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Dental and anaesthetic management of children with dystrophic epidermolysis bullosa

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Background. Epidermolysis bullosa (EB) is a genetic disease associated with fragility and bullous lesions of the skin and mucous membranes. There are various patterns of inheritance and histopathology. The disease is associated with systemic and oral manifestations, among which may be dental decay necessitating oral rehabilitation. General anaesthesia is frequently required for oral rehabilitation in children with dystrophic EB. Paediatric dentists should be aware of the implications of dystrophic EB for dental and anaesthetic management.

Case report. Two siblings with moderate to severe systemic and oral manifestations of dystrophic EB requiring extensive oral rehabilitation for rampant decay are described, including special anaesthetic techniques required for airway management and maintenance of skin integrity.

Conclusion. Dystrophic EB is a rare genetic disorder in which vesiculobullous lesions occur with erosions and scarring of cutaneous and extracutaneous surfaces in the oral cavity. Poor oral hygiene results from efforts to avoid mucosal trauma, resulting in decay. The comprehensive care of children with dystrophic EB impacts not only dental management but anaesthesia administration as well.

Epidermolysis bullosa (EB) is a wide spectrum of rare genetic disorders characterized by marked fragility of the skin and mucous membranes in which vesiculobullous lesions occur in response to trauma, heat, or no apparent cause. The pathophysiology of EB varies, depending on the specific defect in the epithelial/subepithelial connective tissue, with varying severity of blistering up to potentially debilitating scar formation and premature death. More than 20 distinct variants of EB have been identified and classified according to the phenotypic characteristics, mode of inheritance, and the ultrastructural level at which the blisters occur[1,2]. These have further been classified into three major subgroups based on specific level of tissue cleavage: EB simplex usually is dominantly inherited with cytolysis of the basal layer of the epidermis and is characterized by intra-epidermal blistering with relatively mild blistering of the skin and mucous membranes. Lesions typically heal without scarring. Junctional EB is recessively inherited and lesions occur in the lamina lucida or epidermal–dermal interface with variable hemidesmosomal abnormalities. Dystrophic EB is inherited in a dominant as well as recessive form and is usually associated with cleavage in the sublamina lucida plane. There is excessive collagenolysis resulting in reduced or absent collagen VII, a fibrous protein that is the main component of the anchoring filaments. The anchoring fibrils appear abnormal, reduced, or altogether absent and there is diminished epidermal adherence[3–5].

Depending on the type of EB, disease severity may range from mild blistering of the hands, feet, elbows, and knees that heal without scarring, to the more severe recessive form that has cutaneous and extracutaneous features. Cutaneous findings vary and may include blistering, ulcerations, and contractile scars over large body surfaces, cicatricial alopecia, and dystrophic nails. Extracutaneous findings may include the eyes, oral mucosa, teeth, oesophagus (stricture), intestinal tract, genitourinary tract,

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and musculoskeletal system[6–8]. The lesions can become infected leading to dehydration, cellulitis, and septicaemia[9].

Lesions usually start to appear at birth or within the first 6 months of life. Where EB is suspected, there should be a detailed history regarding the patient's age at time of bullae appearance, precipitating factors, types and distribution of blisters, and progression of the injuries. Family history is important to verify the presence of consanguinity and history of similar illnesses in the family pedigree. Further evaluations using enzymatic analysis, electron microscopy, immunofluorescence, and immunohistochemistry are necessary to confirm diagnosis of EB and characterize the histological type[10,11]. Since genetic tests are now available, these are often subsequently used to determine the exact mutation.

Oral manifestations

The extent of oral involvement varies from one EB variant to the next. In the mild forms, small blisters (< 1 cm) may form and heal without scarring. In the more severe forms, cycles of bullae formation, erosion, and scarring may occur at any site in the oral cavity. Over time, oral blistering may lead to obliteration of the vestibule, ankyloglossia, and microstomia. Defective enamel, poor oral clearance of foods, and inability to achieve adequate oral hygiene may lead to rampant decay[13–14].

Systemic manifestations

Children with EB are in a chronically hypermetabolic state due to repeated injury and healing of their skin. Lesions are frequently associated with chronic blood loss, which may lead to chronic anaemia. Energy demands are increased along with the need for increased caloric intake; failure to achieve this intake due to difficulty in eating leads to failure to thrive.

Treatment

There is no specific regimen for managing EB; however, much emphasis has been placed on supportive measures, including wraps with protective gauze to prevent friction and further trauma, palliative care, and surgical correction of excessive scarring in acquired syndactyly and other adhered tissues[14]. Dental care through plaque control and careful prophylaxis is advised. While most individuals with EB can tolerate routine dental treatment, some patients with extensive dental needs or severe soft tissue involvement are best managed under general anaesthesia[15,16]. This report presents the dental and anaesthetic management of two siblings with EB.

Case reports

Two siblings, one boy (age 8 years and 3 months) and one girl (age 4 years and 3 months), were brought to the Pediatric Dental Clinic at the Children's Hospital of Philadelphia (CHOP) for evaluation and treatment. They were referred from Saudi Arabia where they had been diagnosed with epidermolysis bullosa dystrophica. The children were both born by normal deliveries and their parents were identified as first-degree cousins. These children have no other siblings, and no other family member had been identified with the disorder. Subsequent molecular diagnostic testing at CHOP was performed on the boy. He was found to have one mutation in the collagen 7 gene (*COL7A1*, OMIM #120120) and was homozygous for the G2590R mutation in exon 104, characteristic of recessive dystrophic EB (OMIM #226600). Subsequent testing of the unaffected parents revealed that both of them were heterozygous carriers of this gene. No testing of the daughter was done at this time.

Case A

The boy had been followed for his condition by many medical specialties in Saudi Arabia over the previous 7 years. At the time of presentation to CHOP, he had extensive skin lesions in the form of bullae, with some scarring on his trunk (Fig. 1), extremities, neck, and face and had developed decreased mouth opening and acquired contractures and syndactyly of his hands, fingers, and toes. He was unable to open his hands (Fig. 2a) and had no nails on any digits (Fig. 2b). Most of his

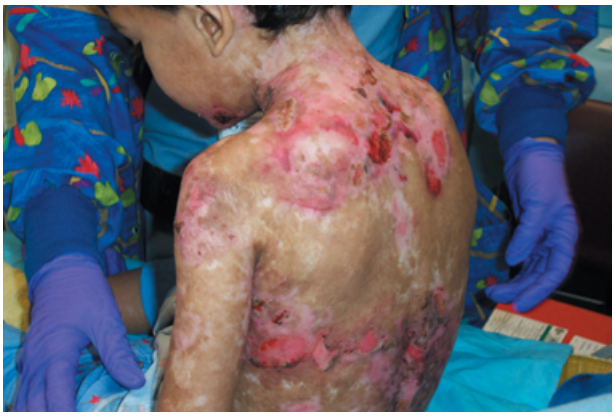

Fig. 1. Vesiculobullous lesions with scarring in a patient with DEB.

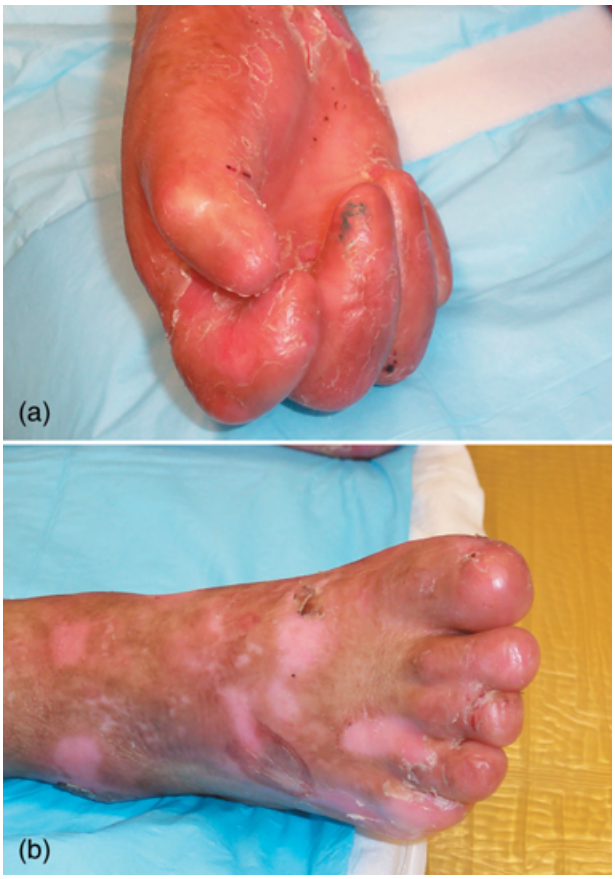

Fig. 2. (a) Scars preventing opening of hand. (b) Loss of nails on extremities.

extremities and torso were covered with dressings to cover the lesions. His history included failure to thrive, hypochromic macrocytic anaemia, and episodes of stridor and respiratory distress. At age 5, he had respiratory failure and was admitted to intensive care, where a decision was made to proceed with conservative treatment, as there was concern that intubation would lead to the development of airway lesions. He was small in stature (18 kg, 108 cm) with growth below the third percentile for his age, despite the hypercaloric formula (two cans of Ensure®, Abbott Laboratories, Abbott Park, IL, USA) ingested daily. His diet otherwise was limited to soft or pureed foods. He had normal cognitive function and attended school. No allergies were reported. Medications included laxatives, iron, zinc, Flamazine® cream (Smith & Nephew Pharmaceuticals Ltd, Hull, UK), artificial tears, and Benadryl syrup. He was scheduled to have surgical correction for the contractures/syndactyly in his hands in the near future. Dental history included an evaluation at a dental clinic in Saudi Arabia when the boy was 7 years old. At this time, he was reported to have lesions of EB both extraorally and intraorally, as well as erosions, dental caries, and abscessed teeth. It was recommended at the time that oral rehabilitation with dental extractions be performed under general anaesthesia. The patient was to be admitted cojointly to the plastic surgery department for hand surgery to minimize the risk for anaesthesia. The patient was subsequently referred to the USA for all necessary treatment. The patient reported a history of pain, particularly at night. Oral hygiene was not practiced due to the formation of bullae following toothbrush trauma. Our dental examination revealed several extraoral and intraoral bullae, no vestibule, as well as severe scarring of the mouth with opening limited to 1 cm (Fig. 3). The tongue was glossy with no fissures or texture, due to previous scarring. He reported difficulty in swallowing. Oral hygiene was very poor and all gingival tissues were inflamed (Fig. 4). He had a mixed dentition with severe dental caries of the permanent first molars and first premolars, as well as the second primary molars. A panoramic X-ray revealed a congenitally missing maxillary right lateral incisor and confirmed that the majority of these teeth were unrestorable, particularly with the patient's limited opening (Fig. 5).

The patient was placed on amoxicillin and instructed to rinse the mouth with water after eating, and apply chlorhexidine with a cotton

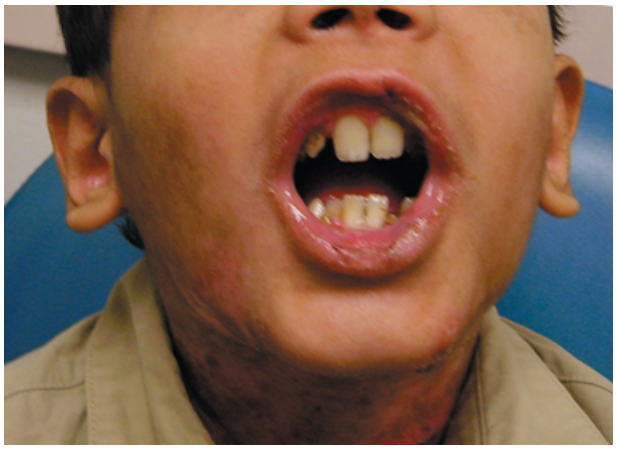

Fig. 3. Severe scarring of mouth with opening limited to 1 cm.

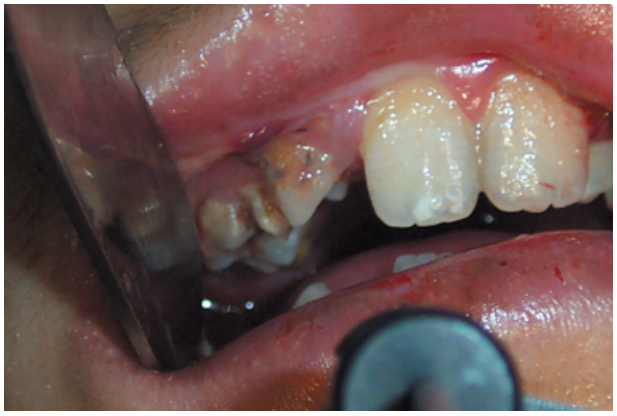

Fig. 4. Dental condition on initial presentation in patient with DEB.

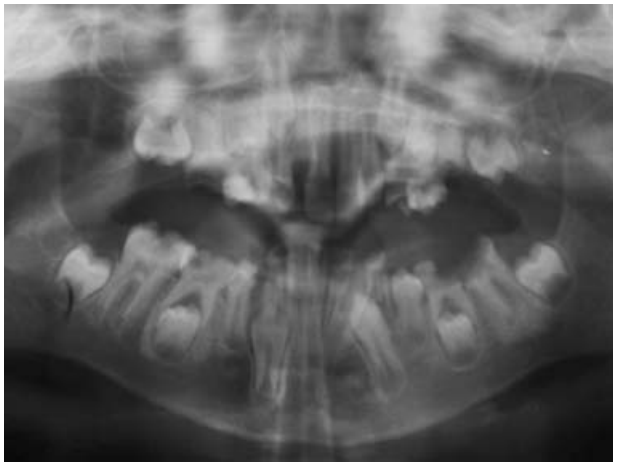

Fig. 5. Panoramic X-ray of patient with DEB.

swab twice daily. The plan was to complete extraction of all posterior teeth under general anaesthesia. After consultation with the plastic surgery division, it was decided to perform all dental rehabilitation prior to hand surgery because of the potential risk of infection to the skin grafts.

Case B

The girl had been followed for EB since early infancy with formation of blisters on her hands and feet since birth. She had a history of scarring of legs and arms and loss of nails by age 45 days. At the time of presentation at CHOP she had blisters in various areas of her body, secondary to friction from clothing, but her disease had not caused functional defects to the degree that her brother had. The skin lesions were being managed by weekly bleach baths by her parents. She also suffered from anaemia and was taking iron when needed. Her medications also included Flamazine cream and one can of Ensure daily. There were no reported allergies or previous hospitalizations. She weighed 13.1 kg and was 97.9 cm in height. She had been followed by the same dental clinic as her brother, where she was noted to have a primary dentition with caries. She was said to have had some preventive and restorative treatment, but was uncooperative for dental care to be completed on an outpatient basis. Oral hygiene was not practiced regularly.

Our dental examination revealed a few extraoral and intraoral bullae. She also had scarring of her mouth and very limited oral opening. Oral hygiene was very poor. A complete primary dentition was evident with multiple carious teeth. No abscessed teeth were evident clinically, although the maxillary anterior teeth were sensitive to touch. Due to the extent of her restorative needs, her limited mouth opening, and poor level of cooperation, it was decided to render treatment in the operating room under general anaesthesia.

Anaesthetic management of cases A and B

Patient A received oral midazolam (Versed®, 0.44 mg/kg; Roche, Basel, Switzerland) as a sedative premedication. Patient B did not receive

Versed because she was having increased problems drinking and swallowing preoperatively. Both patients' anaesthesia was induced with nitrous oxide, oxygen, and sevoflurane through a mask whose contact surfaces were covered with Mepilex® (Mőlnlycke Health Care AB, Göteborg, Sweden) which was held lightly on the face. A clear plastic specimen bag was placed on a finger over which the adhesive pulse oximeter probe was placed, which was then wrapped with Webril. The blood pressure cuff was placed around the upper arm over a layer of Webril. ECG pad adhesive was removed and leads secured to a relatively uninvolved area of skin with Mepilex. An intravenous catheter was inserted in a relatively uninvolved area on the volar surface of the forearm and secured with Mepilex, then wrapped with Coban® (3M, Saint Paul, MN, USA) (Fig. 6). To minimize oro-pharyngeal mucosal trauma and because of limited mouth opening, nasal endotracheal intubation was facilitated with the use of a fibre-optic bronchoscope after the naris was prepared by vasoconstriction with oxymetazoline and dilated with progressively larger soft nasal airways coated with water-based lubricant. A relatively small (4.5 mm) cuffed endotracheal tube was used to minimize trauma and ensure adequate ventilation and to avoid having to change the tube. A 90° metal connector was attached to the endotracheal tube, replacing the plastic 15 mm connector. The eyes were generously lubricated (Lacrilube®, Allergan Inc., Irvine, CA, USA) and closed but untaped under the head dressing. The endotracheal tube was secured to a turban fashioned out of a surgical towel. There was no tape applied to the patient's face (Fig. 7). Anaesthesia was maintained with desflurane, air, and oxygen. Analgesia was provided with intravenous fentanyl (5 μg/kg over a period of 3 h for patient A, and 7 μg/kg over a period of 3.5 h for patient B). Dexamethasone 0.5 mg/kg was administered to both patients to minimize mucosal swelling and nausea. Ondansetron 0.1 mg/kg was administered to both patients. Patient A received no muscle relaxant. Patient B received vecuronium prior to intubation. The patients were positioned supine on the operating table which was covered with a full length gel pad to reduce skin pressure. The gel pas was covered by Chux. Open lesions on the back were covered with silver sulfadiazine 1% cream. All patient transfers were performed by picking up chucks and patient as a unit, not by sliding the patient, to avoid shearing forces to skin surface.

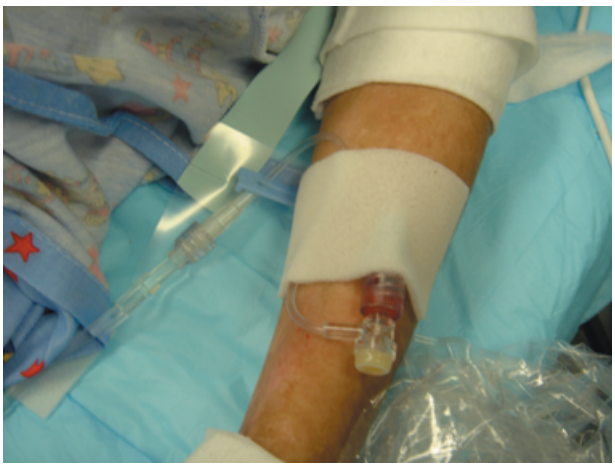

Fig. 6. IV placement secured with Mepilex and wrapped with Coban.

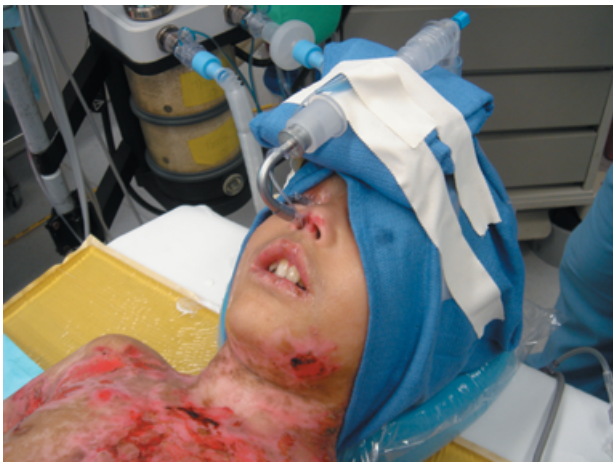

Fig. 7. Endotracheal tube stabilization.

Intraoperative and postoperative dental management of cases A and B

After anaesthetic induction a throat pack was placed. Ampicillin (25 mg/kg) was administered to both patients. All perioral tissues and commisures were protected with lubricant. Treatment consisted of full mouth radiographs,

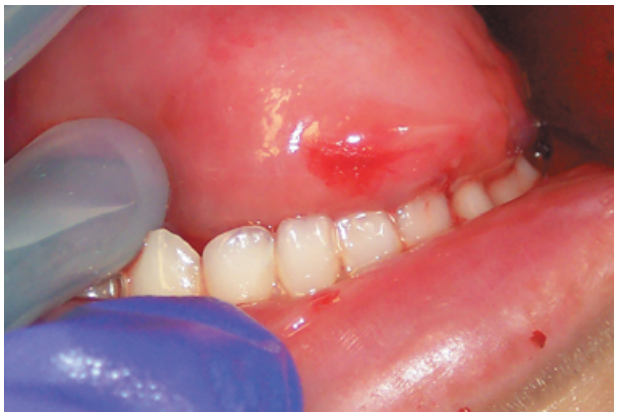

Fig. 8. Bullous formation on the tongue of a patient with DEB.

prophylaxis, and examination in both cases. In the boy, the first premolars were found to have erupted early, but this altered timing ultimately would have no impact on the course of treatment. The manipulation from these procedures was enough to cause bullae formation on the tongue of both patients (Fig. 8). The boy subsequently had all posterior teeth extracted, with most teeth requiring extraction via a buccal approach due to the severely limited opening. Despite an attempt to use as gentle manipulation as possible, extensive sloughing of mucosa resulted. No sutures were placed and haemostasis was obtained with gentle pressure. The girl received stainless steel crowns on all posterior teeth, except for the maxillary primary first molar which was extracted. The maxillary anterior teeth were extracted as well because of severe decay and the decision to limit intraoperative time. Only small surgical suction tips and malleable retractors were used as recommended by Wright[16]. Despite this, some sloughing of tissue was noted in the girl as well. Fluoride varnish was used on the remaining teeth of both patients. The throat pack was removed with no evidence of blistering in either case. At the end of the procedure, if muscle relaxant had been used, neostigmine in combination with atropine was administered at the end of procedure. Patients were extubated uneventfully. There was no trauma, bleeding, or swelling of the airway in either patient, and no prolonged bleeding occurred subsequent to tooth extraction. The patients were taken to the intensive care unit for recovery and airway management. No complications ensued.

Healing of the oral tissues and bullae occurred gradually over a 2-week period, although some mucosal erosion was noted on the palate of the boy. He was continued with pureed and soft foods as well as the Ensure. When oral hygiene was attempted with a soft toothbrush, erosions and bullae would form; therefore, he was advised to discontinue the use of the soft toothbrush and use a disposable oral swab (Toothettes®, Sage Products Inc., Cary, IL, USA) with chlorhexidine to prevent continued trauma. Hard foods were to be avoided as well. A prescription was given for Magic Mouthwash (a mixture of diphenydramine hydrochloride, lidocaine, and an antacid) to be used as needed for oral discomfort. The girl had healing of all tissues with no remaining blistering. All restorations were intact and oral hygiene was reinforced. A soft toothbrush was recommended.

Discussion

The two cases presented here illustrate many features that are characteristic of generalized recessive dystrophic EB[7]. Having unaffected, consanguineous parents suggests an autosomal recessive inheritance form of dystrophic EB[11], and this was confirmed by genetic testing. The oral findings are consistent with what has been described in this condition: blister formation, scarring, vestibular obliteration, microstomia, and extensive dental decay[6–9]. The comprehensive care of children with dystrophic EB can be difficult because of the severe limitations imposed by the condition. This can impact not only dental management but all other specialties as well. Special accommodations need to be provided from an anaesthetic standpoint when these children are to be administered general anaesthesia prior to oral rehabilitation[15–17]. Great care should be exercised to avoid the use of tape on any skin surface and to avoid shearing forces on the skin when moving the patient. Adhesive surfaces are removed from ECG electrodes which are held on the extremities with Webril or on the chest and abdominal surface using Mepilex. In cases of severe skin involvement, ECG monitoring may be omitted, with heart rate

sampled from the pulse oximeter. Mepilex is an absorbent, atraumatic dressing made or polyurethane foam. Although it adheres to the skin, it has no adhesive surface. Pulse oximetry may be accomplished with an adult clip-on probe (not possible if the patient has total pseudosyndactyly of fingers and toes, as in patient A), or with the adhesive strip placed *over a* clear plastic bag covering the hand or foot, then wrapped with Webril or Coban. The IV can be secured with Mepilex then wrapped with Coban.

Although limited mouth opening in many patients with EB necessitates nasotracheal fibre-optic intubation, this route is a good choice for all patients with EB, even with good mouth opening, as oral intubation causes more trauma and bulla formation to the tongue and oral mucosa because of pressure of the laryngoscope on the supraglottic area. The nasal mucosa is composed of pseudostratified cylindrical ciliated epithelium with goblet cells (respiratory epithelium), stratified cuboidal epithelium, and stratified squamous nonkeratinized epithelium, the first two of which are less vulnerable to bulla formation than the stratified squamous keratinized and nonkeratinized epithelium of the oral mucosa, and the tube may be secured more easily without tape than an oral tube. Care should be taken to use a tube small enough to avoid pressure on the skin surface at the entrance to the naris. The tube should be softened by soaking in warm saline and generously lubricated with water-based lubricant prior to insertion in the naris. Oral rehabilitation procedures also are more easily accomplished with a nasotracheal tube. Despite these facts, some authors prefer oral intubation in patients with EB[17].

Although the goal is to preserve the dentition wherever possible, this is often not realistic in these severe cases. Limitations exist due to limited mouth opening, formation of intraoral bullae, and mucosal sloughing with trauma from hard foods and tooth brushing and subsequent difficulty swallowing. These children are often on hypercaloric formulas, which, combined with poor oral hygiene and swallowing issues, results in high caries rates. The development of scarring and hand contractures further complicates oral hygiene issues. Thus, prevention is crucial. Dentists play a central role in early intervention. Patients may require frequent follow-up for cleaning and topical fluoride application. Home-care regimen should include brushing with a soft-bristled toothbrush and regular use of non-alcohol-based fluoride rinses. Dietary counselling may best be managed by a dietician. Unfortunately, the dental prognosis for the children described in this report is not hopeful given their present set of circumstances. The girl may progress to have some of the same difficulties as her brother with advancing age; however, with routine dental care and use of preventive measures for high-risk children, it is hoped that her permanent dentition may be preserved.

What this paper adds

- Dystrophic EB is a rare genetic disorder in which vesiculobullous lesions occur with erosions and scarring on cutaneous and extracutaneous surfaces including lips, tongue, gingiva, and palate.
- A rare case of siblings with dystrophic EB who required extensive dental treatment is presented.
- The comprehensive care of children with dystrophic EB can impact not only dental management but anaesthesia administration as well.
- Guidelines for general anaesthesia management of dystrophic EB patients requiring oral rehabilitation are presented.
- Early intervention with a focus on prevention – strict home-care regimen, dietary counselling, and frequent follow-up with oral health provider – is critical for optimal oral health.

Why this paper is important to paediatric dentists

- This manuscript reviews the clinical features observed in patients with dystrophic EB.
- A review of the dental considerations in the management of dystrophic EB is presented.
- Collaboration with others on the medical team is imperative for optimal care.

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