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Case report

Laryngeal lesion associated with epidermolysis bullosa secondary to congenital plectin deficiency

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ABSTRACT

Introduction: Epidermolysis bullosa (EB) is a congenital disease characterized by fragility of epithelial structures. The skin is the organ primarily affected, resulting in the formation of skin blisters. Some forms of EB may also present mucosal lesions.
Case report: We report the case of a girl with epidermolysis bullosa simplex (EBS) associated with muscular dystrophy secondary to congenital plectin deficiency. She presented severe respiratory tract lesions extending from the oral cavity to the larynx. In particular, we describe our medical and surgical management of the laryngeal lesions, responsible for several episodes of respiratory distress and feeding difficulties.
Discussion: Epidermolysis bullosa simplex associated with muscular dystrophy is a rare hereditary form of EB, as fewer than 50 cases have been reported in the literature. This form is characterized by mucosal lesions involving the upper aerodigestive tract, with consequences for feeding, phonation and breathing. Special care must be taken when performing diagnostic and therapeutic procedures to avoid worsening the lesions of this very fragile mucosa. Tracheotomy is a harmful procedure in these patients and should only be considered as a last resort.

1. Introduction

Epidermolysis bullosa (EB) is a group of genetic diseases characterized by fragility of the dermoepidermal junction. The prevalence of all forms of EB is estimated to be between 5 and 20 per million inhabitants and these conditions affect males and females indifferently [1]. EB is due to abnormalities of the constituent proteins of the dermoepidermal junction, resulting in bullous epithelial detachments. EB is classified into three groups according to the histological features. Epidermolysis bullosa simplex (EBS) represents more than one-half of all forms of EB. EBS is characterized by deep intraepidermal blister formation, usually secondary to a mutation of a gene coding for keratins 5/14. Junctional epidermolysis bullosa (JEB) is characterized by blister formation in the lamina lucida of the dermoepidermal junction. Dystrophic epidermolysis bullosa (DEB) is characterized by blister formation in the lamina densa (25% of all forms of EB). Clinical features vary according to the histological type. A marked variability between individuals with the same subtype of EB is also observed. The clinical course remains unpredictable for each patient and the prognosis is independent of the histological type. Transient forms heal spontaneously, while the most serious forms are fatal during the first days of life.

The circumstances of diagnosis are also variable because EB can present at various ages. In infants, the diagnosis of EB should be considered in the presence of skin blisters over zones of friction, skin erosions following minor trauma and/or delayed healing. In addition to skin lesions, some forms of EB comprise lesions affecting the mucosa of the respiratory and gastrointestinal tracts, genital organs and urinary tract. Lesions of the upper gastrointestinal tract induce odynophagia, which, in severe forms, can be accompanied by true ankyloglossia and progressive oesophageal stenosis. The combination of feeding difficulties and cutaneous protein losses is associated with a high risk of malnutrition, particularly in young infants. Laryngeal lesions are frequently observed in junctional epidermolysis bullosa (JEB) and dystrophic epidermolysis bullosa (DEB), but are rare in epidermolysis bullosa simplex (EBS) [2]. The formal diagnosis is based on histological examination of a skin biopsy with immunohistochemistry. A complementary genetic examination is sometimes necessary to characterize the type of EB, by identification of the mutation responsible.

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We report the case of a young girl presenting with laryngeal involvement in the context of epidermolysis bullosa simplex with congenital plectin deficiency.

2. Case report

We report the case of a female infant, born at term, after an uncomplicated pregnancy to consanguineous parents, who were cousins. The couple's first child had no notable history. Right from the first weeks of life, this baby girl presented skin blisters predominantly involving the extremities, associated with intraoral erosions. She was examined in the dermatology outpatients department at the age 6 months for sternal skin erosions following physiotherapy for bronchiolitis. Histological examination of a skin biopsy revealed detachment of the epidermis with normal underlying dermis. Immunohistochemistry with anti-pankeratin antibody showed labelling of the roof and the floor of the blisters, indicating a diagnosis of congenital epidermolysis bullosa simplex. However, no anti-plectin labelling was observed. Complementary genetic analyses confirmed inactivation of the PLEC gene coding for plectin.

The child was referred to the ENT department at the age of 7 months with dysphonia and blood-stained sputum. Intraoral examination revealed fragile mucosa that bled on simple contact. Nasal endoscopy demonstrated laryngeal erosions involving all of the endolarynx with a fibrous pseudomembrane appearance, extending as far as the glottis, associated with impaired glottic opening despite actively mobile vocal folds with marked reduction of the glottic airway.

At the age of 9 months, she was admitted to the emergency department with rapid onset of respiratory distress on awakening, without fever. Clinical examination revealed inspiratory dyspnoea, intense sweating, agitation and marked intercostal and subcostal retraction. Emergency nasal endoscopy visualized bullous detachments on the epiglottis responsible for supraglottic obstruction. Laryngoscopy under general anaesthesia demonstrated disseminated vestibular lesions with bilateral scarred crico-arytenoid ankylosis and a narrow glottic opening (Fig. 1) with normal subglottis and trachea. Cold instrument release of adhesions was performed during endoscopy. The subsequent course was rapidly favourable in response to medical treatment, comprising high-flow oxygen therapy by Optiflow® (Marseille, France) and corticosteroid nebulization several times a day. After 4 days, the patient was discharged home with inhaled corticosteroids and oral esomeprazole.

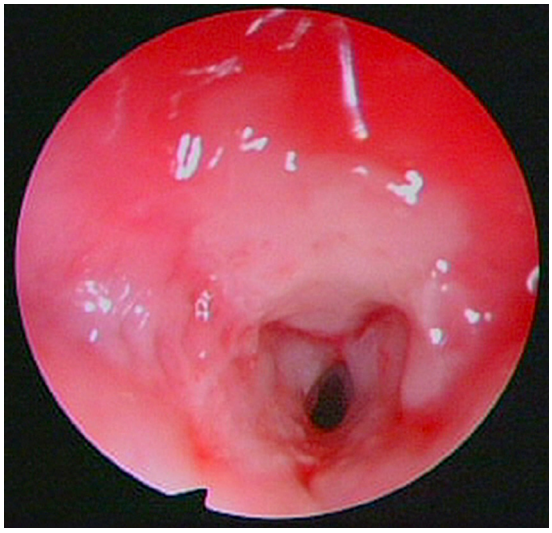

Fig. 1. Laryngoscopy showing a mucosal bulla in the inferior part of the epiglottis, as well as scarring from previous bullae, responsible for stenosis of the marginal zone of the epilarynx, extending to the posterior part of the glottis.

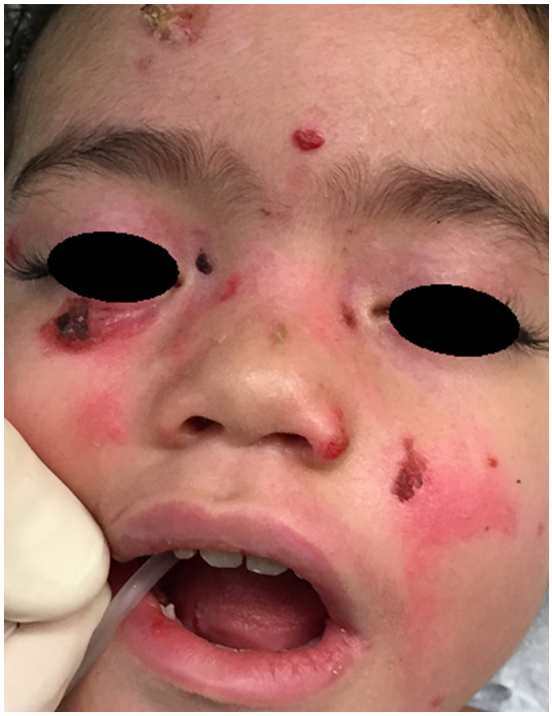

Fig. 2. The face is marked by bullae and sequelae of resuscitation procedures for respiratory distress.

The patient was reviewed in the outpatients department for 6 months. She presented persistent chronic dyspnoea when irritated, with no signs of respiratory decompensation and no impact on feeding or growth. Persistent ulcerated lesions of the oral cavity were observed. The various endoscopic examinations revealed scarred endolaryngeal mucosa, but no bullae or active bleeding. The laryngeal airway remained narrow with limited vocal fold mobility. Inhaled corticosteroid therapy was continued. CT assessment performed at the age of 1 year revealed stenosis of the endolaryngeal lumen, with a normal appearance of the trachea and bronchi.

At the age of 16 months, in a context of progressive deterioration of laryngeal lesions responsible for obstructive respiratory failure and feeding difficulties associated with poor weight gain, it was decided to perform another laryngeal disobstruction procedure. Endoscopic resection of scar tissue mucosal adhesions was proposed rather than tracheostomy, which would be associated with a risk of skin lesions around the tracheostomy tube. The surgical procedure was performed with cold instruments, but required laryngotracheal intubation due to intraoperative ventilatory difficulties. The immediate postoperative course was marked by respiratory distress on extubation, requiring re-intubation. The patient also presented bullous lesions of the skin of the nostril, at the zones of attachment of the nasotracheal intubation tube (Fig. 2). The patient was finally extubated later the same day with adrenaline and corticosteroid aerosol therapy associated with intravenous corticosteroids. The respiratory symptoms rapidly improved, allowing return home after one week of surveillance in hospital.

With a follow-up of 1 year, the patient is in good general health with normal height and weight. She presented persisted respiratory symptoms of dyspnoea and stridor on effort. Follow-up endoscopy revealed persistence of bullous lesions on the right pharyngeal surface of the marginal zone of the epilarynx. Vocal fold mobility remained limited by fibrous ankylosis. It was decided to continue

medical treatment with inhaled corticosteroids, oral esomeprazole and follow-up visits several times a year.

3. Discussion

Mucosal lesions are usually absent in epidermolysis bullosa simplex (EBS), except in the case of epidermolysis bullosa simplex with muscular dystrophy (EBS-MD) [3]. EBS-MD is a rare subtype of EBS (fewer than 50 cases have been reported in the literature), secondary to a mutation of the gene coding for plectin, a protein present in many tissues: skin, muscles, nervous system. Muscle and nerve lesions are variable, and may only appear during adulthood [4]. In contrast, skin lesions are observed by the first days of life, and one-half of infants present mucosal lesions of the upper aerodigestive tract [5,6]. These children develop airway lesions as a result of crying, coughing or episodes of upper respiratory tract infection. Many clinical lesions have been described: inflammation, bullae, erosions, granulation tissue, nodules, mucosal adhesions and stenoses. These lesions can be responsible for stridor, dysphonia, breathlessness on exertion or at rest, or even respiratory distress. Some authors recommend endoscopic examination in all neonates presenting dysphonia in the context of epidermolysis bullosa, but all invasive examinations of the airways are prohibited in the absence of suggestive symptoms [1]. Endoscopic examination is preferably performed with a flexible endoscope, which is less traumatic for the mucosa. Rigid endoscopy under general anaesthesia is sometimes necessary to allow more comprehensive exploration of the laryngeal and subglottic mucosa.

Stridor not associated with any severe respiratory symptoms and not interfering with feeding can be treated medically by corticosteroid nebulization several times a day, frequently combined with antireflux treatment, although the efficacy of this treatment has not been formally demonstrated [7–9].

Endoscopic surgery may be considered in the presence of severe respiratory repercussions. During the operation, the surgical team must be attentive to the patient's fragile skin and mucosa in order to limit iatrogenic trauma. All adhesive dressings, prolonged compression, friction or constriction must therefore be avoided. Some authors recommend lubrication of surgical gloves. The patient should be placed in a neutral position on an operating table equipped with a gel mattress to limit pressure points. Intubation, especially when it is prolonged, can exacerbate the mucosal lesions and create new scar tissue adhesions. A previously lubricated small calibre flexible tube should therefore be used. For the endoscopic surgery, cold instruments are preferred laser to limit the local inflammation. The surgical procedure must be adapted to the intraoperative findings and must be as minimally aggressive to the mucosa as possible. Some authors recommend topical application of mitomycin based on its antiproliferative properties [10]. Surgery is performed under systemic corticosteroid therapy with cautious awakening from the anaesthetic to avoid trauma secondary to postoperative agitation [11].

Tracheostomy is sometimes necessary when the laryngeal stenosis is not accessible to an endoscopic procedure (severe stenosis, tracheal stenosis), but nevertheless raises a number of difficulties, as friction of the tracheostomy tube and repeated tracheal aspiration induce additional lesions of the already vulnerable tracheal mucosa. The tracheostomy tube fixation system can also induce traumatic skin lesions. The course of the respiratory tract lesions in these tracheostomised patients and the possibility of long-term extubation have never been evaluated [7]. Some authors suggest that tracheostomy should be performed in preparation for repeated general anaesthesia, as tracheostomy is less harmful than repeated orotracheal intubation [12,13]. In every case, the decision to perform tracheostomy must be discussed case by case by a multidisciplinary team.

Adequate nutritional intake must be ensured due to the high risk of malnutrition in these patients: increased energy and protein requirements (healing, cutaneous superinfection), decreased intake (odynophagia, oesophageal stenosis), gastrointestinal disorders (constipation, diarrhoea), depression. Fractionated oral feeding with blended foods is recommended. Soft teats should be used in infants. Food supplements are prescribed in the case of high protein and caloric losses.

4. Conclusion

Epidermolysis bullosa is a rare disease that requires multidisciplinary management. Otorhinolaryngologists may be involved in the presence of mucosal lesions of the upper aerodigestive tract with a major impact on feeding and breathing. Serious mucosal lesions are rare in epidermolysis bullosa simples (EBS), apart from the rare EBS with plectin deficiency subtype. No curative treatment for this disease is available at the present time. The management of laryngeal lesions is complex and must be adapted to each patient. Surgery may be necessary in patients with severe airway obstruction. Less invasive endoscopic procedures should be preferred, but require special precautions to limit the appearance of new skin or mucosal lesions. Tracheostomy is associated with high morbidity in these patients and should only be performed as a last resort.

Disclosure of interest

The authors declare that they have no competing interest.

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