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CASE HISTORY REPORT

Early teeth extraction in patients with generalized recessive dystrophic epidermolysis bullosa: A case series

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Abstract

Objectives: To present early teeth extractions as a treatment option in severe dental crowding in patients with generalized recessive dystrophic epidermolysis bullosa (RDEB).

Materials and methods: Three patients with generalized RDEB were treated with early teeth extractions to prevent severe dental crowding.

Results: Two patients had bilateral upper first premolars extraction, and the third patient had permanent maxillary canine extraction. Crowding was avoided, and no further orthodontic treatment was necessary.

Conclusion: Considering the challenges of severe mucosal fragility and microstomia in patients with generalized RDEB, early teeth extractions are a reasonable option as an orthodontic management. This approach reduces the severity of dental crowding as the child gets older and reduces the need for orthodontic appliances. Individual factors such as access to dental care, general health, and oral health have an important impact on the decision-making process. Orthodontic treatment planning should include a multidisciplinary team.

KEYWORDS
orthodontic, rare diseases, skin diseases

1 | INTRODUCTION

Inherited epidermolysis bullosa (EB) is a group of genetic disorders characterized by skin and mucosal fragility. EB presents a wide range of clinical phenotypes with thousands of sequence variants identified in at least 16 structural genes.[1,2]

The current classification system is based on the level of blister formation, recognizing four major types of EB: (a) EB simplex, (b) junctional EB, (c) dystrophic EB (DEB), and (d) kindler EB. In DEB, blistering occurs within the uppermost dermis, just beneath the lamina densa of the basement membrane zone. It is caused by variants in the gene *COL7A1*, encoding type VII collagen.

Patients with DEB can be classified into two major groups by inheritance: dominant DEB (DDEB) with four subtypes and recessive DEB (RDEB) with six subtypes. The most severe and prevalent subtypes of RDEB are *severe*

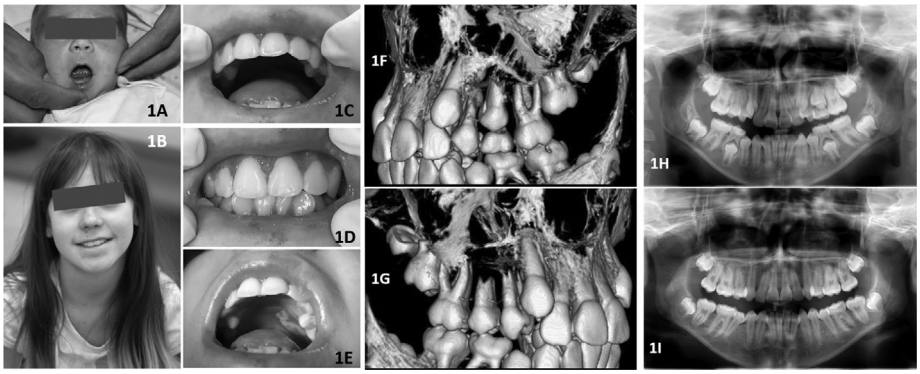

FIGURE 1 Serial extractions in a female patient with intermediate RDEB. Case No. 1. A, First dental appointment at the age of 2 weeks. B, Extraoral photograph at 12 years of age. C and D, After 14 and 24 extractions, upper canines erupted into edentulous space and aligned spontaneously. E, Oral ulcers on the palate at 12 years of age. F-H, Cone beam scan (left and right) and panoramic radiograph revealing no space for upper canine at 9 years old. I, Panoramic radiograph at 12 years of age

RDEB and *intermediate RDEB*.[2] Patients with these subtypes present cutaneous manifestations at birth including blisters, erosions, milia, absent or dystrophic nails, extensive atrophic scarring, anemia, failure to thrive, and progressive acral contractures leading to deformities of the hands and feet. Extra-cutaneous manifestations affect the mouth, esophagus, eyes, stomach, intestine, anus, kidneys, and genital region.[2] Oral manifestations comprise vesiculobullous lesions ranging from small vesicles to large bullae distributed on all the mucosal surfaces, depapillated tongue, significant scarring, and fibrous bands on the buccal mucosa and commissures, resulting in microstomia, vestibular obliteration, and ankyloglossia.[3–8]

Examples of general dental management have been widely reported, including the oral health care for patients with EB best clinical practice guidelines[9]; however, there is limited literature on orthodontic management for this patients group.[10] Serial extractions have been suggested as a treatment strategy to prevent dental crowding, especially for patients with severe forms of EB due to the difficulty in providing conventional fixed orthodontic treatment.[11]

The aim of this article is to present a case series of early teeth extractions in patients with generalized forms of RDEB and to discuss the challenges of early orthodontic management.

2 | CASE REPORT

2.1 | Case No. 1

A 12-year-old girl with *intermediate RDEB* due to compound heterozygous variants c.6527_6528insC and c.8329C>T in the COL7A1 gene (variants are reported in reference to NM 000094 for cDNA). She has been on preventive dental care since the age of 2 weeks old (Figure 1A). The patient lives 785 km from the national EB reference center, however her family was keen to attend frequent EB clinic appointments where she used to see the pediatrician, dermatologist as well as special care dentist. During the last 6 years, she was reviewed by the EB clinic every 3 months.

Her general condition includes severe malnutrition, esophageal stenosis (two balloon esophageal dilations have been required), mild scoliosis, chronic constipation, recurrent corneal ulcers, and fine fiber neuropathy.

At the age of 9, the panoramic radiograph and cone beam confirmed lack of space for maxillary permanent canines to erupt (Figure 1F-H). It was therefore decided to extract the upper first permanent premolars (14 and 24). This helped the permanent canines to erupt into the edentulous space and the teeth to align spontaneously without the need for further orthodontic treatment.

At present, the patient is 12 years old, and her upper teeth are aligned (Figure 1B-E,I). The main EB-related oral features present in this case that pose challenges for conventional orthodontic treatment are as follows: obliteration of the buccal sulcus (vestibule), severe microstomia (22 mm maximal mouth opening), and the development of oral bullae and ulcers in different sites of her oral mucosa on a weekly basis; in addition, she has absence of tongue papillae and palatal rugae (Figure 1E: healing lesion on the palate).

2.2 | Case No. 2

An 18-year-old young woman with *severe RDEB* caused by a homozygous variant c.6527_6528insC in the COL7A1 gene has been on preventive dental care since the age of 4 years and 7 months (Figure 2A). The patient lives 702 km from the national EB reference center. Although the family was

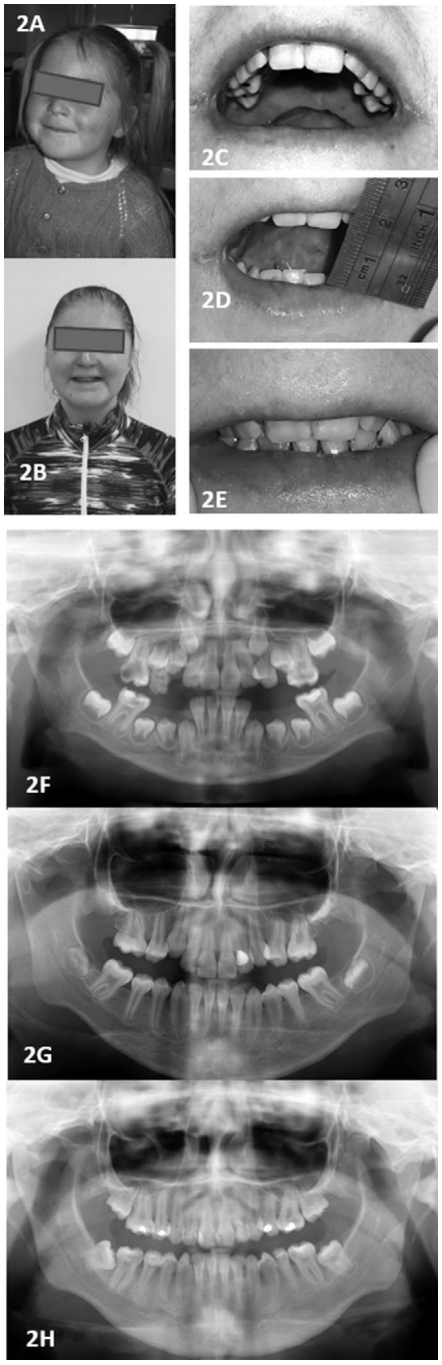

FIGURE 2 Serial extractions in a female patient with severe RDEB. Case No. 2. A, Extra-oral photograph was taken at the first dental appointment (age 4 years and 7 months old). B, The extra-oral photograph at the age of 18 years. C, Intraoral photograph at 18 years old: upper teeth are aligned. D, Severe microstomia, with 13.5 mm interincisal. E, Malalignment of lower arch. F, Panoramic radiograph at 7 years of age, revealing no space for upper canines and severe caries in all first permanent molars. G, Panoramic radiograph at 11 years of age, 6 months after 14-24 and 16-26-36-46 extraction. H, Panoramic radiograph at 18 years of age. Upper canines erupted into edentulous space and aligned spontaneously, together with the alignment of second permanent molars into the space of the first permanent molars

keen to attend regular appointments, they had local difficulties, which led to years of missing appointments.

Her overall health has been stable over the years. She has progressive hand retraction, recurrent urinary infections, chronic constipation, and dysphagia, which required 10 balloon esophageal dilations in the last 18 years, fine fiber neuropathy and vitamin D deficiency.

At the age of 7, an oral panoramic radiograph was taken, confirming insufficient space for the upper permanent canines, as well as deep caries in all first permanent molars (Figure 2F). At the age of 10, it was decided to extract the upper first permanent premolars (14 and 24) to allow positioning of the canines and all the first permanent molars (16, 26, 36, and 46) due to caries. At the age of 11, the canines were erupting into the edentulous space, lower second molars erupted into first molar space, and the teeth aligned spontaneously (Figure 2G).

At present, the patient is 18 years old (Figure 2B-E,H), her upper teeth aligned without the need for orthodontic appliances (Figure 2C). The oral manifestations of EB present in this patient are absence of tongue papillae, vestibule obliteration, severe microstomia (13.5 mm interincisal, Figure 2D), and frequent development of oral bullae and ulcers in different sites of her oral mucosa (Figure 2D and E).

2.3 | Case No. 3

A 10-year-old boy (Figure 3A) with *severe RDEB* due to compound heterozygous variants c.6527_6528insC and c.7708delG in the COL7A1 gene has been on preventive dental care since the age of 14 months. The patient lives 2188 km away from the national EB reference center and can only commit to dental reviews 2-3 times per year.

His general condition includes skin fragility and wounds at different healing stages, severe malnutrition, failure to thrive, vitamin D deficiency, recurrent infections, chronic constipation, dysphagia (requiring eight esophageal dilations to date), pseudosyndactyly, and musculoskeletal contractures.

At the age of 8, the patient developed a painful ulcer on the lower lip, which hindered him from eating solid food (Figure 3B). Supplemental feeds had to be prescribed by the pediatrician, and an emergency appointment was arranged. On examination, severe crowding with protrusion of the upper central incisors was observed, causing the traumatic ulcer on the lower lip (Figure 3C). All four permanents as well as all four deciduous lower incisors were present and crowded. Extraction of bilateral deciduous upper laterals and canines as well as all four lower deciduous incisors were performed under conscious sedations. At the age of 10, the patient returned for a

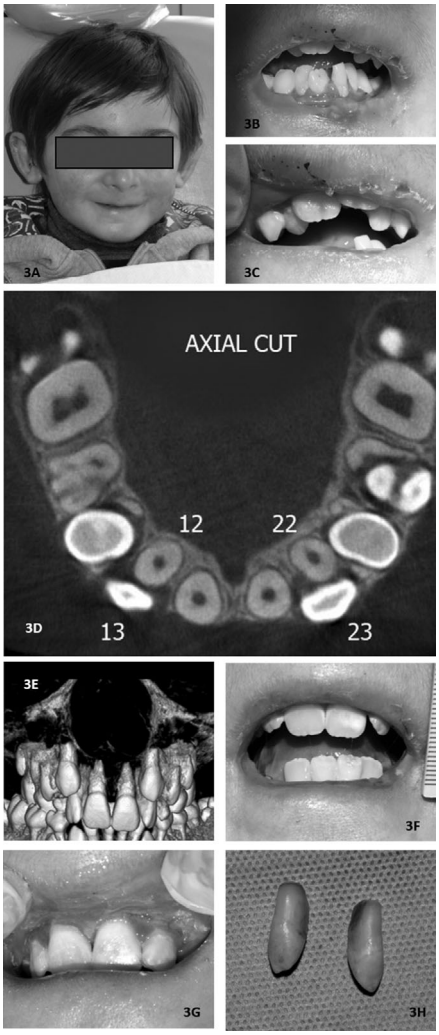

FIGURE 3 Early extractions in a male patient with severe RDEB. Case No. 3. A, Extraoral photograph at 10 years of age. B, Ulcer on the lower lip at 8 years of age. C, Severe crowding of the upper arch at 8 years of age. D and E, Cone beam at the 10 years of age. F, Severe microstomia, 6 mm interincisal distance. G, Healed area of the vestibular flap 1-month postsurgery. H, Extracted right and left maxillary canines with immature roots

review appointment. On examination, the upper and lower incisors had aligned, and the lower lip had no indentation of the upper teeth (Figure 3F). His orofacial conditions include severe microstomia (maximal mouth opening: 17 mm between lips, 6 mm between incisors; Figure 3F), ankyloglossia, and oral vestibule obliteration. The radiographic investigation and cone bean interpretation showing both maxillary permanent canines were labially erupting to both maxillary lateral incisors (Figure 3D,E).

A multidisciplinary team meeting was held; in this case, this involved speech and language therapist, orthodontist, periodontist, and special care dentist. A decision was made to extract both upper permanent canines, taking into consideration the limited mouth opening, the well aligned and sound upper permanent lateral incisors, access to dental services, and the need for future dental treatment (distance to treatment center). Both upper permanent canines were extracted (Figure 3H) under local anesthesia through a vestibular flap. A month after surgery the extraction site had healed uneventfully (Figure 3G).

3 | DISCUSSION

This article reports the experience of managing the orthodontic needs of three patients with generalized forms of RDEB through early extractions. All three patients lived more than 700 km away from the national reference center for EB, presented with severe microstomia and multiple comorbidities such as severe malnutrition, failure to thrive, and esophageal strictures. Considering all these challenges, future orthodontic treatment with fixed or removable appliances might not be a feasible option. Early extractions were a feasible and successful treatment strategy to manage dental crowding. Theses should be planned and performed in the mixed dentition stage. All patients presented in this article had dental extractions between the age of 8 and 10. While cases 1 and 2 had one episode of dental extractions (case No. 1 at age 9 and case No. 2 at age 10), case No. 3 needed two episodes (age 8 and 10). During decision making, careful consideration should be made based on patients' dental developmental stage.

The three cases presented in this article grew favorably, preserving an aligned upper arch after 3 (case No. 1) and 8 years (case No. 2). For patient No. 3, the extractions were performed to prevent dental crowding and damage to the lateral incisor by the upper canine eruption.

Provision of orthodontic treatment for this patient group can be very challenging. Furthermore, there is a lack of reported cases with EB. The best clinical practice guidelines for patients with EB states: "*For patients with RDEB, we strongly recommend serial extractions to prevent dental crowding, as this contributes to high caries risk and periodontal disease.*"[9] This recommendation was made based on the clinical experience of the guideline development group, as there are no previous reports on the benefits of early extractions in EB. Reports on orthopedic and orthodontic management in EB include the use of an interceptive guide of occlusion and a modified twin bock without wire.[10,11] On a more advanced approach, Pacheco and Marques de Sousa Araugio were the first to report a case of fixed orthodontic treatment in RDEB.[12]

It has been suggested that despite the reduced size of the maxilla due to malnutrition and scarring tissue, the dentition is of a normal size, leading to severe anterior crowding that could be solved extracting up to eight teeth in the premolar-molar area.[13] As seen in case No. 3, the

reduced maxillary length and the normal dental size could lead to canine impaction or severe displacement. There are no studies focusing on canine relation in patients with RDEB, but, from clinical experience, during mixed dentition in patients with RDEB there is a higher risk of crowding or displacement, mainly due to the lack of maxillary development.

The multidisciplinary team considered the impact on patients' self-esteem as one of the most relevant factors in the decision-making process for early teeth extractions. The multidisciplinary team involved in the cases presented included a speech and language therapist, orthodontist, periodontist, and special care dentist. Other centers might consider involving pediatric dentists, oral surgeons, and mental health teams. Early extractions will have a positive impact on oral esthetics by allowing appropriate teeth alignment in patients with insufficient space. Access to treatment, oral hygiene, caries, periodontal status, and general health conditions are clinical factors that need to be considered in the treatment planning stage.

4 | CONCLUSIONS

- Early teeth extractions during mixed dentition are reasonable treatment options to prevent dental crowding in individuals with generalized forms of RDEB.
- General health conditions such as failure to thrive and malnutrition may have an impact on facial growth and therefore on dental crowding in RDEB.
- EB-related orofacial features such as microstomia, ankyloglossia, and vestibule obliteration have an important impact on the provision of orthodontic treatment.
- Social factors such as access to specialized treatment centers must be considered during treatment planning stage and prior to decision making.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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