Dystrophic epidermolysis with dilation of esophageal stricture: A case report

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Abstract. Dystrophic epidermolysis bullosa (DEB) is a rare disease and the associated esophageal stricture is frequently complicated by the lack of clinical experience. The present study reported a very rare case of DEB in a 37-year-old male, who was admitted to Shenzhen Hospital (Shenzhen, China) due to an esophageal stricture. The patient received esophageal dilation under digital subtraction angiography. In this patient, dilation therapy was effective and safe. The patient underwent skin biopsies, and histological examination of the resected tissue specimens confirmed DEB diagnosis. The patient was followed up in the Department of Thoracic Surgery, Shenzhen Hospital, for 2 years without any recurrence of esophageal stricture. This is the first case report of dilation therapy in a very rare case of DEB with a satisfactory outcome, but the long-term efficacy needs further observation. In addition, the latest relevant literature was reviewed and it was found that this treatment is uncommonly reported, as is the condition.

Introduction

Dystrophic epidermolysis bullosa (DEB) is a rare disease and the associated esophageal stricture has received insufficient attention. Treatment for such an esophageal stricture is frequently complicated by the lack of clinical experience. The present study described a very rare case of DEB in a 37-year-old male, who was admitted to Shenzhen Hospital (Shenzhen, China) due to dysphagia. DEB is known for its low incidence, reported to range from 3.3 to 5.7 per million people (1). The patient was previously diagnosed with epidermolysis bullosa (EB). In performing a literature search, no significant developments have been documented with respect to the diagnosis and treatment of EB-induced esophageal stricture. Dilation therapy was performed on this patient, which was effective and safe. At the long-term follow-up, the esophageal stricture was alleviated. There has been no significant development in the diagnosis and treatment of ED-induced esophageal strictures and it is often altered by a combination of clinical conditions. To the best of our knowledge, this is the first case report of dilation therapy in a very rare case of DEB with a satisfactory outcome, but the long-term efficacy requires further observations. In addition, the latest relevant literature was reviewed and found that this treatment is uncommonly reported, as is the condition.

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Case report

A 37-year-old male was admitted to Shenzhen Hospital (Shenzhen, China) for 30-year dysphagia and 30-day exacerbation in February 2020. The patient was hospitalized for 17 days. During the stay in hospital, the patient was subjected to standard clinical practices.

On admission, the patient reported dysphagia since early childhood. He was not able to swallow food in one piece but ate liquid foods daily. He did not complain of any other discomforts. In October 2019, the patient visited the Department of Internal Medicine, Division of Gastroenterology of Shenzhen Hospital (Shenzhen, China). The examination results were as follows: Height 165 cm, weight 50 kg, body mass index 28.37 kg/m^2, albumin 29.0 g/l, and hemoglobin 101 g/l. The patient suffered from malnutrition; the dysphagia level was 3.

Upper gastrointestinal radiography revealed a ~48 mm luminal segment of stenosis in the initiation of the esophagus, with the diameter of the narrowest portion of ~2 mm (Fig. 1A). Non-neoplastic stenosis was considered, but no treatment was performed. A total of 3 days before the admission, his dysphagia suddenly worsened, and the patient was admitted to Shenzhen Hospital (Shenzhen, China) for esophageal stenosis as the chief complaint.

The skin lesions in his lower extremities and hands were consistent with the typical skin lesions of DEB (Fig. 1B and C). The patient was previously diagnosed with EB with compound heterozygous mutations in the COL7A1 gene (c.5932C>T, p.R1978*, and c.8065G>A, p.G2689R) (Fig. 1D and E).

The diagnosis of admission was esophageal stenosis and DEB. Related examinations were performed on admission. Preoperative gastroscopy revealed a narrowed esophageal lumen that could not be passed by the ultrathin gastroscope and dilated endoscopically. In February 2020, esophageal dilation under general anesthesia was performed.

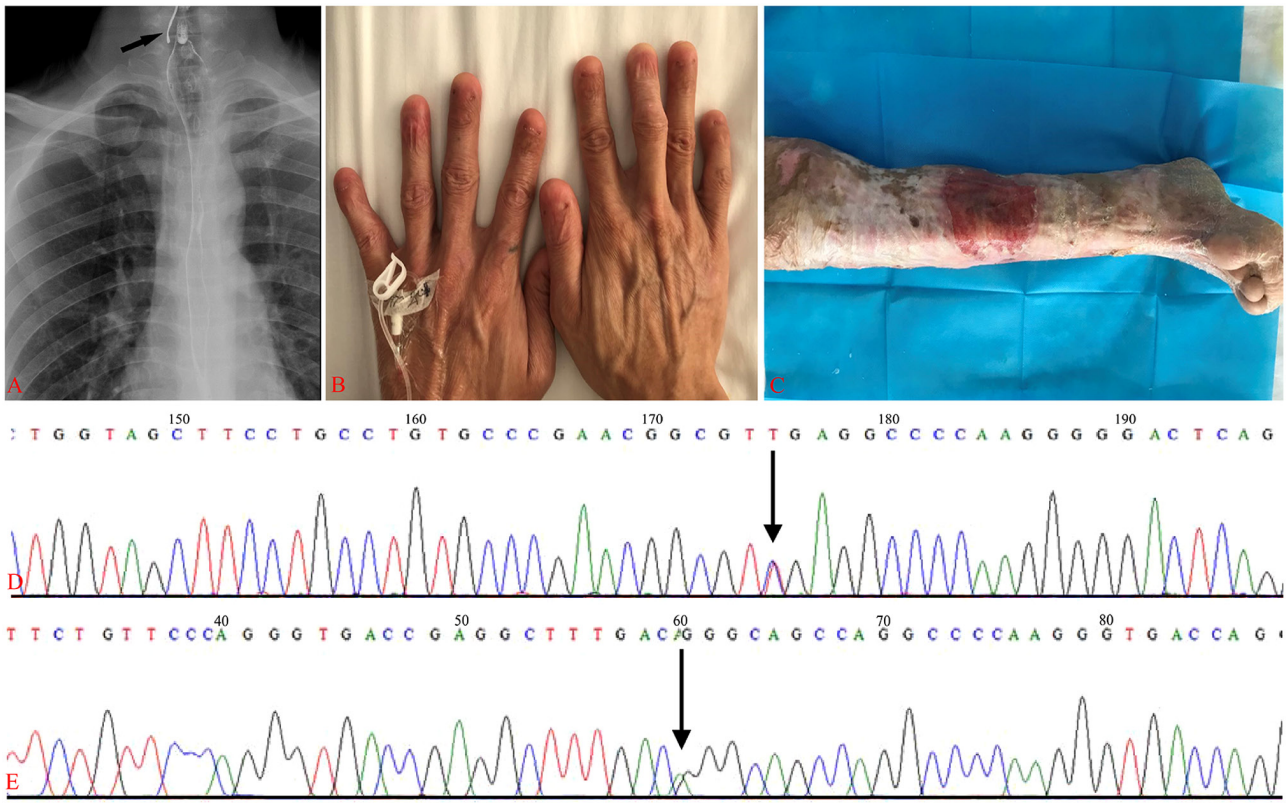

Figure 1. Patient's clinical presentation and results of the genetic analysis. (A) Preoperative upper gastrointestinal angiography of the patient. The lumen at the beginning of the esophagus (the middle of the T6 vertebral body-the upper edge of the T1 vertebral body) showed localized stenosis. The narrowest point was ~2 mm, and the length was ~48 mm. When the esophagus was relaxed, the maximum diameter of the lumen was ~8 mm. (B) The patient exhibited hand lesions consistent with classic dystrophic bullosa. (C) The patient's lower limbs exhibited lesions consistent with classic dystrophic bullosa. (D and E) Results of the genetics analysis.

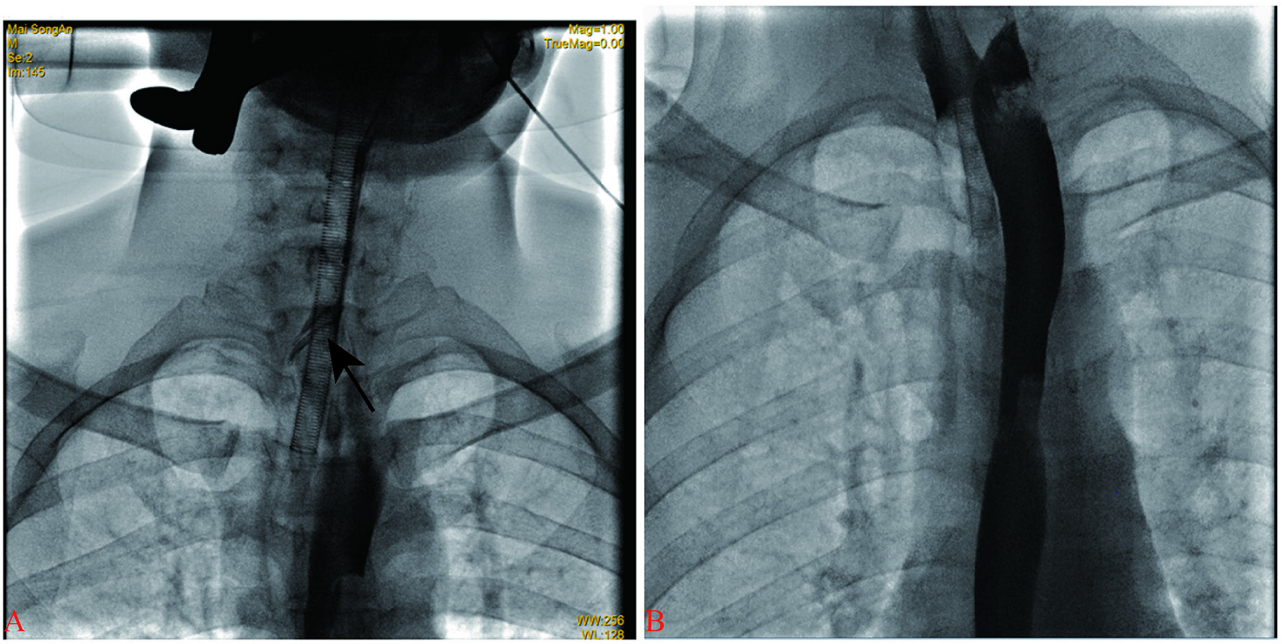

Figure 2. Intraoperative situation of the patient. (A) Intraoperative injection of contrast medium through the stenosis using a cardiac catheter. (B) Visualization of the esophagus with contrast medium after intraoperative dilation.

For the surgical procedure, after anesthesia by transnasal tracheal intubation, the barrel of a 2-ml syringe was put into the mouth of the patient and then a mouth opener was placed given that the patient had moderate difficulty with mouth opening. A 6F catheter with lateral holes for right heart catheterization was innovatively placed to obtain a fluoroscopic

view of the site of esophageal stenosis (Fig. 2A), followed by injection of Iopamidol through the catheter to clearly show the major region with stenosis. Subsequently, a hydrophilic guide wire was inserted through the catheter, while multiple dilators (internal diameter: 5-15 mm) were sent along the guide wire one by one until successful dilation of the esophageal lumen. A gastrostomy tube was indwelled thereafter, with the front cut to allow for free access to the guide wire.

After dilation, the patient could eat semiliquid foods. Considering the favorable outcome of the dilation surgery but recurrent stenosis, a second dilation surgery under digital subtraction angiography (DSA) with general anesthesia was performed 5 days after the first surgery.

Esophagography showed no esophageal stricture (Fig. 2B). The procedure was uneventful, and the patient could consume an ordinary diet after the surgery. The indwelling gastrostomy tube was recommended to be retained for a long period, but the patient declined, citing concerns about its impact on his appearance and not wanting to be seen with the tube in place.

A total of 1 week after the second surgery, the patient could eat ordinary soft foods normally. Ultrathin gastroscopy showed multiple patchy mucosal congestions in his glottis and a narrowed pharyngoesophageal segment, ~21 cm away from the front teeth and with an ulcerated surface covered with white fur but without bleeding, that could be passed by the gastroscope (Fig. 3A). The pharyngoesophageal segment 21-28 cm away from the front teeth presented with denuded mucosa and white fur but without stenosis or active bleeding. The remaining esophageal mucosa was normal.

Since cutaneous squamous cell carcinoma is a common cause of death in patients with DEB, a biopsy of skin lesions in his bilateral lower extremities was performed. Biopsy pathology suggested EB, but no malignant tumor was found (Fig. 3B and C).

The patient's diagnosis on discharge was esophageal stenosis and DEB. In the follow-up, the patient could eat semi-liquid foods normally within 2 years after discharge, and no dilation surgery was required.

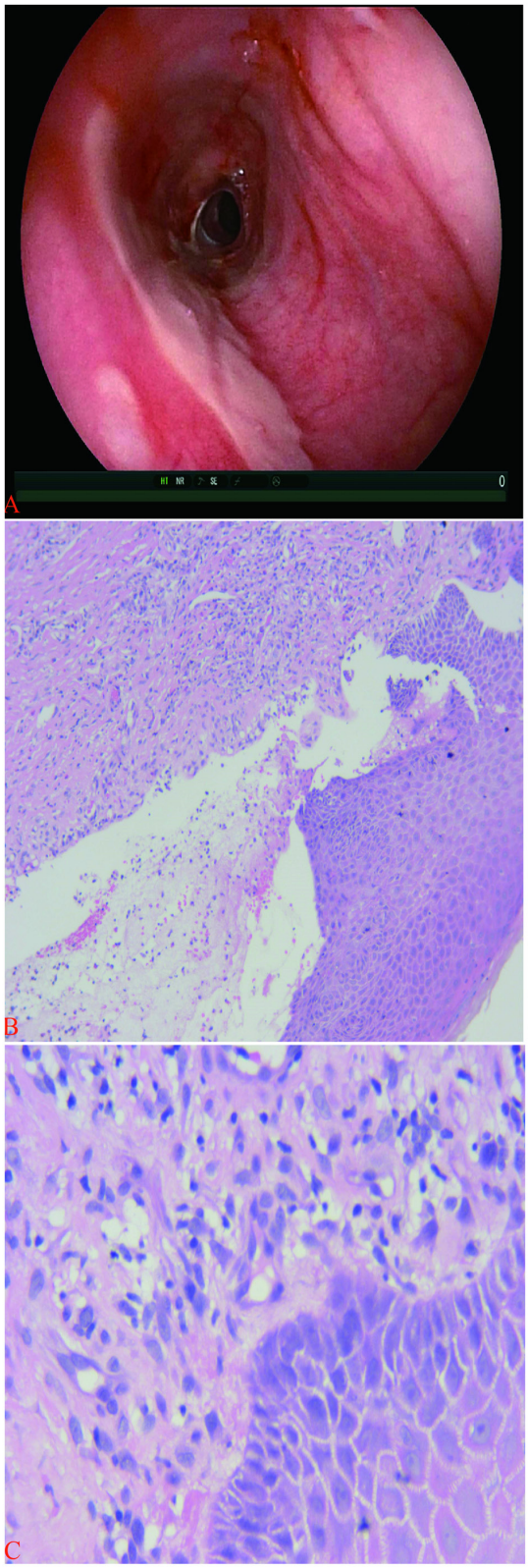

Figure 3. Clinical findings of the patient. (A) Postoperative review of the patient's with gastroscopy. (B) Histological findings from skin biopsies. Postoperative hematoxylin and eosin staining; magnification, x100. (C) Histological findings from the skin biopsies. Postoperative hematoxylin and eosin staining; magnification, x400.

Discussion

EB represents a group of heterogeneous, inherited mechano-bullous diseases presenting with skin and mucosal fragility resulting from mutations in structural proteins within human skin. All types or subtypes of EB are rare. Statistically, as of 2002, the estimated overall incidence and prevalence of EB in the U.S. was 1/53,000 and 1/125,000, respectively, while similar data could be found in certain European countries (2). There are no race or sex differences in the prevalence of EB (3). According to the ultrastructural level within which fissures develop in EB-affected skin, the latest International Consensus Meeting on Diagnosis and Classification of EB classified EB into four major types (4): Epidermolysis Bullosa Simplex (EBS), Junctional Epidermolysis Bullosa, DEB, and Kindler Syndrome (Table I). In addition, EB can be classified by features such as lesion distribution (localized or generalized), lesion severity and extracutaneous involvement.

EBS is the most common type of EB, although certain cases present with a recessive inheritance pattern. Type VII collagen gene COL7A1 is a DEB-causative gene (5). Studies have suggested that the site and type of mutations in the COL7A1 gene can lead to DEB with different types and medical conditions (6,7). According to the pattern of inheritance, DEB can

Table I. International Consensus Meeting on Diagnosis and Classification of EB.

Epidermolysis bullosa type	Ultrastructural site of skin findings
Epidermolysis bullosa simplex	Intraepidermal, basal keratinocytes, basal layer
Junctional epidermolysis bullosa	Intra-lamina lucida at the epidermal-dermal junction
Dystrophic epidermolysis bullosa	Sub-lamina densa, anchoring fibrils above the dermal papilla
Kindler syndrome	Intraepidermal, intra-lamina lucida and sub-lamina densa

be subdivided into dominant (DDEB) and recessive (RDEB). In the present report, the patient had compound heterozygous mutations in the COL7A1 gene (c.5932C>T, p.R1978* and c.8065G>A, p.G2689R). In addition, it was noted that both the patient and his twin brother had RDEB, which was moderately generalized.

In a clinical setting, it is widely considered that RDEB is more severe than DDEB and the prognosis tends to be worse (8). DEB infants are positive for the Nikolsky sign shortly after birth, presenting with blistering and erosion, with the blister wall being thin and fragile (9). In the meantime, the skin all over the body simultaneously presents with milia, atrophy and scars, while the devastating damage to the four limbs can lead to skin atrophy and severe deformation (10,11). The patient in the present report had typical skin lesions associated with EB. In addition to whole-body skin lesions, patients with EB may also exhibit oral damage and conjunctival involvement concurrently with manifestations such as anemia and growth retardation. Upon gastrointestinal involvement, 1/3 suboesophageal mucosa is usually involved, resulting in difficulty in opening the mouth (12), which was also observed in the present patient. Esophageal stenosis was reported to occur in ≥80% of RDEB patients before the age of 25 years. It can further exacerbate malnutrition, and severe cases usually require a gastrostomy tube for complementary feeding.

There have been certain reports on EB-related esophageal stenosis; however, treatment modalities are varied (13). According to the authors' experience, esophageal stenosis that cannot be dilated in any case is uncommon in the clinic. Since the patient in the present study had difficulty in opening the mouth, a mouth opener was placed after transnasal tracheal intubation for anesthesia and then dilation with a conventional conical Maloney bougie under DSA was performed. Considering that the narrow part could not be passed by the ultrathin endoscope preoperatively, we innovatively applied right cardiac catheterization to the narrow part followed by placement of dilating bougies with varying inner diameters along a hydrophilic guide wire. After the first dilation, a gastrostomy tube was indwelled. The second dilation 5 days after the first dilation contributed to significant improvements in the esophageal stenosis in this patient. A previous study in 126 RDEB patients reported an interval of 5 years between two dilation surgeries (13). At 1-year of follow-up, no recurrent stenosis was observed in this patient. The case presented here has a significant impact on the clinical management of DEB patients with esophageal stenosis. As the majority of patients present with stenosis in 1/3 sub-esophagus, esophageal stenting may be a viable alternative to surgery or other dilation modalities despite certain discomforts and potential risks such as esophageal rupture. For certain patients with recurrent stenosis after dilation, gastrostomy tube indwelling can be performed for complementary feeding (14).

The present case report has some limitations. First, additional verification of similar cases and longer follow-up periods are required to support these findings. However, the case is very rare, and a long period of time is required to collect additional similar cases. Second, it was not possible to perform genetic testing on immediate family members of the patient as they did not cooperate due to cost concerns.

At present, there is no specific therapy for DEB, while symptomatic treatment remains the mainstay for the management of patients when symptoms occur. Current clinical treatments for DEB primarily focus on avoiding skin damage, reducing the risk of complications such as infection and malnutrition, and improving the quality of life. A variety of novel therapies, such as cell therapy, targeted therapy and gene editing/engineering of induced pluripotent stem cells, have emerged in recent years, which hold promise for DEB treatment (15-18). Given the genetic identity of DEB, prenatal diagnosis in families with a proband is the most fundamental and effective intervention for the management of DEB at present. To the to the best of the authors' knowledge, this is the first case report of dilation therapy in a very rare case of DEB with a satisfactory outcome. These findings suggest that dilation therapy is effective and safe to perform in the clinic for DEB treatment.

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Availability of data and materials

The datasets used and/or analyzed during the current are available from the corresponding author on reasonable request.

Authors' contributions

MW, JY and JK contributed to the conception and design of the study, prepared the material, and collected and analyzed the data. MW drafted the manuscript. DL, QG, XZ and JZ

analyzed patient data. All authors were involved in revising and editing the manuscript. All authors have read and approved the final manuscript. MW and JZ confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any potentially identifiable images or data included in this article.

Competing interests

The authors declare that they have no competing interests.

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