International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 08, Issue 12, December 2023,
https://doi.org/10.23958/ijirms/vol08-i12/1794

Case Report

Esophageal Stenosis as a Rare Mode of Revelation of Hereditary Epidermolysis Bullosa: Report of Three Cases

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Received 26 November 2023; Accepted 12 December 2023; Published 15 December 2023

Abstract

Dystrophic epidermolysis bullosa (DEB) is a heterogeneous group of rare genodermatoses with multiple variants and multi-organ involvement, including digestive system with esophageal stenosis. We describe in this paper 3 unusual cases of hereditary epidermolysis bullosa revealed by dysphagia. The first one is a 77-year-old man admitted with chronic dysphagia, cutaneous erosions and a complete loss of fingers and toenails. Gastroscopy with skin biopsies and barium swallow confirmed a hereditary epidermolysis bullosa. He was treated by pneumatic dilatation. The second case is a 60-year-old female admitted because of dysphagia. She was on good condition but had lingual erosions and anonychia affecting fingernails and toenails, with esophageal stenosis. The skin biopsy confirmed the DEB. She was treated successfully with pneumatic dilatation. The third case is a 15-year-old male who was transferred to our department for management of esophageal stenosis. The physical examination showed malnutrition and dehydration with bullous lesions and anonychia. The diagnostic of DEB was confirmed and he was treated by pneumatic dilatation. Dysphagia can rarely reveal an esophageal stenosis complicating a DEB, and can be treated successfully by pneumatic dilatation.

Keywords: ***Hereditary epidermolysis bullosa, Dermo-epidermal cohesion, Dysphagia,* Esophageal stenosis, Pneumatic dilatation.**

Introduction

Hereditary epidermolysis bullosa (HEB) is a genodermatosis classified into four groups based on the cleavage level in the skin: Dystrophic epidermolysis bullosa (DEB), Epidermolysis Bullosa Simplex (EBS), Junctional Epidermolysis Bullosa (EBJ) and Kindler Syndrome. DEB can be classified into two subtypes based on the mode of transmission: the recessive form (RDEB) with the severest subtype known as Severe RDEB, and the dominant form (DDEB). The clinical manifestations of DEB are bullae and mucocutaneous erosions, due to the extreme fragility of the skin and mucous membranes. It is characterized by the mutation of the COL7A1 which encodes type VII collagen. Mucosal involvement in severe forms mainly affects the mouth, esophagus and anus [1].

Esophageal stenosis during dystrophic epidermolysis bullosa is a serious complication, responsible for dysphagia, with a negative impact on the quality of life of patients. The management is difficult, because the recurrences are frequent.

We report 3 cases of dystrophic epidermolysis bullosa, all revealed by dysphagia, and treated successfully with endoscopic balloon dilatation.

Cases reports

Case 1

A 77-year-old male was admitted to the department of gastro-enterology of Mohamed VI University Hospital Center, with a progressively severe dysphagia, including initially only solids. He became unable to swallow liquids or food for two weeks. There was no weight loss. He didn't have any pathological history other than tobacco use.

On physical examination, the patient was on good condition, with a body mass index of 23.2 kg/m^2, and no signs of malnutrition. The abdominal examination was normal. The patient presented multiple cutaneous erosions and a complete loss of fingers and toenails (**Figure 1a and 1b**). Laboratory tests and the nutritional assessment did not reveal any abnormalities.

A gastroscopy was performed, and had shown a regular esophageal stenosis 12 cm from the dental arches, that could not be traversed. The barium swallow test demonstrated an extensive stricture involving the upper and middle thirds of the esophagus (**Figure 2**). Skin biopsies of erosions were done, and showed subepidermal cleavage with a neutrophilic infiltrate. Furthermore, there was a loss of immunofluorescence for type VII collagen.

The clinical manifestations associated with these histopathological findings allowed to confirm the diagnosis of hereditary epidermolysis bullosa. The esophageal stenosis was treated by 3 endoscopic balloon dilatations, with no reported complication. Corticosteroids were also prescribed for the mucocutaneous involvement. After a 3-year follow-up, our patient is able to swallow without any difficulties.

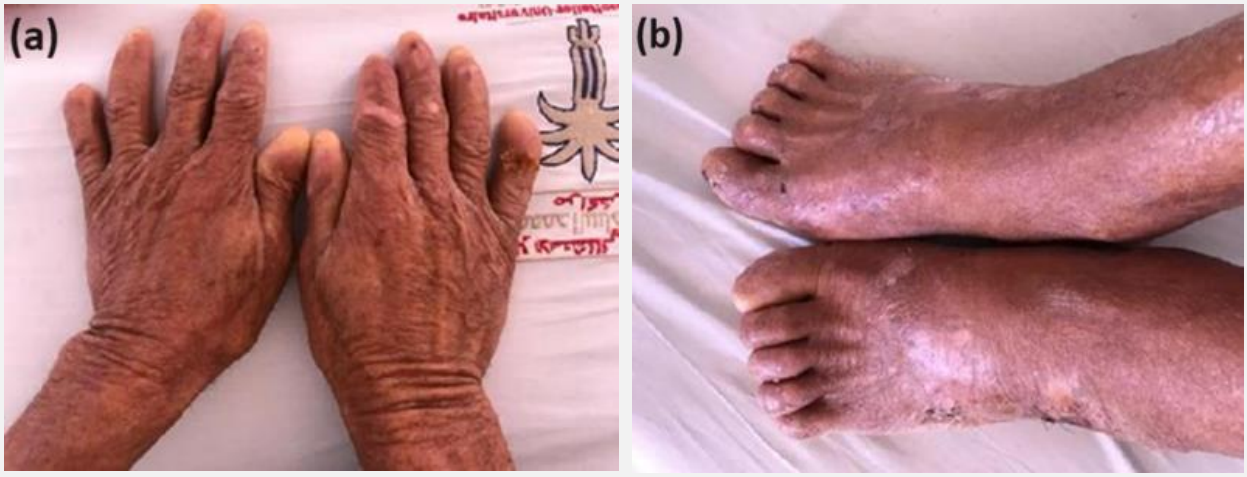

Figure 1: Complete loss of toe (b) and fingernails (a) in the first case

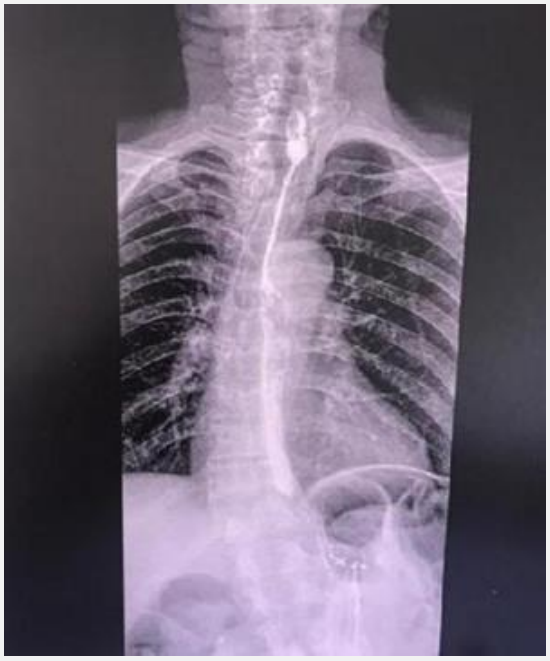

Figure 2: Extensive stricture of the upper and middle thirds of the esophagus on a barium swallow

Case 2

A 60-year-old female, with a history of thyroidectomy, was admitted to our department because of a dysphagia. This symptom has been present for several years, and has progressively worsened. On physical examination, the patient was on good condition, without any signs of malnutrition or dehydration. Her body mass index was 22.1 kg/m^2. There were no abnormalities on abdominal examination. However, we noticed lingual erosions and anonychia affecting fingernails and toenails (**Figures 3 (a,b) and 4**).

Laboratory tests and the nutritional assessment did not reveal any abnormalities. A gastroscopy was performed, and had found a regular stenosis of the upper third of the esophagus that could not be traversed. A barium swallow test was performed, and had confirmed the stricture of the upper third of the esophagus, extending over 3cm. The stomach's morphology was normal.

In view of the benign aspect of the stenosis, the presence of suggestive skin manifestations and the family bond with our first patient, an epidermolysis bullosa was strongly suspected, and a skin biopsy was performed. The examination of the skin biopsy by Immunofluorescence (IF) showed a reduced staining of collagen VII, which allowed us to confirm the diagnosis of DEB. The esophageal stenosis was treated by 2 endoscopic balloon dilatations, with no reported complication. After one year, our patient is able to swallow without any difficulties. A family investigation was carried out in order to screen possible cases, but the other family members did not have any suggestive dermatological or digestive symptoms.

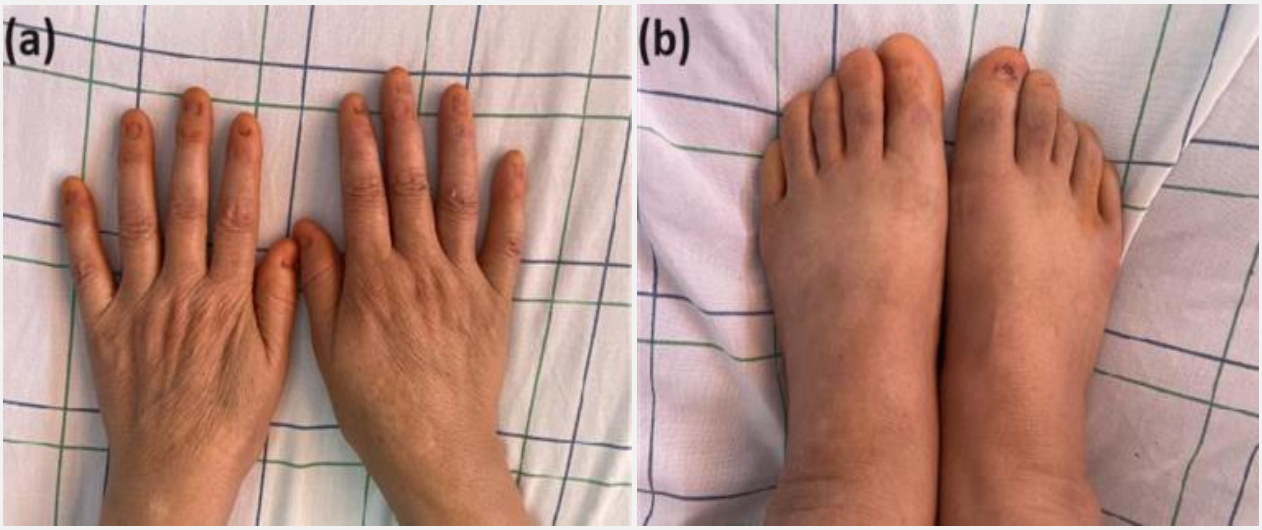

Figure 3: Complete loss of toe (b) and fingernails (a) in the second case

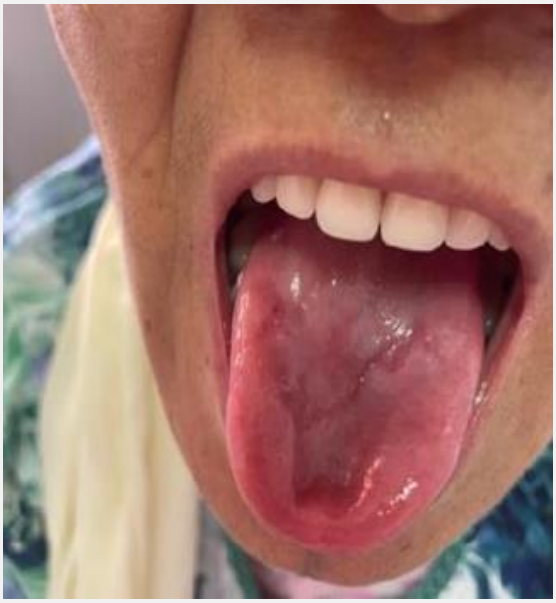

Figure 4: Lingual erosions

Case 3

A 15-year-old, full-term male was transferred to our department for management of esophageal stenosis. He was the product of a normal vaginal delivery and had a birth weight of 3.2 kg. The parents were not related. He did not have any brothers or sisters. He was initially admitted for investigation of progressive dysphagia to solids which has started five years before. Besides, since birth, he had suffered from extensive bullous lesions, occurring at the slightest trauma.

A barium swallow test was previously performed, and had showed two regular esophageal strictures. The first one was located at the junction between the upper and middle third of the esophagus, and the second one at the lowest third, extending over 39mm (**Figure 5**). Our initial physical examination showed that the patient was undernourished and dehydrated. His body mass index (BMI) was 14.3 (<3rd percentile). His abdominal examination was normal. However, we were able to highlight multiple erythematous and hypopigmented macular lesions associated to anonychia affecting fingernails and toenails (**Figure 6a and 6b**). There was poor oro-dental hygiene with scars of the mouth and dystrophic teeth.

The blood count was normal, but the level of serum albumin was low. A gastroscopy was performed, and had found a regular esophageal stenosis 22 cm from the dental arches, that could not be traversed. A skin biopsy with examination by IF showed that staining for collagen VII was reduced. Thus, the diagnosis of DEB was established and we performed 3 endoscopic balloon dilatations allowing weight gain and improvement of digestive symptoms with a follow-up of 2 years.

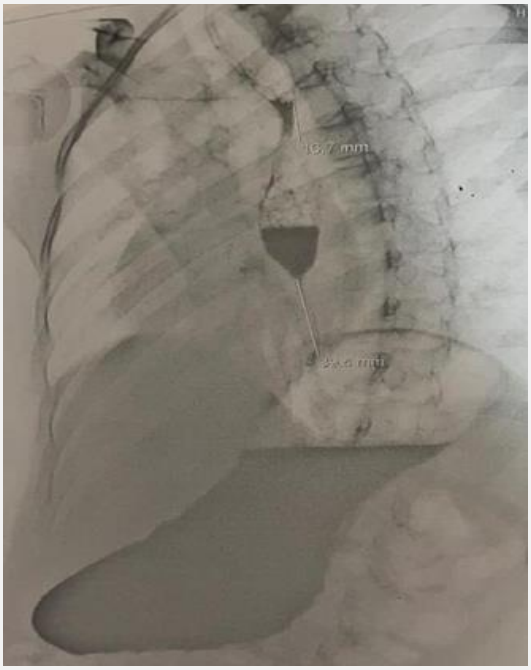

Figure 5: Two esophageal strictures on the barium swallow

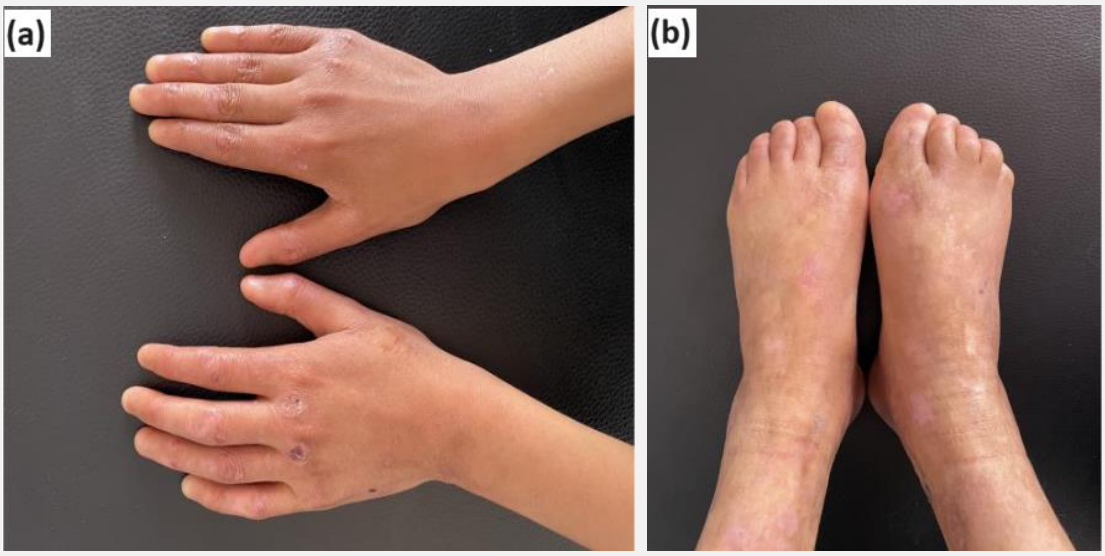

Figure 6: Complete loss of toe (b) and fingernails (a) in the third case

Discussion

DEB is a rare, genetically inherited disorder affecting dermo-epidermal cohesion. It is responsible of an extreme skin fragility, resulting in blisters, erosions and scars even after the slightest trauma [2]. It is a rare disease, affecting approximately 1/50000 newborns [3]. It was first described in 1886 by the German dermatologist Heinrich Koebner [4]. It has a wide range of clinical presentations ranging from localized skin lesions to extracutaneous manifestations, with eyes, nose, oral cavity, upper respiratory tract, digestive and genitourinary system involvement.

Serious complications can occur in multisystem forms, including esophageal stenosis. Dysphagia is the main symptom. The stenosis is secondary to a fibrosing process, caused by repeated traumas while swallowing hot or solid food. These traumas lead to a cleavage between the epithelium and the lamina propria, responsible of the esophageal stricture [5]. The stenosis can be single or multiple [6]. Esophageal involvement is mainly described in the Severe RDEB (33%). There appears to be no sex predilection for this complication. In most series, the stricture occurs in the upper third of the esophagus (50-70%). Also, the middle third is affected more often than the distal third. In 25% of cases, patients have multiple strictures [7]. Most commonly, the fibrosing process of the esophagus starts in childhood, but can remains silent, leading to late diagnosis.

The presentation in adults is rare. The esophagus's stenosis can be diagnosed based on the swallow barium. The upper gastrointestinal endoscopy can also confirm the diagnosis, but should be avoided, since the endoscope's trauma may result in esophageal bulla and hemorrhage. Esophageal strictures can lead to multiple complications, including malnutrition, anemia, vitamin deficiency, and aspiration pneumonia. Some cases of perforation have been reported. There does not appear to be an increased risk of esophageal carcinoma [5]. The management of esophageal strictures is essentially based on pneumatic dilatation. The bougienage should be avoided since it causes tangential shearing pressure, rather than vertical one, leading to more trauma and eventually new strictures [7]. Pneumatic dilatation is therefore the gold standard treatment of the esophageal stenosis complicating the DEB. It is a safe and effective method to relieve dysphagia, even if it is often temporary. The multidisciplinary care, including an expert team of endoscopists, dermatologists, and anesthesiologists is mandatory. The anesthetic team should avoid the orotracheal intubation, and be

available to face any difficulty or complication during the dilatation [8]. There are no guidelines regarding the dilatations' protocol, but in most cases, more than one dilatation is necessary [9].

Regular monitoring is therefore essential. Thus, the treatment of esophageal strictures in DEB remains difficult, and represents a challenge for endoscopists [10]. Adjuvant therapies have been proposed in refractory cases, including local or systemic corticosteroids, mitomycin C and injection of triamcinolone topical. The results were satisfying [11,12,13]. Some authors suggest their use before resorting to surgical treatment, that can be aggressive [14].

Besides esophageal stenosis, other digestive manifestations have been reported, including gastroesophageal reflux disease (GERD), esophageal atony, intramural pseudodiverticulosis, constipation, or even anal stenosis.

To our knowledge, only a few cases of esophageal strictures revealing a DEB in adults have been described in the literature [3]. The two first cases we reported are particular since they were both diagnosed, above the age of 60, of esophageal strictures, with un uncompromised nutritional status.

Conclusion

Esophageal stricture during DEB is a serious complication and can be difficult to manage. The gold standard treatment is pneumatic dilatation, which can be repeated if necessary. Regarding to multisystem involvement, the management of patients with DEB should be based on a multidisciplinary approach that also includes psychotherapy. Until then, no curative treatment is available. Recent advances of pathomecanisms of different subtypes of DEB will allow to develop some new targeted therapies such as gene-, protein- and cell- based therapies [15].

Ethics approval and consent to participate

Not applicable.

List of Abbreviations

DEB: Dystrophic epidermolysis bullosa
HEB: Hereditary epidermolysis bullosa
EBS: Epidermolysis Bullosa Simplex
EBJ: Junctional Epidermolysis Bullosa
RDEB: Recessive Dystrophic epidermolysis bullosa
DDEB: Dominant Dystrophic epidermolysis bullosa
IgG: Immunoglobulin G
IF: Immunofluorescence
BMI: Body mass index
GERD: Gastroesophageal reflux disease

Conflicts of Interest:

The authors declare that there is no conflict of interest regarding the publication of this paper.

Funding

None

Acknowledgements

None

References

[1] Fouad Nejjari, Tarik Adioui, Hassan Doulhoussne, et al., "Epidermolysis bullosa: an exceptional cause of dysphagia." *PAMJ, Volume 1, Article 27, 25 Nov 2019 | 10.11604/pamj-cm.2019.1.27.21035, 2019.*

[2] T. Okada, F. Sasaki, H. Shimizu, et al., "Effective Esophageal Balloon Dilation for Esophageal Stenosis in Recessive Dystrophic Epidermolysis Bullosa", *Eur J Pediatr Surg;16: 115–119 c, 2006*.

[3] A Ksia, S Mosbahi, M Ben Brahim, et al., "Esophageal strictures in children with epidermolysis bullosa", *Archives de Pediatrie,19:1325-1329; 2012*.

[4] Agata Michalak, Halina Cichoż-Lach, Beata Prozorow-Król et al., *BMC Gastroenterology, 18, Article number 47, 2018*.

[5] Paola De Angelis, Tamara Caldaro, Filippo Torroni et al., « Esophageal stenosis in epidermolysis bullosum". *Journal of Pediatric Surgery, 46, 842–847, 2011*.

[6] A. Marchal, L. Goffinet, A. Charlesworth, et al., « Un cas particulier d'épidermolyse bulleuse dystrophique », *Sciences du Vivant [q-bio]. hal-01731882, 2011*.

[7] Maria Rosaria Marchili, Giulia Spina, Marco Roversi et al., "Epidermolysis Bullosa in children: the central role of the pediatrician", *Orphanet Journal of Rare Diseases 17:147, 2022*.

[8] Antje Gottschalk, Stefan Venherm, Thorsten Vowinkel et al., "Anaesthesia for balloon dilatation of esophageal strictures in children with epidermolysis bullosa dystrophica: from intubation to sedation", *Curr Opin Anaesthesiol;23:518-22, 2010*.

[9] Patrícia Santos, Carolina Simões, João Lopes et al., "Endoscopic balloon dilation of oesophageal stenosis in a patient with recessive dystrophic epidermolysis bullosa", *Gastroenterol Hepatol. 2018*.

[10] Zhen Xu, Tianqiao Huang, Min Pan, et al., "Case Report: Recessive Dystrophic Epidermolysis Bullosa With Severe Esophageal Stenosis: A Case Report and Literature Review", *Br J Biomed Sci 79:10200, 2022*.

[11] Morikawa N, Honna T, Kuroda T, et al., "High dose intravenous methylprednisolone resolves esophageal stricture resistant to balloon dilatation with intralesional injection of dexamethasone", *Pediatr Surg Int; 24: 1161-1164, 2008*.

[12] Berger M, Ure B, Lacher M, "Mitomycin C in the therapy of recurrent esophageal strictures: hype or hope?", *Eur J Pediatr Surg; 22: 109-16, 2012*.

[13] Hirdes MM, van Hooft JE, Koornstra JJ, et al., "Endoscopic corticosteroid injections do not reduce dysphagia after endoscopic dilation therapy in patients with benign esophagogastric anastomotic strictures", *Clin Gastroenterol Hepatol; 1(7):795-801.e1.2013*.

[14] Dall'Oglio L, Caldaro T, Foschia F, et al., "Endoscopic management of esophageal stenosis in children: new and traditional treatments", *World J Gastrointest Endosc, 8(4):212-9, 2016*.

[15] Wally V, Reisenberger M, Kitzmüller S, Laimer M, "Small molecule drug development for rare genodermatoses - evaluation of the current status in epidermolysis bullosa", *Orphanet J Rare Dis, 15(1):292, 2020*.