that does not cause any form of trauma, not even when removed, minimizing pain and trauma to the wound and perilesional area because it creates a tight seal around the edges of the wound.¹⁶⁻¹⁸ If these materials are not available, it is enough to lubricate abundantly and cover with elastic bandages.

Cables, electrodes and lines were covered with a tubular bandage (*Tubilast*[®]). Eye protection is also paramount: it is contraindicated to use traditional taping, and the recommendation is to use preservative-free ocular gel or a wet hydrogel dressing.

It has already been mentioned that airway management may pose some difficulty. The evidence for intubation safety in the simple and dystrophic forms of EB cannot be extrapolated readily to Herlitz EB because of the greater degree of involvement of the respiratory mucosa and associated malformations. Our patient came into the operating room already intubated, but, nonetheless, airway management material was meticulously prepared.

Monitoring must be reduced to a minimum and, in a short procedure, pulse oximetry and electrocardiography may be enough. For blood pressure monitoring, the number of readings must be reduced and the cuff must be padded appropriately. In complex or long procedures, invasive blood monitoring may be required.¹⁹

Regarding intra-operative pharmacological management of EB, loco-regional anaesthetic techniques are preferred over general anaesthesia.^{12-15,20} If general anaesthesia is used, all conventional intravenous induction agents are considered safe. Sevoflurane was used for maintenance although there is no evidence in the literature regarding superiority of inhaled agents over intravenous anaesthesia in this group of patients.¹⁴ There is a general tendency to premedicate with atropine in order to diminish secretions. Regarding muscle relaxants, it is better to avoid depolarizing agents, while rocuronium and atracurium are considered safe. Succinylcholine has been used with satisfactory results, although it must be used with caution due to the possibility of inducing hyperkalemia and because fasciculations may create friction.^{12,14}

Pain in EB is usually treated inadequately. We underscore the importance of adequate intra- and post-operative pain management. Analgesia with morphine or fentanyl and midazolam may be required 30-45 min before dressing changes. Remifentanyl might be a good option, but no reports have been found about its use in this group of patients.²¹⁻²³

In conclusion, adequate perioperative management of patients with EB may pose a challenge to the anaesthetist and, ideally, it must be performed in referral hospitals by an experienced, multidisciplinary team. Meticulous preparation of the

anaesthetic and surgical material and a rigorous assessment of the airway and the skin lesions minimize the risk of complications and sequelae. It is important not to forget the degree of extracutaneous involvement and potential adverse conditions (malnutrition, anaemia, etc.) that may need correction before surgery.²⁴

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Conflicts of interest

The authors have no conflicts of interest to declare.

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