Case Report
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Junctional Epidermolysis Bullosa Associated Laryngeal Stenosis: A Case Report and Review of Literature

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Abstract

Introduction:

Introduction: Junctional Epidermolysis Bullosa (JEB) is a rare subtype of the Epidermolysis Bullosa which itself is a rare genetic disorder. While mucosal involvement of pharynx and oesophagus has been reported, laryngeal involvement is rare.

Case Report:

A 7-month-old male child who was known to have Junctional Epidermolysis Bullosa presented to the emergency department with respiratory distress associated with a stridor which was eventfully found to have multiple level laryngeal stenosis.

Conclusions:

Longitudinal cohort studies are required to determine the long-term outcome and the anticipated behavior of epidermolysis bullosa in patients with laryngeal manifestation to avoid unnecessary surgical interventions.

Keywords: Airway, Junctional Epidermolysis Bullosa, Laryngeal Stenosis.

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Introduction

Epidermolysis Bullosa is a rare genetic disorder characterized by the formation of skin blisters secondary to minor trauma and when ruptures, it heals by scar formation. Based on the type of inheritance, it is divided into four sub-types: Simplex, Dystrophic, Junctional and Hemidesmosome Epidermolysis Bullosa (1). We hereby present a rare case of a male child with Junctional Epidermolysis Bullosa complicated with multi-level laryngeal stenosis.

Case Report

A 7-month-old male child presented to the emergency department with a sudden onset of respiratory distress associated with a stridor. He was cyanosed on presentation and had an oxygen saturation of 80 % despite non-invasive mask ventilation. The child was known to have Junctional

Epidermolysis Bullosa with a positive family history of the same condition. He was diagnosed in another hospital shortly after birth by skin biopsy and DNA analysis from a bulla lesion in the right upper limb.

Because of his status, the decision was taken to proceed with in-theatre endotracheal intubation -/+ tracheostomy given his Junctional Epidermolysis Bullosa disease. In the theatre, mask induction by oxygen and sevoflurane was done followed by the administration of 1mg/kg bolus propofol. Video laryngoscopic examination showed multiple ulcerations in the soft palate, posterior pharyngeal wall and oedema of the epiglottis obscuring the glottis with generalized oedema of the supraglottis. However, endotracheal intubation with a size three uncuffed tube was successful.

The patient was admitted to the pediatric intensive care unit (PICU) under the impression of Supraglottitis. He was treated with intravenous antibiotics and supportive care. He was extubated after 2 days and discharged uneventfully on day five of his admission. 6 months later, at the age of 13 months, he presented to the emergency department with a fever associated with cough, respiratory distress, and stridor.

His overall condition was distressed with multiple skin lesions, nasal ulcers, bilateral auricular ulcers, and multiple oral ulcers (Figure 1).

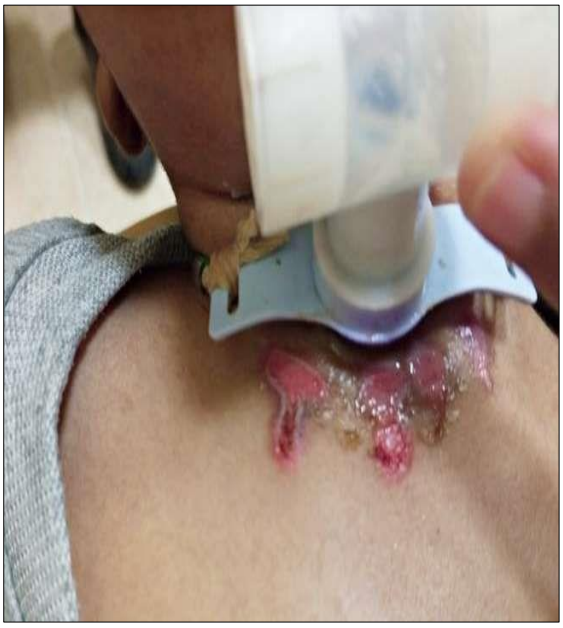

Fig 1: skin lesions beneath the tracheostomy tube flange

He was admitted to the PICU with fluctuating saturation despite non-invasive mask ventilation. The decision was taken to do an airway assessment and proceed with again either endotracheal intubation or surgical tracheostomy in the theatre. After induction, a video laryngoscopy was done and revealed an anterior glottic web with ulcerative epiglottis. A size three uncuffed endotracheal tube was inserted with difficulty and surgical tracheostomy was done in the same setting. He was kept on mechanical ventilation for 3 days in the PICU and then gradually weaned off until recovered.

He was discharged on tracheostomy after completing 7 days of intravenous antibiotics and supportive medication. 3 months later, at the age of 16 months, the patient attended the ENT OPD for review and first tracheostomy tube change.

The parents gave a history of complete aphonia on crying with minimal secretions upon suctioning. Given the previous airway assessment findings, repeated airway assessment and tracheostomy tube in the theatre were advised. In theatre, a suspension direct laryngoscope was done and revealed a thickened and deformed epiglottis with inter arytenoid granuloma, causing mechanical immobility of the vocal cord with a negative jostle sign (Figure 2).

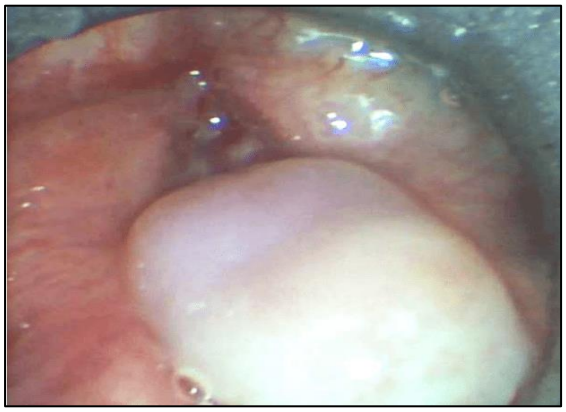

Fig 2: large bulla setting on the inter arytenoid mucosa blocking the glottis view

A thick anterior glottic web was seen and the subglottis could not be visualized. Trans-stomal tracheoscopy was done and showed normal trachea up to the carina. The tracheostomy tube change was done uneventfully.

Counseling sessions were conducted with the parents regarding the critical nature of the child's sole reliance on tracheostomy as the primary airway. Given the nature of the disease, the tracheostomy tube was changed to a durable Duratwix-type tracheostomy tube to avoid unnecessary airway manipulation or tracheal mucosal injuries due to tube change. To date, the child is still on routine follow-up and his next tube change is due at the age of 22 months.

Discussion

Epidermolysis Bullosa is a rare heterogenous hereditary disorder. It is characterized by the formation of cutaneous or mucosal bullae in response to minor trauma after which the bullae rupture, ulcerate, and heal by scar formation (1). This healing process leads to the disturbance of the normal anatomy and physiology of the affected tissue. There are four subtypes of Epidermolysis Bullosa: Epidermolysis Bullosa Simplex, Dystrophic Epidermolysis Bullosa, Junctional Epidermolysis Bullosa and Hemidesmosomal Epidermolysis Bullosa. While this classification is based on the type of inheritance and its genotype, the clinical manifestation of each subtype is also discrete. Junctional Epidermolysis Bullosa has been observed to be more commonly associated with head and neck manifestations (2). The head and neck manifestations are divided into cutaneous manifestations and mucosal manifestations. The cutaneous head and neck manifestations include ulcerations over the nasal vestibule, auricle, and lips which can lead to vestibular stenosis secondary to scar and trismus in severe cases (2,3). The mucosal manifestations include aerodigestive tract ulcerations which can lead to dysphagia. Dysphagia - secondary to esophageal strictures- is the most common head and neck manifestations of JEB (3). Laryngeal involvement, in contrast, is uncommonly reported. Airway compromise due to active bullae in the supraglottis or scaring due to a ruptured bullosa in the supraglottis and glottis have been reported (4). Ida et al reported seven patients with laryngeal manifestations and Lyos et al reported five children with Epidermolysis Bullosa. Five out of which three children of Lyos et al were tracheostomy dependent due to the laryngeal involvement and one child died due to acute airway obstruction (3,5).

Moreover, Davies et al reported the death of a 22-month-old child with acute airway obstruction on Epidermolysis Bullosa background and confirmed on postmortem evaluation to have narrow laryngeal airway and granulation tissue replacing the laryngeal epithelium (6).

Whether it is secondary to the infective inflammatory process, food bolus trauma to the supraglottis, aggressive cough, or voice abuse-associated tearing pressure of the mucosa, the exact provoking factors of laryngeal bullae are unknown. Endotracheal intubation, however, can be considered a provoking factor resulting in mechanical injury to the supraglottic, posterior glottis and subglottic mucosa (7). Gonzalez et al advocated for early tracheostomy in children with Epidermolysis bullosa-associated respiratory distress to avoid laryngotracheal trauma associated with intubation whether prolonged or recurrent due to the lack of predictive prognostic indicators for the condition (8).

In our case, the patient was intubated electively, and the laryngeal findings were identified 6 months after extubation. Nevertheless, the sequela of scar formation is unreversible and based on its location, depleting symptoms can emerge. Scaring of the epiglottis can cause thickening of the cartilage and tubular appearance which can narrow the airway channeling to the glottis resulting in

dyspnea, stridor, and hoarseness of voice. Interarytenoid bullosa can result in immobile vocal cords secondary to fibrosis and hence stridor with airway obstruction. Subglottis involvement can result in subglottic stenosis. While it is noteworthy to observe that the limited documented case reports of laryngeal manifestations in Junctional Epidermolysis Bullosa report lesions on the mucosa of the supraglottis, particularly over cartilaginous structures such as the epiglottis and arytenoids. While, Dystrophic Epidermolysis Bullosa is linked to mutations in the COL7A1 gene which provides instructions for the synthesis of type VII collagen, Junctional Epidermolysis Bullosa is associated with mutations in genes that encode proteins crucial for the formation of the basement membrane, a critical structure in the skin rather than the mucosa (1). However, existing treatment strategies emphasize symptom management rather than a curative approach. In contrast to Epidermolysis Bullosa Acquisita, an acquired autoimmune disorder occurring in adulthood, the formation of bullae in Epidermolysis Bullosa is not prevented by immunosuppression therapy and corticosteroids (1).

Furthermore, the correlation between active skin lesions and ongoing mucosal disease, as well as the predictive capacity of such lesions for bullae formation, remains unknown. Palinko et al reported a successful management of glottic stenosis in a 4-year-old child with epidermolysis bullosa using CO2 Laser lysis with temporary suture lateralization of the arytenoid to avoid adhesion (9). 3 years post-intervention, Palinko reported that the child was symptom-free. Although the morbidity associated with epidermolysis bullosa is high, Wall et al reported rare surgical management of three adult patients with epidermolysis bullosa with laryngotracheal stenosis. One patient in Wall et al report was already tracheostomy dependent and developed left main bronchus stenosis. The three patients required frequent dilatation and the outcome did not modulate the course of the airway status (7). However, the cumulative risk of developed laryngotracheal stenosis is 39.8% by the 6 years and 5% at the age of 30 years, which makes laryngotracheal stenosis a paediatric airway challenge while squamous cell carcinoma is the main mortality in the adult population of Epidermolysis Bullosa (4,10, 11). To date, there is no cure for epidermolysis bullosa, and the current treatment strategies focus on symptomatic relief. New-generation research focuses on addressing the underlying genetic mutation: gene replacement therapy, protein, and cell-based/stem cell therapies (1).

Conclusion

Epidermolysis Bullosa is a genetic disorder with a challenging course in which multi-level laryngeal stenosis is a life-threatening morbidity in the pediatric population. Scattered case reports describe the trials of endolaryngeal surgical interventions; however, longitudinal cohort studies are required to determine the long-term outcome and the anticipated disease behaviour in this group of patients to avoid unnecessary surgical interventions. We advocate for early tracheostomy once indicated.

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Conflict of interest and funding

we addressed no conflict of interest, and no funding was required.

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