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Case Report

Role of Oral Lesions in Diagnosing Generalised Recessive Dystrophic Epidermolysis Bullosa- A Rare Case Report

Amit D. Ramchandani[a], Aarti Singh[b] and Abhishek Singh Nayyar*[c]

[a]Assistant Professor, Saraswati-Dhanwantari Dental College and Hospital and Post-Graduate Research Institute, Parbhani, Maharashtra, India
[b]Assistant Professor, Maulana Azad Dental College and Hospital, New Delhi, India
[c]Associate Professor, Saraswati- Dhanwantari Dental College and Hospital and Post-Graduate Research Institute, Parbhani, Maharashtra, India

***Corresponding Author**
Dr. Abhishek Singh Nayyar
44, Behind Singla Nursing Home,
New Friends' Colony, Model Town,
Panipat-132 103, Haryana, India
Phone number: 073509 90780
E-mail: singhabhishek.rims@gmail.com

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Abstract

Epidermolysis bullosa (EB) is a heterogeneous group of genetically determined, vesiculo-bullous disorders characterized by blister formation in response to mechanical trauma. Three major subgroups, simplex, junctional, and dystrophic EB, contain more than 20 genetically and clinically distinct subtypes. Herewith, we are presenting a case report of a patient diagnosed with a milder variant of generalised recessive dystrophic epidermolysis bullosa with specific oral and cutaneous lesions, previously named as non-Hallopeau-Siemans subtype.

1. Introduction

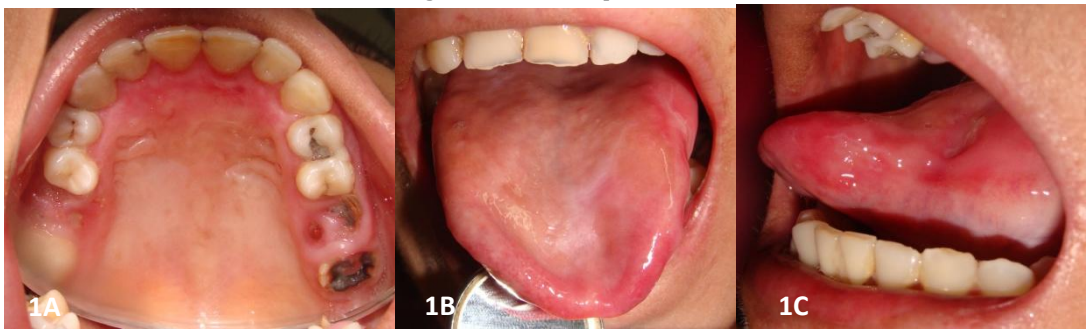
Epidermolysis bullosa (EB) comprises a group of genetically determined skin fragility disorders characterized by blistering of the skin and mucosa following mild mechanical trauma. Dystrophic Epidermolysis Bullosa (DEB) is a subtype of EB with a well understood pathogenesis. The main presenting feature of DEB is trauma induced blisters followed by healing with scarring. The dystrophic forms of EB are characterized by deformities of the skin including coalescence of the fingers, nail changes and milia formation, and have either autosomal recessive (RDEB) or dominant (DDEB) inheritance.[1] Prevalence of DEB is not known precisely though it is found to occur in all races worldwide with equal predilection in both the genders.[2] There are three main subtypes of RDEB- severe generalized RDEB (formerly named Hallopeau-Siemens RDEB), non-Hallopeau-Siemens RDEB, and inverse RDEB. Each has its onset at birth. The most severe subtype, severe generalized RDEB, is clearly one of the most devastating multi-organ, genetically transmitted disorders seen in mankind. Prototypic findings include generalized blistering at birth which are progressive and often lead to mutilating scarring of the skin, corneal blisters or scarring[3], profound growth retardation[4], multifactorial anemia, failure to thrive (less common than in JEB-H), esophageal strictures[4], and debilitating hand and foot deformities ("mitten deformities"; pseudosyndactyly etc.). The non-Hallopeau-Siemens RDEB, on the other hand, has similar but milder manifestations [5], as presented here.

2. Case Report

A 25 year old female patient reported to the outpatient Department of our institute with complaints of multiple decayed teeth and difficulty in maintaining oral hygiene. Parents reported that she had been having oral and skin blisters since birth for which she had been diagnosed as a case of Epidermolysis bullosa five years back at some private dermatology clinic and was under medication since then. Her family history was not significant. The members of her family reported that she usually avoided brushing and used to have soft diets since birth to avoid trauma to the structures in her oral cavity.

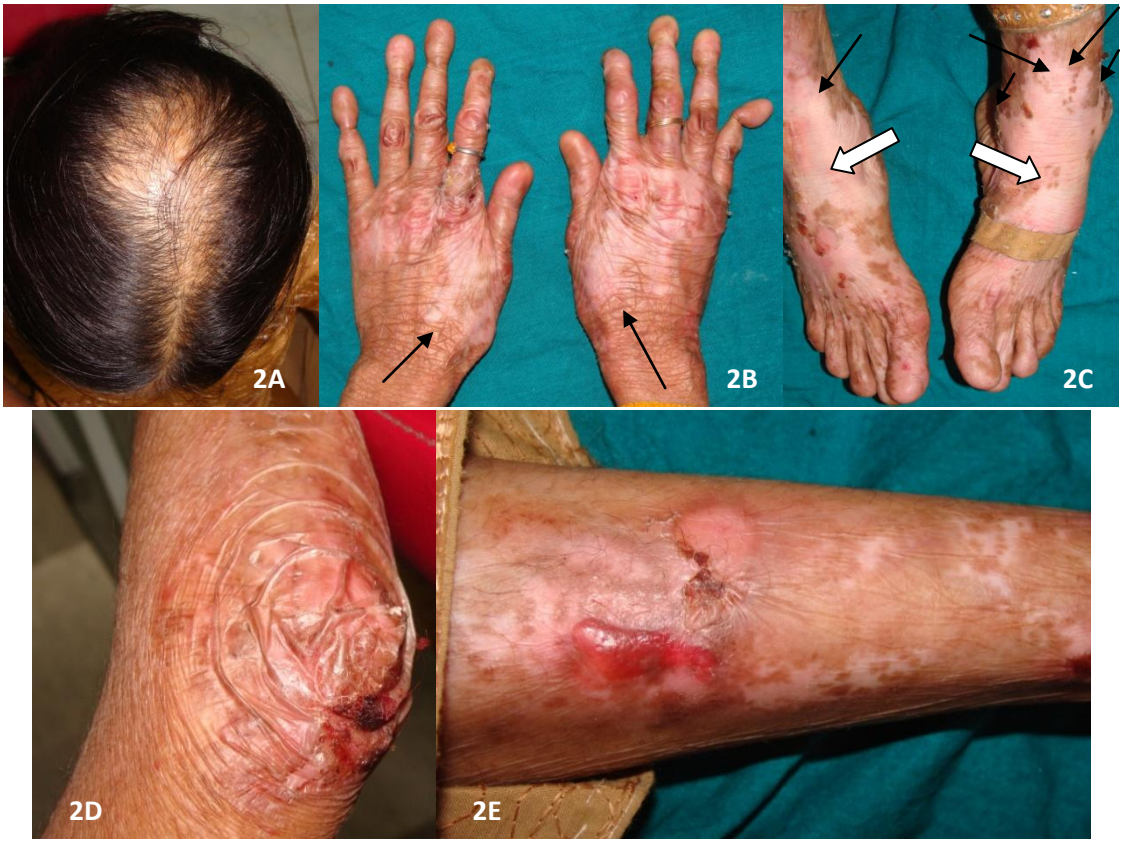
General physical examination revealed a dwarf and thinly built physique with normal phonation. Toe nails and finger nails were missing with atrophic nail beds (Fig.2B and C) and constricted distal inter-phalangeal joints of fingers. Skin on the arms, legs, neck, and face was dry, wrinkled, atrophic and shiny with hypopigmented confluent scars present along with encrustations at some places (Fig.2B-E). Fresh bullae were present on the skin surface with serous hemorrhagic fluid. Scarring alopecia was also evident on the scalp (Fig.2A). Intra-orally, generalised mucosal atrophy and pallor were seen. There was complete atrophy of the lingual mucosa with loss of filliform papillae (Fig.1B and C) and palatal mucosa with loss of rugae pattern (Fig.1A). All the permanent teeth were present with grossly carious posterior teeth. All the non-carious teeth were intact in morphology and appearance (Fig.1A). Hence, based on the clinical findings, the case was provisionally diagnosed as dystrophic recessive epidermolysis bullosa (RDEB) (non-hallopeau type). Histopathological examination of skin revealed dermo-epidermal split, and immunopathological examination revealed that collagen band VII was absent at basement membrane zone (BMZ), while keratin IV and laminin band V showed a normal pattern. After correlating the clinical and histopathological findings, the diagnosis of DREB was confirmed. Extraction of the grossly carious teeth was advised and patient was counselled to maintain good oral hygiene avoiding cariogenic food.

Figure.1: Intra-oral pictures



A: Pale, shiny, atrophic oral mucosa, while all the teeth are normal in appearance and morphology with grossly carious posterior teeth;
B: Pale, atrophic, shiny surface of tongue with loss of papillae;
C: Atrophic tongue mucosa with ulceration irt left lateral aspect of tongue.

Figure.2: Extra-oral pictures



A: Sparse hair and scarring alopecia irt parietal region of scalp;
B: Atrophic scarring and post-inflammatory hypopigmented areas in a flame shaped, sock-like distribution (arrows) and wrinkled skin of forearm, with complete absence of nails and with shrunken atrophic nailbeds and constricted distal inter-phalangeal joints;
C: Atrophic scarring with hypopigmented areas in a flame shaped (thin arrows) and sock-like (thick arrows) distribution and wrinkled skin with complete absence of nails irt lower extremity;
D: Skin on the elbow has become shiny, wrinkled, atrophic and crusted after repeated blistering;
E: Fresh bulla formation on skin, containing serous hemorrhagic fluid, with surrounding hypopigmented scars due to previous blisters

3. Discussion

There are four major types of inherited EB: EB simplex (EBS), junctional EB (JEB), dystrophic EB (DEB), and Kindler syndrome.[6] These differ not only phenotypically and genotypically but more importantly by the site of ultra-structural disruption or cleavage. Intra-epidermal blistering is the hallmark feature of EB simplex. EB simplex patients are then further sub-classified based on whether blisters arise within the basal or suprabasal layers of the epidermis.[7] In contrast, JEB and DEB patients develop their blisters within the lamina lucida and beneath the lamina densa of the skin basement membrane zone ("dermo-epidermal junction"), respectively. In Kindler syndrome, multiple cleavage planes may be seen within the same biopsied specimen of skin.[8]

DEB further occurs as recessive (RDEB) and dominant (DDEB) forms. There are mutations in the COL7A1 gene, encoding type-VII collagen which is the major component of anchoring fibrils, in RDEB. [9,10] The resulting abnormal structuring in type-VII collagen prevents the organizational structuring of the anchoring fibrils.[10] In RDEB, bullae are present at birth or appear in early infancy, especially affecting the hands, feet and lower legs in a flame shaped or sock-like distribution and leave atrophic scarring after healing.[11] In our case as well, the lesions and hypopigmented scars typically presented in a flame shaped and sock-like distribution on feet (Fig.2C) as well as hands (Fig.2B). Although whole of the skin was fragile, the main sites of predilection for blister development were those subjected to repeated friction or trauma, and were seen on the knees (Fig.2D), elbow, hands (Fig.2B and E), and feet (Fig.2C), back of the neck, shoulders, and spine. Chronic ulcers tend to become covered with a slough, often associated with heaped up crusting and scarring. Hair growth on scalp and body was impaired and scarring alopecia was evident (Fig.2A) as expected

[5]. Pseudosyndactyly may result in mitten-like deformity of hands apart from prolonged disuse of hands that results in bony resorption and muscular dystrophy [12], as was apparent in our case (Fig.2B), constricted inter-phalangeal joints and thin, atrophied fingers. Non-cutaneous epithelia are also at risk of developing blisters, erosions and scars. Oral lesions may be severe, leading to marked ankyloglossia and microstomia. The gingivae are fragile and even gentle brushing may induce epithelial disruption and bleeding resulting in poor oral hygiene. The lingual papillae are lost and the surface of tongue becomes smooth, shiny and atrophic was also apparent in our case (Fig.2B), with constricted inter-phalangeal joints and thin, atrophied fingers. Non-cutaneous epithelia are also at risk of developing blisters, erosions and scars. Oral lesions may be severe, leading to marked ankyloglossia and microstomia. The gingivae are fragile and even gentle brushing may induce epithelial disruption and bleeding resulting in poor oral hygiene. The lingual papillae are lost and the surface of tongue becomes smooth, shiny and atrophic [12]. This was clearly evident in our case too (Fig.1B and C). In RDEB, esophageal strictures and pseudosyndactyly are of particular importance, since they occur early in childhood and continue to negatively impact the functionality of these patients throughout their lives. [4] Similarly, about 30% of severe generalized RDEB patients have signs of pseudosyndactyly as early as 2 years of age and virtually 100% develop this by age 20.[5] Although secondary caries occurs, no primary enamel defects exist in any type or subtype of dystrophic EB [12,13], as seen in our case (Fig.1A). Enamel hypoplasia is seen exclusively in all subtypes of JEB and is therefore a highly useful diagnostic finding.[14] Chronic renal failure, the result of post-streptococcal glomerulonephritis or renal amyloidosis, occurs within the RDEB subtype, and may eventually lead to death in about 12% of the patients.[13] A low but real risk of potentially fatal dilated cardiomyopathy (cumulative risk of 4.5% by age 20, 30% of whom eventually die of this complication) exists in patients with severe generalized RDEB. Although the exact etiology is still not known, data suggest the possibility that this may result from a micronutrient deficiency (carnitine; selenium) or chronic iron overload.[15] Although the risk of infantile death from any cause is low in RDEB, nearly all patients with severe generalized RDEB will develop at least one cutaneous squamous cell carcinoma (arising as early as within the second decade of life), and most (about 87% by age 45) will, then, die of metastatis the same within five years of the time of diagnosis of the primary malignancy, despite treatment. Rare children with severe generalized RDEB are also at risk of developing malignant melanoma (cumulative risk of 2.5% by age 12) although none of the latter has been reported to result in metastasis. [16] General physical development is retarded. Most patients are very thin and have a short stature. Sera levels of the various vitamins and trace elements are found to be low and natural killer cell activity is impaired. [17] A more common RDEB subtype, which was diagnosed in our case, and formerly known as non-Hallopeau-Siemens RDEB (probably best referred to as generalized mitis RDEB), has a similar but less severe cutaneous involvement and a much lower risk of esophageal strictures, corneal injury, and hand or foot deformities [16], which tend to be more localised and similar to those seen in the classical dominant dystrophic EB [18]. Growth retardation and anaemia are extremely uncommon. However, these patients still have a significant risk of developing squamous cell carcinomas (47.5% by age 65), although the risk of death from metastases (60% by age 65) is lower than that which is seen in severe generalized RDEB.[16]

4. Conclusion

There is no effective treatment for epidermolysis bullosa, only palliative care is given. In case of severe oral lesions, nutritional support must be provided as coarse foods are not well tolerated, and a high caries rate is often the norm. Autologous skin grafting can be performed on non-healing skin lesions.[19] Preventive strategies include topical fluoride application to prevent dental caries and physical removal of bacterial plaque supplemented with chemical inhibition by the use of chlorhexidine gluconate mouthwash. Neutral pH sodium fluoride mouthwashes compared to the acidic ones as the latter cause discomfort during oral ulceration. Nutritional advice is always warranted and helps in reducing the suffering of the patients. [19]

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