

## Hereditary epidermolysis bullosa: Report of two cases

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يعتبر مرض تسليخ الجلد الفقاعي أحد الأمراض الوراثية والذي يتميز بوجود فقاعات وتقرحات على الجلد وعلى الأغشية المبطنة للفم. وله أهمية في طب الفم والأسنان لما يتميز به من ظواهر فموية وصعوبات علاجية. يتضمن هذا التقرير الظواهر الفموية والخطة العلاجية لنوعين مختلفين من هذا المرض.

Epidermolysis bullosa (EB) describes a group of genetically determined disorders, characterized by blistering of the skin and mucosa. It is of dental interest because of its specific oral manifestations and management problems. Oral manifestations and management outline of two different types of EB are described.

### INTRODUCTION

Hereditary epidermolysis bullosa (EB) is a group of rare genetically transmitted disorders that have several methods of inheritance with various degrees of severity and expression.<sup>1, 2</sup> It is a multiracial disorder that is characterized by the formation of vesicles and bullae on the skin and mucous membranes. The vesicles may arise spontaneously or from minor trauma. In some varieties of EB, high room temperature may precipitate blisters.<sup>3</sup>

The pathogenesis of these disorders is unknown. Bullae formation has to do with various basic defects including structural and biomechanical abnormalities of keratin, hemidesmosomes, anchoring fibrils, anchoring filaments, and altered skin collagenase.<sup>4</sup>

Hereditary EB is classified into three major categories which have been further subdivided on the basis of their clinical phenotypes and modes of inheritance.<sup>1,4</sup> The three types of hereditary EB are simplex, dystrophic and junctional. In simplex EB, the disease appears at birth or shortly after and is characterized by the development of bullae, mainly limited to the hand and feet. Extracutaneous organs and nails are rarely involved. The lesions heal without residual scarring or

pigmentation.<sup>2</sup> In the dystrophic form of EB, the disease also appears at birth. The skin lesions appear on the ankles, knees, elbows, hands, and feet. The nails are severely dystrophic or absent. Oral lesions are also observed and the mucosal lesions tend to heal with scar formation in the mouth, oropharynx and conjunctiva. These patients present with microstomia and ankyglossia.<sup>2</sup> In junctional EB, lesions tend to appear at birth, bullae and erosions usually form on the side of trauma on hands and feet resulting in atrophic scars. Dystrophy of nail and oral lesions is common.<sup>2</sup>

Nowadays, there is an increased knowledge about clinical characteristics of different hereditary EB subtypes including oral and dental involvements. Clinicians managing patients with EB must be familiar with different subtypes of this disease so that they may accurately predict the prognosis and develop an optimal treatment approach. Recessive dystrophic EB presents the most severe oral involvement which complicates optimal dental treatment delivery, while patients with simplex EB can be treated as normal patients. Dental literature has described successful dental management under general anesthesia for patients having even the most severe forms of EB.<sup>5-7</sup>

The purpose of this study was to present the oral and dental manifestations of two different cases of EB, namely recessive dystrophic EB and EB simplex, and to discuss the dental management as well as the different problems confronting

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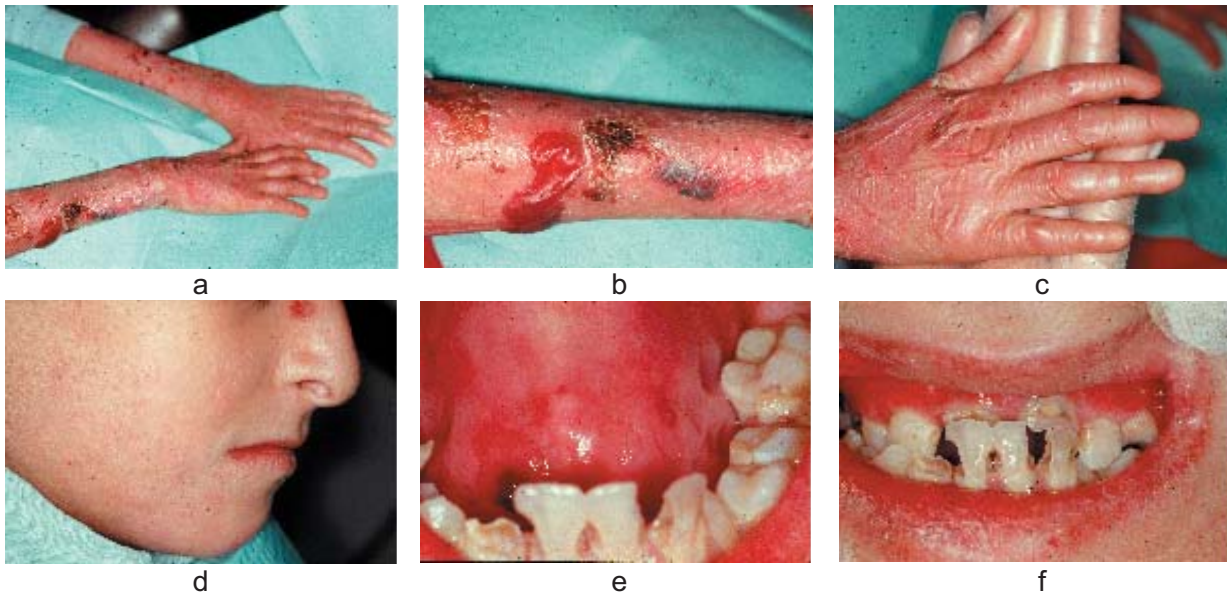
## CASE REPORTS

### Case 1

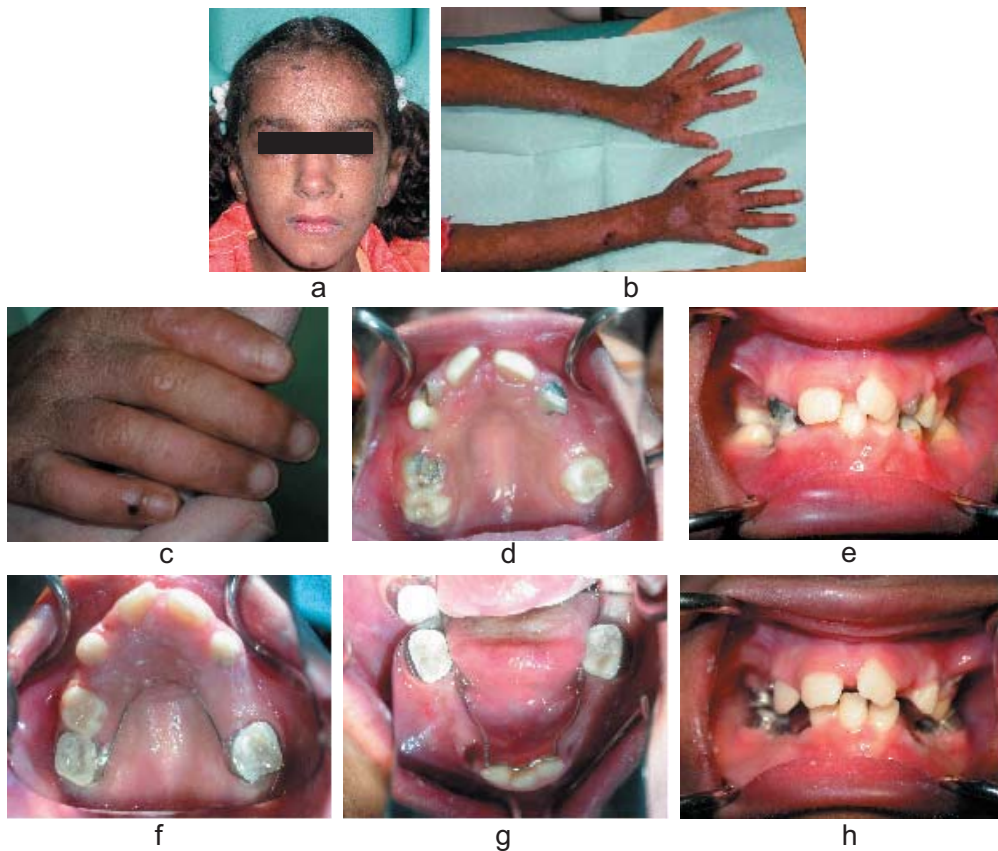
A 10-year-old Saudi girl presented for dental care at the Pediatric Dentistry Clinic of the College of Dentistry, King Saud University in Riyadh, Saudi Arabia. Medical history revealed that the patient is a known case of recessive dystrophic EB. The patient was anemic and suffering from multiple eye infections as well as upper respiratory tract infection. The patient had been managed only by palliative treatment of the skin with Flumazine cream. She had only one dental visit for incomplete root canal treatment of the upper central incisors, which was done in a private clinic. Family history revealed that there was no previous history of family skin disorders or consanguinity. The patient has two siblings (8-year-old sister and 6-year-old brother) who are severely affected by dystrophic EB. Extra-oral examination showed multiple bullae and vesicles all over the body with severe hands and legs involvement (Fig. 1a). The vesicles were large, red and infected. In addition, there were multiple scarrings and pigmentation (Fig. 1b). There was complete absence of finger nails (Fig. 1c), but the face was not severely involved although there were multiple skin milia (Fig. 1d). The patient was underweight. Intra-oral examination showed diminished oral opening, multiple vesicles and bullae, obliteration of the sulcus, ankyloglossia and tongue atrophy (Fig. 1e). Oral hygiene was very poor with thick plaque deposition. The teeth were hypoplastic with severe rampant caries affecting the permanent upper and lower incisors and the remaining primary teeth (Fig. 1f). The patient had class III malocclusion, the upper incisors and upper molars were in crossbite (Fig.

1f). OPG examination revealed that all permanent teeth were present except the third molars, with pulp involvement of the upper centrals, lower centrals and lateral incisors.

Treatment was planned to extract all the remaining roots of the upper and lower primary molars, to use fissure sealant and preventive resin restorations as indicated for all newly erupted teeth, to apply topical fluoride, to carry out composite restorations of small caries and to do root canal treatment for all pulpally involved permanent teeth. Oral hygiene instructions were given to the patient to use small-headed soft toothbrush and to use chlorhexidine mouth rinse twice a day. On the second visit, the father said that the patient could not use chlorhexidine mouthwash since it "burns the tongue and mucosa". Fissure sealant, preventive resin restorations and composite restorations were performed with difficulty since the patient could not open her mouth wide. Isolation and suction were achieved with caution. Formation of vesicles occurred after using saliva ejector (Fig. 1e). In the third visit, one extraction was done under intraligamentary injection of local anesthesia with some difficulties because the patient was uncooperative and could not be restrained. Then the patient failed to come for two visits. There was consultation with the anesthesiologist to continue treatment under general anesthesia. The anesthesiologist advised not to use general anesthesia approach because the case was severe and there was a possibility of developing airway obstruction due to blister formation and also due to recurrent upper respiratory tract infections. Patient was given appointment to complete extraction and to be referred to the endodontist for treating pulpally involved teeth but the patient failed to attend subsequent appointments.



**Fig. 1.** Dystrophic epidermolysis bullosa. (a) Severe hands involvements with bullae and vesicles. (b) Large, red, and infected vesicle. (c) Complete absence of finger nails. (d) Non-severe multiple skin milia scattered on the face. (e) Tongue atrophy with fresh vesicle. (f) Hypoplastic teeth with severe rampant caries. Upper incisors are in crossbite.



**Fig. 2.** Simplex epidermolysis bullosa. (a) The face with multiple bullae and vesicles. (b) Multiple bullae and vesicles on the hands which ended up with erosions but no scarring. (c) Nails are not dystrophic. (d) Oral mucosa without bullae. (e) Mild hypoplastic upper permanent incisors with carious primary canines. (f,g and h) After treatment was completed.

### Case 2

A 6-year-old Saudi girl presented for dental care at the Pediatric Dentistry Clinic, College of Dentistry, King Saud University in Riyadh. Medical history revealed that the patient is a known case of simplex EB. She had only been managed by palliative treatment for the skin lesions with fucidin ointment and potassium permanganate. Family history revealed that there was no previous history of family skin disorders or consanguinity. The patient had two previous emergency dental visits. Extraction of two teeth was done at these visits with some management difficulty. Then the patient was referred to the Pediatric Dentistry Clinic.

Extra oral examination showed multiple bullae and vesicles scattered on the face (Fig. 2a). They are maximal in the upper and lower limbs which ended up with erosions but no scarring (Fig. 2b). Some lesions had post healing hypopigmentation. There were no milia and no nail dystrophy (Fig. 2c). The patient was underweight. Intraoral examination showed no bullae on the oral mucosa at the time of the first examination (Fig. 2d). The mother gave history that oral bullae decreased as the child got older. Permanent upper central incisors were mildly hypoplastic with multiple carious lesions of other teeth (Fig. 2e). OPG examination showed that all permanent teeth were present except the third molars. There was an apical radiolucency around the lower primary canines and molars.

Treatment was planned to extract non-restorable primary teeth, to do composite restorations for small carious lesions and fissure sealant for all first permanent molars, to construct upper Nance and lower lingual arch space maintainers to be inserted and to apply fluoride therapy. Oral hygiene instructions were given to the patient. Treatment was carried out

as planned after behavior modification. Extraction was done under infiltration injection. Suction was used with caution to avoid formation of bullae. Treatment was completed without bullae formation. Patient was put on recall program every 3 months (Figs. 2 f, g, h).

## DISCUSSION

Signs and symptoms of the first case were pathognomonic of dystrophic EB, a recessive type since the eye involvement and the presence of cutaneous milia or small epidermoid cysts can be distinguished from the dominant type.<sup>2</sup> Nails are usually involved often being dystrophic or absent. Bullae are usually manifested at or shortly after birth arising at the site of pressure or trauma or appearing spontaneously. In older children, hands, feet, knees and elbows are most often involved. The fluid contained in the bullae is sterile at first but it may become secondarily infected and then contain blood. Upon healing, the bullae are often followed by keloidal scars causing contraction and pigmentation. The scars may lead to the loss of the bony structure or to interference with growth.<sup>2,8</sup> Severe anemia is commonly seen in recessive dystrophic EB and is presumed to be secondary to malabsorption and chronic iron loss through mucosal erosions and ulcerations.<sup>2,9</sup> Treating hereditary EB still consists of palliative topical care. There are no known cures. Phenytoin was suggested for treatment but its efficacy has not been proven.<sup>10,11</sup> Eroded skin surfaces are best covered with nonadherent dressings after applying a topical antibiotic such as bacitracin, silver sulfadiazine, or mupirocin.<sup>12</sup> Oral nutritional supplements including iron and zinc may be partially beneficial in managing individuals suffering from anemia, and liquid preparations high in protein and calories may help patients with growth retardation.<sup>13,14</sup>

Individuals with recessive dystrophic EB exhibit most severe oral involvement, which is characterized by complete obliteration of the sulcus, ankyloglossia and the absence of lingual papilla as a result of continuous blistering and scarring.<sup>15</sup> Microstomia is often severe with this type of EB which result from either intraoral or peri-oral blistering with subsequent scar formation.<sup>8</sup> Oral milia do not usually occur in this form of EB despite their widespread prevalence on the skin and despite the presence of severe oral involvement.<sup>15</sup> Regarding enamel hypoplasia and rampant caries, it was shown that dental enamel from patients with recessive dystrophic EB is essentially normal in terms of its chemistry.<sup>16</sup> Caries prevalence among patients with dystrophic EB is significantly higher than among healthy people.<sup>17,18</sup> The high caries experience is probably related to some factors such as the presence of the soft tissue involvement, which leads to alterations in the diet (soft and frequently high carbohydrate). This increases oral clearance time due to limited tongue mobility and vestibular constriction, and creates an abnormal tooth/soft tissue relationship as the buccal and lingual mucosa is firmly positioned against the tooth. Furthermore, these individuals often lack the ability to routinely practice normal preventive measures such as oral hygiene or the use of oral rinses.<sup>8</sup> Class III malocclusion may result from atrophy of maxilla with resultant relative mandibular prognathism, secondary to generalized growth retardation. Patients with severe recessive dystrophic EB are prone to develop crowded dentition. The incisors often are inclined lingually. This may result from small alveolar arches secondary to generalized growth retardation and collapsed dental arches which are secondary to soft tissue constriction.<sup>8</sup>

Dental management of patients with recessive dystrophic EB includes some difficulties. The presence of microstomia prevents adequate examination and delivery of dental treatment.<sup>5</sup> Formation of bullae after simple dental procedures and the use of suction also added to these difficulties. Preventive measures which included fissure sealants, preventive resin restorations, dietary advice and oral hygiene instructions were delivered to this patient with very hard approach. Extraction of one remaining root was done under intraligamentary injection of local anesthesia to avoid infiltration, which might cause tissue separation and bullae formation.<sup>8</sup> Patient was uncooperative during this procedure although the extraction was very simple but the patient could not be restrained to avoid formation of skin bullae. Consultation with anesthesiologist was done to treat the patient under general anesthesia. Successful dental management under general anesthesia had been reported in the dental literature,<sup>5-7</sup> but due to the presence of recurrent upper respiratory tract infection and the possibility of developing airway obstruction during or after the operation, which may require emergency tracheostomy,<sup>19,20</sup> the anesthesiologist advised against the use of tracheal intubation. Intubation was reported as extremely difficult in a case of severe microstomia which limited oral accessibility and visibility and resulted in the swelling of the epiglottis.<sup>16</sup> It appears that due to the complications of treatment required by patients with HEB, there is a tendency for such patients to lose interest in regular dental appointments.

Sucralfate which is a complex salt of sucralfate and aluminum hydroxide has proven to be an effective prophylactic and therapeutic modality in the treatment of pain and blisters in the oral cavity on patients with dystrophic EB. It is also attributed to a decreased cariogenic

potential and the inhibition of the growth of cariogenic streptococci.<sup>21</sup>

The goal of dental therapy is preservation of the dentition. Unfortunately, this may not be possible because many of these patients are not brought to the dentist or do not seek dental care until acute dental problem arises as in these cases. This is mainly because too much concentration has been placed on the patient's medical status.<sup>22</sup>

Preventing dental caries is most challenging in patients with recessive dystrophic EB since they often are faced with an extremely cariogenic diet and are least able to perform routine preventive procedures. Preventive measures can be best accomplished by using soft bristled, small-headed toothbrush with fluoride containing tooth paste, systemic fluoridation when appropriate, daily fluoride rinse, chlorhexidine mouth rinse and diet counseling.<sup>23</sup> Initiating a preventive program when the patient is young will allow the oral health to be successfully managed before the development of problems become so severe that treatment is difficult to accomplish. All patients with recessive dystrophic EB should be referred for dental evaluation by the age of one year, and such patients should be maintained on a frequent recall schedule so that preventive measures and treatment strategies can be monitored and modified to the patient's needs. Diet constitutes a major difficulty in caries control. Due to the complex systemic nutritional demand of these patients, diet may best be managed with the help of a dietitian.<sup>5</sup>

The second patient is a case of EB simplex. Skin blisters and vesicles were present all over the body and concentrated in the extremities which ruptured and healed without scar leaving hypopigmented areas. Extraoral and intraoral milia were not seen in this patient and neither was nail dystrophy

which are characteristic of EB simplex.<sup>2,3,5</sup> No oral bullae were seen at the time of examination. Oral blistering tends to be few and small in size and tends to heal rapidly without scarring.<sup>12</sup> In addition, oral involvement in EB simplex appears to occur most commonly during the early childhood period.<sup>12,24</sup> As the child matures, less oral involvement usually occurs and this disease becomes self-limiting.<sup>3,25</sup> This patient did not develop ankyloglossia or vestibular obliteration because oral lesions when they existed, healed without scarring. The teeth were mildly hypoplastic although earlier, there were reports of severe enamel hypoplasia in cases of EB simplex.<sup>25</sup> Generalized severe enamel hypoplasia is limited to junctional EB types.<sup>14,23</sup> Rampant caries involved primary teeth, while newly erupted permanent teeth were free of caries.

Treatment was carried out as planned. This included the use of local anesthesia, extraction, composite restorations, fissure sealants and cementation of space maintainers. Patients with EB simplex have no intraoral abnormalities related to their disorder and therefore are treated in the manner of a normal patient.<sup>5,26</sup> Individuals with this form of EB require few alterations in their dental care and maybe treated much like any other patient. The practitioner should, however, carefully question any individual with EB as to the fragility of the mucosa because dental therapy can precipitate oral blistering even in some mildly affected patients.<sup>25</sup>

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