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Anesthetic implications in epidermolysis bullosa dystrophica

Epidermolysis bullosa is a genetic mechanobullous disease of the stratified squamous keratinizing epithelium that affects the skin and mucous membranes. Its primary feature is the formation of blisters after minor shearing trauma to the skin or mucous membranes that can result in debilitating, even life-threatening scarring. The disease presents special problems for the anesthesia provider because the equipment used to deliver anesthesia and monitor vital signs may cause serious postoperative complications. The challenge is to maintain patency of the airway and use monitoring technology without damaging epithelial surfaces, which could result in permanent scarring. Successful anesthetic management of a patient with epidermolysis bullosa is possible if precautions with anesthetic instrumentation are observed.

Key words: **Bullae, collagenase, epidermolysis bullosa dystrophica, regional anesthesia, skin disease.**

Introduction

Epidermolysis bullosa (EB) is a group of genetically determined diseases characterized by abnormal fragility of the skin and mucosa. The disease mainly affects the stratified squamous keratinizing epithelium of the skin; however, blisters can occur on virtually any mucosal surface. The blisters usually occur at sites of pressure or friction but can occur spontaneously in the most severe forms of the disease. Resolution of the blisters can result in severe scarring. The prognosis of this disease varies with the type of EB present. Some patients have sporadic blistering that does not interfere with their livelihood, but others have widespread blistering of the skin and mucosa, resulting in scarring that can be life threatening. Blistering can occur not only on the skin but also in the esophagus, ocular surface, and trachea.[1]

The importance of EB to anesthesia providers lies in the serious sequelae that can occur if proper precautions are not taken with anesthetic instrumentation. Routine instruments used for delivery of anesthesia and monitoring of vital signs may cause serious postoperative complications. A variety of general, regional, and local anesthetic techniques have been used successfully in adults with EB. For infants and children with this disorder, anesthetic management usually consists of general anesthesia delivered by mask or endotracheal tube, or intravenous (IV) or intramuscular anesthesia.

Case history

The patient was a 22-year-old woman who had been diagnosed with the dystrophic type of EB at birth. The patient's medical history included numerous operations for esophageal strictures and webbing of her fingers. She was very knowledgeable about her disease, and her longevity could be attributed to the excellent care and management of her disease by medical professionals and her family.

The patient sought treatment for esophageal dilatation. In preparation for the procedure, a string with a weight attached was passed through her nose and swallowed to guide the esophageal dilators. This was done in the surgeon's office, and at that time the preanesthetic evaluation was performed. During the preoperative evaluation, it was noted that her mouth opening was smaller than at previous admissions. Upon further examination of the airway, it was determined ankylosis of the temporomandibular joint had increased. The risks of a difficult intubation and the alternatives available for establishing an airway, including tracheotomy, were discussed at that time. The possibility of difficult IV access also was discussed. Nausea and vomiting had occurred after 3 of the previous anesthetics, and prophylaxis with metoclopramide and intraoperative odansetron had not eliminated the problem.

Upon admission, the patient's body weight was 56 kg, and her height was 1.62 meters. Skin erosions were present on the elbows, between the knees, and on the ankles. Small erosions were present on the anterior surface of the hands and forearms, and there were minor flexion contractures of the fingers on both hands. The results of all laboratory tests were within normal limits. Premedication was omitted due to unpleasant extrapyramidal effects experienced by the patient when sedated with benzodiazepines in the past.

In preparation of the operating room (OR), a full-bed-size sheep skin pad was placed on the OR table, and the room temperature was increased to avoid hypothermia. For transport to the OR, the patient moved herself to the stretcher, and upon arrival she moved to

the OR table without assistance, decreasing the risk of skin trauma. All points of contact with the sheets and padding were checked for wrinkles and folds that could produce pressure on the skin.

Anesthesia monitors were specially prepared for use with this patient. Any device that would touch the skin had been lubricated with 1.0% hydrocortisone cream. All adhesive had been removed from the electrocardiogram pads, leaving the gel sphere, and the wires were wrapped with cotton padding. Cotton padding was wrapped around the patient's upper right arm, and the blood pressure cuff was gently applied. A finger clip pulse oximetry probe was attached to the patient's left index finger. Heart sounds were monitored with a precordial stethoscope, which had been lubricated with steroid cream and placed over the left chest. Temperature was monitored with an axillary probe, with the patient's arm fully adducted to increase accuracy of the reading. Fiberoptic equipment was on standby, and a tracheotomy tray was in the OR.

In the past, obtaining IV access had been difficult with this patient; for this procedure, the patient requested the use of nitrous oxide to allow for amnesia and analgesia while IV access was attempted. The cuff of the face mask was lubricated with hydrocortisone cream and placed gently on her face. The patient's left arm was wrapped with cotton padding, and the tourniquet was applied with minimal tension. A 20-gauge IV catheter was placed in the left arm after 5 attempts. The IV catheter was secured with 1 small piece of paper tape and wrapped securely with cotton padding.

After the patient received 100% oxygen for 3 minutes, induction began with lidocaine, 2 mg/kg IV, followed by propofol, 2.0 mg/kg. Ventilation by mask was established, and rocuronium, 0.08 mg/kg, was administered. A peripheral nerve stimulator was not used due to its adhesive electrodes.

Isoflurane was added to deepen the anesthetic in the event of a difficult intubation. The laryngoscope blade, endotracheal tube, and cuff had been lubricated with the hydrocortisone cream. After 90 seconds, laryngoscopy was attempted using a number 2 Miller laryngoscope blade. The oral opening was small, and exposure of the epiglottis and vocal cords was unsuccessful on first attempt. On the second attempt, the intubation was successful; however, trauma to the lower lip and buccal mucosa had occurred. The cuff on the endotracheal tube was inflated with just enough saline to seal at approximately 22 cm water pressure. The endotracheal tube was secured with umbilical tape, which was wrapped in cotton padding and wrapped around the patient's neck. The eyes were lubricated with ophthalmic ointment.

The surgeon began the esophageal dilatation by attempting to expose the esophagus with the laryngoscope and visualize the string that was passed through the patient's nose during the preoperative period. Due to excessive strictures, the string had not passed down the esophagus and was curled in the posterior pharynx. Esophageal dilators in graduated sizes were lubricated and passed orally in succession to attempt dilatation. Each dilator became progressively more difficult to pass. Even with the utmost care, trauma to the oral cavity and esophagus could not be avoided. Suctioning the oropharynx with a standard suction catheter was difficult, due to the accumulation of the hydrocortisone cream in the posterior pharynx. A tonsil suction tip was used with great care to avoid contact with the mucosa. The muscle relaxant was reversed, and spontaneous ventilation returned within 5 minutes. Return of the protective reflexes was the criterion used for extubation. When the patient was able to respond to verbal commands, the endotracheal tube was removed without difficulty. Upon arrival to the postanesthesia care unit the patient complained of nausea and vomited twice. The presence of blood and steroid cream (used for lubricant) in the stomach was thought to contribute to the nausea.

Twelve hours postanesthesia, the patient was hoarse and complained of a lump in her throat. Humidified oxygen, via an open face mask, had been used to provide moisture to the airway since recovery began. The patient was discharged home in 24 hours without sequlae.

Three months elapsed, and the hoarseness was still present. It seemed to be worse in the early morning and the late afternoon. An examination by an otolaryngologist, via flexible laryngoscopy, demonstrated bilateral functioning vocal cords and no scarring visible in the larynx.

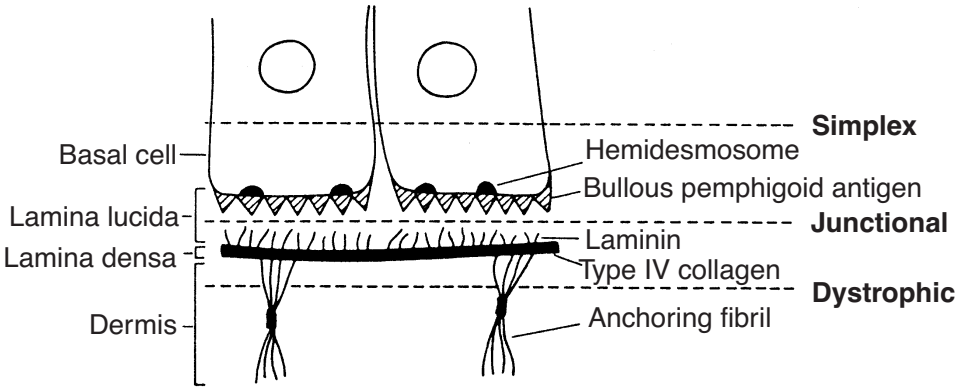
Discussion

Fox[2] first described EB in 1879. It encompasses an array of autosomal dominant and recessive conditions that may have either localized or generalized dermatological manifestations. The incidence is 1 in 300,000 live births.[3] This disease is usually detected soon after birth or in early childhood due to the appearance of bullae and erosions of the skin that can become infected and/or hemorrhagic.

Classification

More than 20 different subtypes of EB are now recognized.[4] There are 3 major classifications of epidermolysis bullosa, based on the precise location at which blistering or separation occurs. The fundamental abnormality in this disease is an increase in collagenase activity, which leads to collagen degeneration.

Figure 1. Ultrastructure of the basement membrane zone showing the level of split in different types of epidermolysis bullosa*



*Reproduced with permission from Lin AN, Carter DM. [5]

This results in the splitting of the various epidermal layers or at the transition between epidermis and dermis (Figure 1).[5] The separation of the epidermal layers result in formation of bullae, and in dystrophic forms, subsequent healing with scarring.[6]

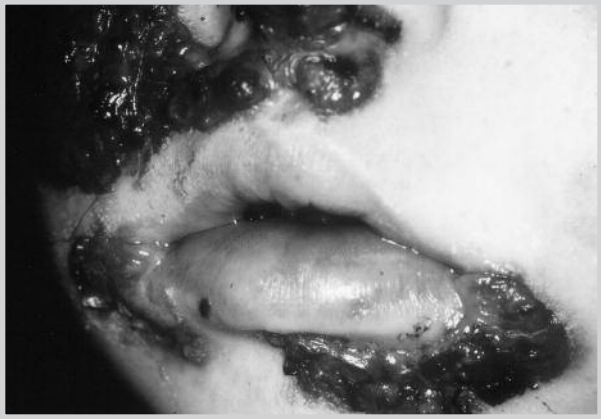
Epidermolysis simplex is the most superficial type of EB. It is characterized by intraepidermal blistering and minimal mucosal involvement, and it usually follows a benign clinical course. Junctional EB, the least common form, is diagnosed when blistering or separation occurs between the basal cells of the epidermis and the lamina lucida. It is usually identified at birth by severe blistering, and many of these patients die during infancy. Epidermolysis bullosa dystrophica occurs at the level of the dermis below the lamina densa. In the recessive form, blistering and scarring can be severe (Figure 2). Patients with dystrophic EB are prone to development of squamous cell carcinoma, which behaves aggressively and may metastasize widely.[7]

Extracutaneous involvement

Mucosal involvement can be severe in junctional and dystrophic forms of EB. The most common area for mucosal blistering is in the gastrointestinal tract. Esophageal stricture that could lead to complete luminal obstruction is a common manifestation, along with microstomia, esophageal webs, and iron deficiency anemia from chronic blood loss at the site of the lesions.[8] Malnutrition and protein losses from exudating lesions contribute to the anemia and hypoalbuminemia that may accompany this disease.

Secondary infection of bullae, primarily with *staphylococcus aureus* and beta-hemolytic *streptococci*,

Figure 2. A young patient with epidermolysis bullosa*



*Lesions are the result of shearing forces on the skin from application of a face mask.

occurs frequently with all forms of EB.[9] Oral lesions can produce severe adhesions, such as cleavage of the tongue to the palate or the floor of the mouth.[10,11] Laryngeal involvement is rare because that tissue is pseudostratified, columnar, ciliated epithelium, whereas the oral, pharyngeal, and esophageal mucosa is stratified squamous epithelium. Laryngeal bullae are most common in the junctional form of the disease.[12] Dental involvement also is common. Because teeth have an ectodermal structure like the skin, this disease affects the quality of the enamel and increases susceptibility to dental caries.[13] An association between certain types of porphyria and EB has been suggested, due to similar cutaneous manifestations and hepatic enzyme deficiencies. The incidence of patients having both diseases at the same time is rare, possibly coinci-

dental, and when patients with EB are tested for porphyria, the results have been uniformly negative.[14] Renal insufficiency has been reported, which may be related to amyloidosis (an accumulation of fibrillar proteins in the kidney that affect renal function).[15] Because of these associated disease states, morphine and barbiturates have been avoided. Fingernails and toenails are usually absent, and ocular movement may cause corneal ulcers and scarring (Figure 3).

Treatment

There is no cure for any of the forms of EB. Treatment consists of administration of corticosteroids systemically to limit scarring and the use of phenytoin to reduce collagenase activity or synthesis.[16] One of the most important aspects in the treatment of EB is the avoidance of any type of trauma to the skin or mucous membrane. A program of cutaneous hygiene minimizes the risk of infection and the resultant scarring from the bullous lesions.

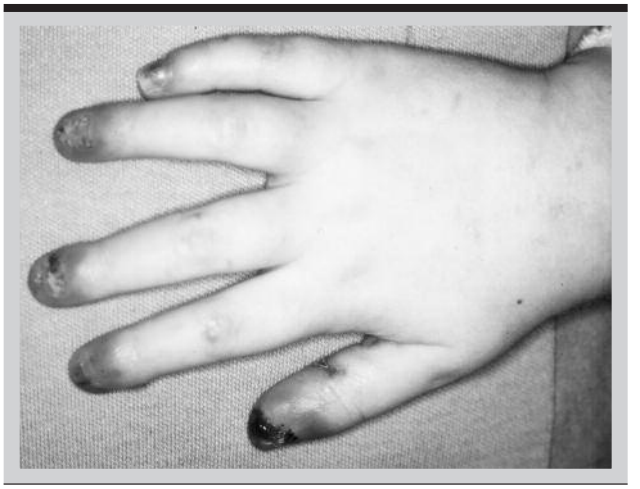
Anesthetic management

The patient with EB presents numerous problems when surgical interventions that require anesthesia are necessary. Because of the extraordinary degree of cutaneous and mucosal fragility that can be present in the patient with EB, any form of anesthetic instrumentation may induce blister formation. Equipment and techniques routinely used in the induction and maintenance of general anesthesia can be the source of serious postoperative complications. Laryngoscopy, endotracheal tubes, face masks, blood pressure cuffs, electrocardiogram electrodes, laryngeal mask airways, and adhesives of any type can induce blistering, possibly resulting in infection and debilitating scarring. Even without instrumentation, spontaneous laryngeal blisters have been reported in patients with junctional and dystrophic EB.[14]

Skin care is one of the most important aspects of conducting any procedure on the patient with EB. The sheets beneath the patient should be free from creases, and foam padding or bandages should protect the patient's heels and elbows. Hydrocortisone ointment, 0.5% to 1.0%, should be applied prophylactically to all sites where pressure or friction is likely to occur. Though widely recommended, the rationale for steroid cream is unclear, since EB is not an inflammatory disorder. Any nonmedicated lubricant should be sufficient.[14] Letting the patients move themselves to and from the operating table may reduce skin damage.

Any equipment that touches the patient's skin should be padded with cotton and/or coated the some type of lubricant; eg, Vaseline gauze or steroid cream.

Figure 3. The hand of a patient with a 6-year history of epidermolysis bullosa*



*Fingernails are absent, and fingers are "stubbed."

Padding and lubrication also should be used under the chin during airway management to avoid skin damage from pressure of the anesthetist's hand. Adhesive should be removed from monitoring equipment, especially equipment with an adhesive interface. The electrocardiogram monitor leads can be placed on the padding under the patient, and the patient's body weight can hold the leads in place. The use of a standard finger probe with pulse oximetry may be difficult in the patient with syndactyly secondary to EB, necessitating the use of a clip or flexible probe. During certain minor procedures, monitoring may consist of a pulse oximeter alone.[4]

The surface of the limb where the blood pressure cuff is placed should be wrapped with soft cotton gauze before the cuff is applied. It has been demonstrated that direct pressure on the skin, ie, cycling of the blood pressure cuff, does not have the same damaging effect to the skin, if well padded, as friction or shearing forces. For major procedures, intra-arterial monitoring can be used.

Intravenous access and security is usually a problem. Intra-arterial and/or IV catheters should be secured by means of elastic bandages, cotton wrapping, or sutures. It often is necessary to insert a central venous catheter. Due to difficult venous access, inhalation induction may be required. Adequate premedication is essential during inhalation induction to prevent struggling that could lead to skin damage.

All IV and inhalation agents currently in use for induction and maintenance are safe to use in patients with EB, unless concomitant disease states, such as porphyria, contraindicate their use.

The use of muscle relaxants in EB patients has been

controversial. Several sources have suggested that the fasciculations produced by succinylcholine may result in skin damage, and that hyperkalemia resulting in cardiac arrhythmias could occur due to muscle wasting occasionally found with EB.[4] There are no reported complications with the use of nondepolarizing muscle relaxants.

In some patients, skin contractures around the eyes can prevent them from closing during anesthesia. Eye ointment and lubricated eye pads should reduce the risk of corneal damage. Corneal blister formation may occur spontaneously despite proper care.[17]

Struggling during emergence from anesthesia increases the risk of skin damage and bullae formation. Oxygen masks should be avoided in the postanesthesia recovery area as the sharp edges can damage skin. Pain should be controlled to avoid excessive movement in an attempt to eliminate the painful stimuli. Pediatric patients may struggle on waking from anesthesia, causing skin damage; the parents of these children should be present in recovery to reassure them on awakening.

Nausea and vomiting frequently accompany emergence from anesthesia when esophageal dilatation is performed. The reverse peristalsis that occurs during vomiting produces excessive pressure and friction in the esophagus and could result in esophageal bleeding or rupture. Prophylactic antiemetics may decrease the incidence and/or severity of the nausea and vomiting.

Use of regional anesthesia

Regional anesthesia is a reasonable alternative that avoids all contact with the oropharyngeal mucosa. Care must be taken when disinfecting the skin at the puncture site. The preparatory solution must be poured over the site; rubbing of the skin must be avoided. Local infiltration of the skin should not be performed due to the risk of bullae formation at the needle puncture site and potential skin sloughing. Epidural, spinal, caudal, and brachial plexus blocks have all been used successfully in patients with EB. If regional blockade does not provide adequate surgical conditions, supplementation with IV sedation would be acceptable. In the pediatric population, the use of swaddling or restraints could augment lesions or create new ones.[1]

Summary

Rigorous attention is necessary to prevent exacerbation of existing lesions and the formation of new lesions in patients with EB. In addition to the concerns of skin trauma, a thorough preoperative evaluation should assess other associated conditions, such as anemia, chronic infections, contractures, dehydration, and malnutrition.[1] Airway management should be performed with the utmost care, and if the procedure allows, regional anesthesia could be a reasonable alternative.

Some of the earliest case reports on this devastating disease described patients as having skin like "cotton wool." These patients are a challenge for all anesthesia providers, and with adequate preoperative planning among all providers, a favorable anesthetic and postoperative course is possible.

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