Anaesthesia for children with junctional epidermolysis bullosa (letalis)

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The anaesthetic management of two children with junctional epidermolysis bullosa, formerly called the letalis form, is described. Anaesthesia for children with this disease has not been described previously. Special precautions were taken to avoid mucosal injury and some customary monitoring devices were omitted. The previous anaesthetic literature, which discusses related but distinct forms of bullous skin diseases, is reviewed. The special concerns which relate to airway management in this disease are discussed.

Epidermolysis bullosa (EB) comprises a spectrum of severe mucocutaneous blistering disorders which are of concern to anaesthetists because of a propensity of skin and mucosa to form large bullae after trivial contact. The anaesthetic difficulties presented by some such patients have been described previously. We recently anaesthetized two patients with a distinct form of the disease – junctional epidermolysis bullosa (JEB; formerly called EB letalis or Herlitz disease) – which has not been reported in the anaesthesia literature. This report describes their anaesthetic management and reviews the anaesthesia literature pertaining to the related disorders, focusing on the controversy regarding the safety of endotracheal intubation in such patients. Although formerly considered fatal within the first year of life, JEB now carries a potential prognosis for survival well into childhood.[1,2] It is, therefore, increasingly likely that anaesthetists will encounter these children and the anaesthetic challenges they present.

Key words

GENETIC FACTORS: epidermolysis bullosa; COMPLICATIONS: epidermolysis bullosa; ANAESTHESIA: general.

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Case reports

Case 1

A 3.7 kg nine-week-old female presented for urgent placement of a central venous line (CVL). She was the 3.1 kg product of a full term uncomplicated pregnancy. There were bullous lesions on her fingertips at birth; these soon spread widely and a clinical diagnosis of junctional epidermolysis bullosa was made. She was managed at home with careful skin care by her mother. Hospitalization at nine weeks was required because of diarrhoea and dehydration. Her skin had widespread denuded, weeping areas involving face, back, perineum and extremities. There were scattered bullae as well. Sepsis developed, but as venous access was impossible to maintain she was treated with oral fluids and intramuscular antibiotics. Over the next day she became hypothermic, neutropenic, markedly anaemic and stuporous. A decision was made to place a central venous line for intravenous antibiotics, fluids and blood products.

The operating room was prepared with a high ambient temprature (22°C) and radiant warming lights. The operating table was covered with sheepskin. Electrocardiogram electrodes with the adhesive outer ring removed were placed gel-side-up on the table and a satisfactory trace was obtained when the baby was placed on them. A 24G teflon catheter was placed percutaneously in a scalp vein and was secured with a suture. Intravenous normal saline and antibiotics were given followed by atropine (0.1 mg) and ketamine (0.5 $mg \cdot kg^{-1}$). Oxygen was delivered by a mask held close to, but not touching, the face. A lubricated precordial stethoscope was held against the left chest throughout the procedure and the superficial temporal pulse was palpated. Neither blood pressure cuff nor doppler was used.

Once the baby was sedated, she was positioned for a right internal jugular vein cut-down. Her limbs were secured with well-lubricated gauze pads under curlex restraints. The surgical field was gently blotted with prep solution and the drapes sewn in place. Placement of a

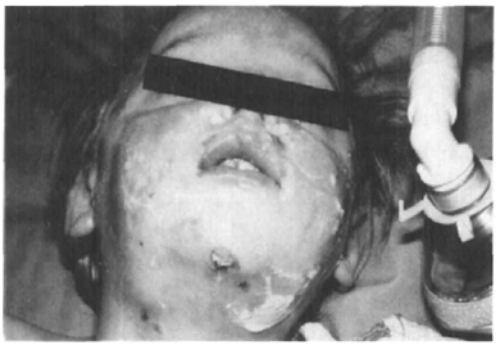

FIGURE 1 Case #2. Face and neck showing nasal excoriations, thinning of hair and circumoral irritation.

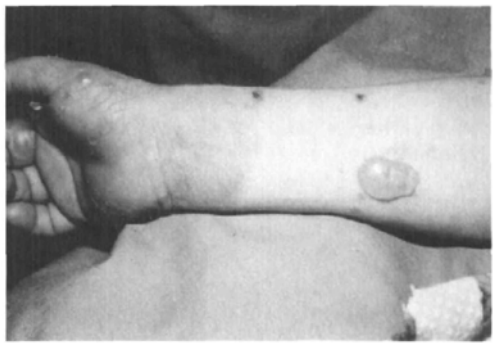

FIGURE 2 Case #2. Forearm and hand demonstrating acute blistering and chronic changes distal to the shirtsleeve line. There is no scarring or digit fusion.

silastic CVL followed uneventfully. Anaesthesia was maintained with incremental doses of ketamine (0.5 mg·kg^{-1}dose^{-1}); a total of 3.5 mg·kg^{-1} was given during the 90 minute procedure. The baby breathed spontaneously at 22–28 breaths·min^{-1} throughout. Heart rate was maintained at 140–160 beats·min^{-1} and a good peripheral pulse was palpable. At the conclusion of the procedure the CVL was secured with sutures and the exit site covered with gauze; no adhesive dressing was used. There were no new skin lesions following removal of drapes and restraints.

The child was transferred to the intensive care unit and treated with intravenous antibiotics and blood products. Clinical deterioration continued and she developed disseminated intravascular coagulation. Circulatory collapse ensued and she died two days later. Her trachea was never intubated. Autopsy showed bullae covering 40 per cent of the skin surface. Microscopically, in the skin, there was separation between the basal cells of the epidermis and the basement membrane of the dermis, consistent with JEB. The tongue and tracheal mucosa were ulcerated and the gastric mucosa was also involved.

Case 2

A four-year-old white male with the diagnosis of JEB was scheduled for dental restoration and circumcision. He was the product of an uncomplicated pregnancy and delivery but recurrent infections had prompted multiple hospitalizations in the neonatal period. Subsequently meticulous skin care at home had stabilized his condition and he currently functioned at age-appropriate levels in nursery school, albeit with restricted activity. Medications included prophylactic antibiotics and anabolic steroids. Physical examination showed mild nasal excoriations, multiple scalp blisters with areas of alopecia, circumoral irritation without scarring or contracture and several small buccal blisters; the tongue was spared (Figure 1). There were areas of moderate blistering on the trunk and severe blistering on all contact surfaces of the extremities without scarring or digit fusion (Figure 2). Haematocrit was 34.7 per cent and weight was 16 kg.

The patient was admitted directly to the recovery room on the morning of surgery. Anaesthesia was induced with methohexitone (30 mg·kg^{-1}) administered rectally. (No perirectal lesions were detected preoperatively.) Once asleep, the patient was placed on a sheepskin and transported to the operating room where he was lifted directly onto the operating table on the same sheepskin.

A lubricated stethoscope was applied to the precordium. Additional monitoring consisted of visual assessment of respiration and palpation of a peripheral pulse. Anaesthesia was deepened with 50 per cent nitrous oxide in oxygen and incremental concentrations of halothane delivered by a mask held close to, but not touching, the face. This permitted an intravenous catheter to be started without a struggle. The mask was removed and anaesthesia maintained with an infusion of ketamine (20–60 μg·kg^{-1}·min^{-1}). The patient breathed spontaneously throughout the procedure.

A pharyngeal screen consisting of one layer of fine mesh gauze was placed to trap debris during the dental restoration but still permit unimpeded ventilation. surgical suction was directed away from mucosal surfaces. Retraction was done by the surgeon's lubricated fingers rather than by instruments. Following the successful dental restoration there were no new oral lesions.

The patient was transported to the recovery room on the

TABLE Classification of epidermolysis bullosa

Name	*Other designation*	*Clinical features*	*Histology & pathogenesis*
Non-scarring forms			
EBS – generalized	EBS-Koebner	Onset: birth/infancy. Generalized bullae: heals without scarring. Nails spared. Teeth normal. Dominant inheritance	Intra-epidermal bullae due to cytolysis of sub-nuclear cytoplasm in basal epidermal cells.
EBS – localized	Weber-Cockayne	Onset: after infancy. Bullae localized to limbs. No scarring. Dominant inheritance.	
Junctional EB	Letalis; Herlitz	Onset: birth/infancy. Generalized bullae. Little to no healing. No scarring. Hands and feet relatively spared. Pan-mucosal involvement. Recessive inheritance.	Separation between basal cell of fermal layer. Hypoplasia of hemidesmosomes on EM.
Scarring forms			
EBD-D	Hyperplastic; dystrophic	Onset: birth. Limbs involved, mouth spared. Bullae heal with scars. Dominant inheritance.	Dermatolytic lesions beneath BM with decreased anchoring fibrils. Collagen fibre dissolution. Associated with abnormal collagenase.
EBD-R	Hallopeau-Siemens	Onset: birth. Generalized bullae with limbs most involved. Prone to syndactyly; marked nail dystrophy. Severe peri-oral scarring with microstomia. Teeth dysplastic. Recessive inheritance.	

EB = epidermolysis bullosa; EBS = epidermolysis bullosa simplex; EBD = epidermolysis bullosa dystrophica; D = dominant; R = recessive; BM = basement membrane; EM = electron microscopy.

same sheepskin. He was kept overnight for observation but no complications occurred and he was discharged home the following morning.

Discussion

Epidermolysis bullosa comprises a family of related but distinct diseases. Although the formation of mucocutaneous bullae is common to all, they can be separated on the grounds of genetics, history, clinical features and histology and ultrastructure.[1,2] The crucial features which distinguish JEB from other forms of EB are: severe generalized blistering dating from birth, absence of scar formation, pan-mucosal involvement (skin, gastrointestinal, genitourinary, respiratory[2,5,6] and probability of early demise (usually from sepsis). In contrast, the other form of special interest to anaesthetists, EBDR, is notable for marked scar formation affecting the extremities (often with fusion of digits). Also involved are the mouth, tongue and oesophagus; ankyloglossia, microstomia and oesophageal strictures are common.[7] Laryngo-tracheal involvement has been reported in rare cases.[8] Survival into adulthood is common.[4,9] Teeth are severely dysplastic in both forms.[9] These two diseases have such distinct appearances on light and electron microscopy (see Table) that each can be diagnosed pre-natally from fetal skin biopsy. In infancy the clinical presentation of the two forms may be similar and microscopic analysis of skin biopsy may be needed to make the differential diagnosis; older children can be distinguished on clinical grounds.

Previous reports of anaesthesia in EB have dealt with the EBDR and EBS forms exclusively. There are many excellent reviews of the anaesthetic considerations for these specific disorders, beginning with Wilson's in 1959[10] and continuing into recent literature.[1,4,11–17] Several general guidelines for anaesthetizing all patients with EB can be drawn from these reports.

Preoperative assessment must consider the likelihood of anaemia, dehydration, electrolyte abnormalities and poor nutrition. Various drug therapies have been used (with mixed results)[1,6] and if in use may alter management (notably steroids, phenytoin and vitamin E). Underlying renal diseases may exist.[11] Airway patency may be a problem in EBDR because of microstomia and carious teeth.[7]

Anaesthetic management must, above all, emphasize prevention of the slightest trauma to skin and mucosal surfaces. Positioning must minimize pressure and all contact points must be well-padded and lubricated. Shearing forces are most damaging[11] and adhesive devices must not be used (severe bullae formation having been reported following their removal).[11] Monitors must thus be applied in novel ways or avoided. Pulse oximetry using a non-adhesive sensor would have made a valuable contribution to patient safety but was not available at the time these anaesthetics were given. Pressure from a firmly applied anaesthesia mask is clearly harmful[10] and oral airways are equally traumatic.[18]

The above considerations make good preoperative

rapport between patient and anaesthetist vital to smooth induction. The need for adequate premedication has been emphasized.[11] Special induction methods – such as those using intramuscular[15] or rectal[17] medication – may be needed in children to forstall struggling.

A variety of anaesthetic techniques have been described in EBDR. The most common operations required by these patients are dental restorations, separation of fused digits and repair of oesophagel strictures. Peripheral procedures have been done under anaesthesia using both volatile agents (by open mask[13] and headboxes) and ketamine. Intraoral procedures have been done during anaesthesia using insufflation of volatile agents[14] or parenteral ketamine and spontaneous ventilation.[15,19] Anaesthesia for an emergency Caesarean section was successfully given utilizing halothane by mask.[18]

The most controversial aspect of anaesthetic care for EB patients is the safety of tracheal intubation. It must be emphasized that previous reports pertain only to the EBDR form of the disease. Early reports expressed concern that intubation would produce intratracheal bullae and subsequent airway obstruction.[10,13] But intraoral surgery has been done successfully with endotracheal techniques[3,7] and open-chest surgery has been done with tracheal intubation, paralysis and controlled ventilation, without laryngeal complications.[4–16] The overwhelming impression from the literature is that intra-tracheal lesions are not produced in EBDR patients by cautious intubation using a lubricated, undersized tube.[4,7,12,16] One large series reported no laryngotracheal complications in 131 endotracheal anaesthetics.[7] (It should be noted that difficult intubations were common in this series and several patients could not be intubated.) But this study did find new oral lesions were common after intubation. The same findings were reported in virtually every study in which the airway of patients with EBDR was manipulated. One theory to explain the apparently greater resilience of the tracheal (versus oral) mucosa in EBDR is that its epithelium is of a histological type (ciliated columnar) which is more resistant to disruption than that of the oral cavity (which has squamous epithelium).[18] Laryngeal stenosis has been reported in a few EBDR patients who had never been intubated.[8,20] These patients may represent a previously unrecognized subset of EBDR who are prone to laryngeal damage, but details in these reports are lacking.

Unfortunately, it is difficult to generalize the historical evidence about tracheal intubation in EBDR to patients with JEB. These are two different diseases with distinct histo-pathologic appearances. The responses of epithelial surfaces to trauma in the two conditions is quite different, as evidenced by the marked tendency for scar formation in EBDR and the absence of scarring in JEB (see Table). JEB is a condition which affects *all* mucosal surfaces, including the respiratory epithelium. In fact, involvement of the tracheal epithelium in the absence of airway instrumentation has been shown in several cases of JEB[2,5,6] as well as our Case 1. Thus one cannot necessarily extrapolate from the evidence in EBDR and assume that tracheal intubation in patients with JEB is safe. Given present data, elective tracheal inntubation in patients with JEB cannot be recommended.

Because the safety of endotracheal anaesthesia in JEB is unproven, we chose as a maintenance technique parenteral ketamine and spontaneous ventilation, even for intra-oral surgery. In addition, we found careful inhalation anaesthesia without face-mask contact was helpful during induction of our Case 2. this induction was facilitated by rectal medication, which was well tolerated despite theoretical concerns.[6]

The safety of tracheal intubation in an infant or child with severe bullous skin disease may well depend on the particular form of the disease. Distinguishing JEB from EBDR is particularly important. Thus an accurate diagnosis of such a patient – which will require consideration of the clinical and historical features of the illness as well as perhaps histopathologic analysis of the skin – is necessary to optimally plan his anaesthetic management.

In summary, we report two cases of anaesthesia in JEB, a disease which is no longer uniformly lethal in infancy[2,5] and which anaesthetists may encounter with increasing frequency. Special precautions to avoid epithelial trauma were taken, necessitating deviation from usual practices: no adhesive devices were used, blood pressure was estimated by palpation without a cuff and anaesthetic masks were never placed in direct contact with a patient's face. Rectal methohexitone and open-mask inhalation induction were used in an older patient. Tracheal intubation was specifically avoided. Intravenous ketamine with spontaneous ventilation was well tolerated during peripheral and oral surgery. Preoperative planning among anaesthetists, surgeons, parents and patient (where appropriate) was crucial to a smooth perioperative course. Airway manipulation in JEB, as in any form of EB, should be minimized. If unavoidable, such manipulation must be meticulous because of both proven and theoretical risks of bullae formation in the pharynx and trachea. The safety of endotracheal intubation in JEB, despite its apparent feasibility in EBDR, remains to be shown.

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Résumé

On décrit la conduite anethésique chez deux enfants souffrant d'épidermolyse bulleuse jonctionnelle, antérieurement appelée forme mortelle. L'anesthésie chez les enfants souffrant de cette maladie n'a pas été décrite antérieurement. On a pris des précautions particulières afin d'éviter des lésions aux muqueuses et certains appareils de monitorage habituels ont été omis. On fait une revision des écrits anesthésiques antérieurs discutant de formes reliées, mais différentes, de dermatose bulleuse. On discute des inquiétudes particulières concernant l'entretien de la perméabilité des voies respiratoires dans cette maladie.