Clinical Reports

Twelve hour anaesthesia in a patient with epidermolysis bullosa

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Epidermolysis bullosa (EB), an inherited disorder presents clinically with recurrent cutaneous blister formation with possible involvement of mucous membranes and other organs. The sequelae of this disease pose multiple challenges to the anaesthetist and operating room team. Recent literature describes several anaesthetic techniques for the short surgical procedures this patient population may undergo. We describe the anaesthetic technique employed in a 28-yr-old woman with recessive dystrophic epidermolysis bullosa who underwent 12 hr reconstructive surgery followed by a review of the literature that includes a recent description of the possible association of EB with at least two distinct neuromuscular diseases. A detailed description of airway and skin management is described in addition to preoperative concerns. We conclude that a prolonged operative procedure can be undertaken successfully in this population with minimal sequelae involving skin integrity and airway management.

L'épidermolyse bulleuse (EB) est une affection héréditaire caractérisée par la formation de phlyctènes avec la possibilité d'une atteinte des muqueuses et d'autres tissus. Les séquelles de cette maladie présentent à l'anesthésiste et à l'équipe chirurgicale plusieurs défis. La littérature récente décrit plusieurs techniques anesthésiques pour les interventions de courte durée que doivent subir ces malades. Nous décrivons ici la technique anesthésique utilisée auprès d'une femme de 28 ans affligée d'épidermolyse bulleuse dystrophique soumise à une chirurgie de reconstruction. Nous poursuivons avec un survol de la littérature dont celle qui établit un lien possible de l'EB avec au moins deux maladies neuromusculaires distinctes. La gestion des voies aériennes et de la peau, et les préoccupations peropératoires

sont décrites avec précision. Nous concluons qu'une intervention de longue durée peut être réalisée avec succès et ne comporter que des séquelles minimales pour la peau et les voies aériennes.

Inherited epidermolysis bullosa (EB) is a rare (1:300,000)¹ group of disorders that is characterized by the spontaneous or traumatic development of bullae on the skin and mucous membranes. It encompasses a collection of subdivisions that can be broadly classified into scarring (dystrophic) and non-scarring (simple). Further subclassifications are based on mode of inheritance and expressions occurring in varying intensities suggesting allelic mutation.¹⁻⁵ (Table) Bullae formation above the basement membrane of the dermal-epidermal junction is termed non-scarring. Healing of these lesions usually occurs without much scarring unless infection develops.

In dystrophic epidermolysis bullosa, separation occurs at the dermal-epidermal interface. Elevated plasma collagenase concentrations are found in these patients and have been implicated in the formation of blisters.¹ The blistering that occurs from separation heals slowly and may produce scarring even in the absence of infection. The repeated cycles of blistering and scarring produce contractures and deformities of the hand. The web spaces are gradually lost as the epidermal scar creeps distally until the digits are encompassed in an epidermal cocoon.⁶ The recessive mode of inheritance suffers the greatest deformities. In addition to skin blisters, mucous membranes of the mouth, pharynx, oesophagus, and anus are commonly affected. Oesophageal strictures develop and inadequate dietary intake results in malnutrition and anaemia.^{7,8} Oral scarring can result in microstomia and immobility of the tongue. Possible airway obstruction and laryngeal stenosis can occur from these bullae.⁹

The patients pose a particular challenge to the anaesthetist, both in airway management as well as in maintenance of skin integrity. Several anaesthetic case reports have been documented. However, none addresses the issue of a prolonged anaesthetic course in a patient with this disease and the subsequent implications.^{2,12-20}

Key words

COMPLICATIONS: epidermolysis bullosa.

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TABLE Classification of types of epidermolysis bullosa (EB)

Disorder	Characteristics
I Nonscarring EB	
(a) EB simplex, generalized	Autosomal dominant. Begins at birth or very early in life. Generalized blister formation, especially at pressure sites. Oral blisters rare. Aggravated by warm weather. Nails and teeth normal. Mildly to moderately incapacitating.
<i>Pathology:</i>	Intra-epidermal blister formation as the result of cytolysis of the basal membrane.
(b) EB simplex, localized	Autosomal dominant. Blisters occur exclusively on limbs. Mildly to moderately incapacitating.
<i>Pathology:</i>	As in I (a).
(c) EB junctional form	Autosomal recessive. Begins at birth. Generalized blister formation. Often lesions around mouth. Sometimes tracheal lesions. Severe anaemia and retarded growth. Death usually occurs before the second year of life.
<i>Pathology:</i>	Subepidermal blister formation with splitting occurring immediately above the basal membrane.
II Scarring EB	
(a) EB dystrophica, dominant	Autosomal dominant. Begins in childhood. Particularly affects limbs. Oral lesions rare. Teeth and nails normal. Hypertrophic scars often occur on healing. Moderately incapacitating.
<i>Pathology:</i>	Subepidermal blister formation. Splitting occurs immediately below basal membrane. Reduction in, or total absence of, anchor fibrils.
(b) EB dystrophica, recessive	Autosomal recessive. Begins at birth or in early childhood. Severe, generalized blister formation. Atrophic scars are frequent after healing. Fusion of fingers common. Nails absent. Teeth dysplastic. Usually severe lesions of oesophagus and oropharynx. Anemia. Severely incapacitating. Death usually occurs before 30th year of life.
<i>Pathology:</i>	As in II (a).
(c) Acquired EB	No evidence of heredity. Begins in adult life. Blisters do not become inflamed and remain localized. Oral lesions very fleeting. Underlying disease should be excluded.
<i>Pathology:</i>	Subepidermal blister formation. Splitting immediately below basal membrane. Amorphous matter beneath the basal lamina.

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We report a 12 hr plastic surgery operation on a patient with recessive dystrophic epidermolysis bullosa and

the steps taken to ensure protection of the skin and airway.

Case report

A 28-year-old 47 kg woman, previously diagnosed with recessive dystrophic epidermolysis bullosa, was admitted for an elective free flap to the right hand with release of syndactyly. The disease had been diagnosed on clinical grounds at the age of five years. She had a past medical history of multiple oesophageal dilations secondary to cervical oesophageal scarring, three Caesarean sections, and a subtotal thyroid lobectomy; the latter were performed under general endotracheal anaesthesia. Thiopentone and succinylcholine were used in previous anaesthetics. Intubations in the past were noted to be difficult. The previous operations were of less than two hours duration and were complicated by the immediate postoperative development of bullae over the coccyx, heels, elbows and scapulae although no oral bullae were noted. On physical examination, she was noted to have moderately scarred, thin, atrophic extremities and manifested alopecia, nail dystrophy, scattered areas of gross bullae in various stages of healing, and marked syndactyly of the fingers. There was evidence of microstomia with severe overbite, poor dentition, and limited temporomandibular joint mobility. She had no visible oral lesions. Laboratory results showed haematocrit of 29%, haemoglobin $9.6 \text{ mg} \cdot \text{dl}^{-1}$, sodium $140 \text{ mEq} \cdot \text{L}^{-1}$, potassium $3.5 \text{ mEq} \cdot \text{L}^{-1}$, chloride $101 \text{ mmol} \cdot \text{L}^{-1}$, blood urea nitrogen $16 \text{ mg} \cdot \text{dl}^{-1}$, and creatinine $0.6 \text{ mg} \cdot \text{dl}^{-1}$.

Since a free flap was to be obtained from the left hand to cover the right hand, a right external jugular silastic catheter was placed and sutured without local infiltration or the use of tape. Because of the risk of aspiration and a difficult intubation, premedication consisted of ranitidine 50 mg *iv*, glycopyrrolate 0.2 mg *iv*, and lorazepam 1 mg *iv*. Limb and precordial ECG leads were made with Johnson and Johnson adhesive pads (4768DV), reported to be innocuous by the patient, and NDM silver ECG electrodes adhered to these with 3M double-stick discs. Because the free flap was to come from the left arm, the left thigh was wrapped with web role and a thigh blood pressure cuff placed. A pulse oximeter probe was positioned on the big toe and cotton rolls were placed below the patient's scapulae, buttocks and heels. The operating room table was padded with an egg crate mattress and sheep skin. An endotracheal tube (ETT) and MacIntosh blade were soaked in viscous lidocaine and the face mask wrapped in xeroform gauze. In addition, the patient's chin was covered with xeroform gauze to minimize skin trauma induced by finger support of the mandible.

Because of this disease's possible association with por-

phyria and her difficult airway, anaesthesia was induced with ketamine 75 mg ($1.5 \text{ mg} \cdot \text{kg}^{-1}$) *iv*. Once it was ascertained that an airway was established and in order to facilitate tracheal intubation, muscular relaxation was obtained with succinylcholine 100 mg ($2 \text{ mg} \cdot \text{kg}^{-1}$) *iv*. A Macintosh #2 blade was used because of the patient's small mouth and a 6.0 mm ETT was successfully passed into the trachea. On direct laryngoscopy, the patient was found to have the characteristic grey pharynx and erythematous epiglottis. A fiberoptic scope was available should laryngoscopy fail and an awake intubation be required. The possibility of tracheostomy for airway control was discussed and a tracheostomy set was available in the OR. The ETT was wired to tooth #6, the lips lined with xeroform gauze, and further instrumentation of the airway avoided. Positive-pressure ventilation was initiated after intubation. The eyes were closed after placement of ocugel bilaterally, a bladder catheter with a temperature probe was inserted, and a precordial stethoscope was adhered to "Johnson and Johnson" adhesive tape over the left chest. Anaesthesia was maintained with isoflurane 0.5 MAC and a continuous fentanyl infusion adjusted to heart rate and blood pressure response from 0.5 to $2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$.

The skin was prepared for surgery by pouring hexachlorophene soap over both upper extremities and right thigh. The arms were wrapped with web roll and tourniquets were applied. Total tourniquet time was 118 min on the left and 120 min on the right with no evidence of bullae formation on release. The position of the patient's head, lower extremities, and pulse oximeter was changed every two hours. Anaesthesia and surgery proceeded uneventfully. Prior to emergence, 2 ml lidocaine 4% were given through the ETT. When the patient responded to verbal stimuli and demonstrated return of muscle strength, the cuff was deflated to determine the patient's ability to breathe around the ETT. Once this was confirmed, the trachea was extubated after careful suctioning of the mouth. The total anaesthetic time was 12 hr 25 min. The patient was seen 24 and 48 hr later and only developed bullae over the dorsum of the hands. She was discharged nine days postoperatively in stable condition.

Discussion

Treatment of epidermolysis bullosa is directed at prevention of frictional trauma to the skin and frequent skin lubrication.³ This standard appears to apply successfully to a prolonged anaesthetic course in a patient undergoing plastic reconstructive surgery. An extensive literature review supported the techniques employed and raised several issues of interest regarding the management of the rare yet complex disease entity.

Patients with EB are most likely to require the care of an anaesthetist for plastic reconstruction of extremities, dental procedures, labour and delivery, and possible gastro-oesophageal surgery including monitored anaesthetic care for oesophageal dilatations. Coordination of surgical, anaesthesia and nursing teams is essential when preparing for a case in a patient with EB. Preoperative considerations for the anaesthesia team include pre-existing metabolic derangements, reduction in frictional trauma, and meticulous airway control with anticipation of possible difficult airway and aspiration secondary to oesophageal strictures.²¹ In addition to malnutrition and anaemia with subsequent fluid and electrolyte imbalances,⁸ secondary amyloidosis, hypercoagulable states, porphyria,¹⁰ and two distinct neuromuscular diseases^{11,25} (muscular dystrophy and myasthenia gravis) have been associated with the disease. Suggested preoperative tests include complete blood count, urinalysis, electrolytes, and blood urea nitrogen.¹² Preoperative medications include glycopyrrolate for control of airway secretions and H2 blockers particularly in patients with a history of oesophageal strictures. These may be given *iv*, *im* or *po*; *im* injections have been used successfully without sequelae.^{13,14}

Skin protection and integrity is a major challenge as minimal friction may lead to blistering and subsequent scarring. The patient's skin must be examined and the degree of wound healing notes as they are at risk of developing staphylococcal bacteraemia. Friction tends to be more harmful than perpendicular pressure. Adhesive tape, tourniquets, blood pressure cuffs, alcohol wipes, ECG electrodes, temperature probes, bladder catheters and even subcutaneous local anaesthetic infiltration have been associated with cutaneous trauma.² Web rolls placed beneath cuffs have prevented frictional trauma. Intravenous or intra-arterial catheters should be sutured in place and the eyes protected with ointment and not taped close. Friction from masking may be prevented by avoiding excessive pressure and the use of xeroform around the nose (Figure). Tape or adherent strips should be avoided; securing the ETT to a tooth provides a safe alternative. Preparation of the skin for intravenous placement as well as surgery consists of pouring the appropriate solution onto the area to avoid frictional scrubbing.

Oral alterations of the soft and hard palate are common, including microstomia, impaired tongue mobility, and severe dental caries. The cervical oesophagus is usually involved with recurrent strictures and lesion formation, placing the patient at increased risk of gastro-oesophageal reflux.²¹ Gentle airway manipulation is of utmost importance as oral bullae formation has been associated with tongue adhesion to the hard palate, facial trauma, pulmonary infections, and airway obstruction.

FIGURE Use of zerofoam gauze to protect face from frictional trauma from face mask.

Fisher *et al.* reported a case of a neonate with epidermolysis bullosa lethalis that developed airway obstruction from a large fibrosing bulla above the vocal cords.^{23,24} On the other hand, in a review by James *et al.*, tracheal intubation was performed on 131 occasions over 22 yr with only six patients developing bullae on the tongue and none with airway compromise.²⁴ Intubation is advocated in this review as the majority of the facial bullae that developed were related to the use of a face mask. If indicated, a smaller ETT and laryngoscope blade lubricated with a water soluble gel are optimal. Where intubation is deemed difficult, an awake oral or nasal fibreoptic intubation is appropriate.²¹ The use of a laryngeal mask airway (LMA) has been described.²¹ This technique could potentially cause damage to the pharyngeal mucosa. If an LMA is to be used, it should be very well lubricated and inserted with care to avoid mucosal damage. Further studies on the safety of using an LMA in patients with EB and needed before advocating its use.

Ketamine, thiopentone and propofol have been used safely and effectively for induction of anaesthesia.²¹ Use of ketamine predominates in the literature involving anaesthetic techniques in EB because of a presumed association with porphyria, although this has never been substantiated in the literature.¹⁰ Ketamine does have properties that are advantageous to patients with EB including maintenance of spontaneous respiration while providing amnesia and analgesia. Certain authors suggest that barbiturates should be used with caution in patients with EB although barbiturates have been used without incident including previous anaesthetics in our case.²¹ The use of propofol has been used in patients with EB.

Both nondepolarizing and depolarizing muscle relax-

ants have been used in patients with EB without untoward effects. Autosomal recessive transmitted EB with phenotypic features characteristic of severe types have been linked with neuromuscular diseases, notably myasthenia gravis and muscular dystrophy.^{11,25} Neimi *et al.* proposed transmission by a common gene.²⁵ However, the possibility exists of the coincidental occurrence of two separate inherited disorders.¹¹ A thorough interview regarding weakness and family history is essential in identifying those who may be predisposed to muscular dystrophy. Succinylcholine should be used with caution in these patients. If suspicion exists, diagnosis can be confirmed with the presence of elevated serum creatinine kinase and aldolase as well as an open muscle biopsy.^{11,25}

In the past, regional anaesthesia has been avoided secondary to possible skin sloughing by local anaesthetic infiltration and by the possible development of infection by adjacent bullae. However, there are several successful reports of spinal and epidural placement for a Caesarean section,^{16,17} caudal epidural anaesthesia in children,^{18,20} and brachial plexus anaesthesia.¹⁹ A regional technique avoids possible severe complications associated with airway manipulation; therefore, if the site meets the requirements for a safe anaesthetic, it is an effective method for providing anaesthesia in a patient with epidermolysis bullosa.

In summary, a patient diagnosed with epidermolysis bullosa presents a challenge to the anaesthetist but can undergo a prolonged anaesthetic while still maintaining skin integrity and preventing airway trauma. This disease entity shows considerable variability in its severity. Discussion with the patient about the severity of disease and the patient's ability to tolerate certain tape products may allow the anaesthetist to tailor the anaesthetic management.

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