Case Report

Periodontitis and Hereditary Epidermolysis Bullosa: A Rare Case Report and Review

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ABSTRACT

Hereditary epidermolysis bullosa (EB) refers to a group of rare genodermatoses and mutational impairment of the structural and functional integrity of skin, i.e., intra-epidermal adhesion and dermo-epidermal anchorage. It is a group of inherited heterogenous mechano- bullous disease that appears on the skin (Fragile) and mucosa (mucous membrane) in the form of blisters associated with minimal mechanical trauma. It is a dermatological condition formed in severe auto-immune disease. EB dystrophica has been presented with various oral manifestations, and earlier dental treatment was restricted to an extraction of all permanent teeth with a construction of complete denture. However, patients suffering from EB also respond well to conventional periodontal therapy. We present the case report of the 20-year-old female patient diagnosed with EB, who reported with the chief complaint of gingival bleeding and difficulty in chewing food due to the mobile teeth. A comprehensive interdisciplinary treatment planning was employed. We find this case report interesting, being one of the rare conditions, reporting periodontal alterations in the patient suffering from EB.

Key words: Epidermolysis bullosa, inherited, mechano-bullous, blisters, periodontitis

INTRODUCTION

Epidermolysis bullosa (EB) syndrome is an inherited rare connective tissue, chronic non-inflammatory mechano-bullous skin disease.[1] It encompasses a group of heterogeneous diseases of the skin and mucous membranes that have a tendency to grow and share the characteristic feature of the formation of blisters and erosions in response to minor mechanical trauma. These include hair, nail and tooth abnormalities, ocular findings, and fragility of the epithelia in upper respiratory, urogenital, and gastro-intestinal tracts.[1-3] Particularly interesting are two forms of EB, one associated with late onset muscular dystrophy and another one with congenital pyloric atresia.[3]

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EB simplex (EBS) appears either on the skin or mucosa or both as a result of trauma or mechanical irritation and is characterized by the formation of recurrent blisters or bullae which heals with atrophic scarring. The skin is made up of three layers the epidermis, the dermis and the hypodermis. In healthy individuals, anchoring proteins such as collagen and laminins are important for the maintenance of the basement membrane zone (BMZ) underlying the epithelium. In EB patients, epidermis and dermis layers are mostly altered or lack some of the anchoring proteins that hold them together. As a result, the skin is extremely fragile, and minor mechanical action such as rubbing, pressure, or friction can separate the layers of the skin or mucosa and form blisters.[2]

The three main discriminants features are:

1. The presence of epidermal cysts (milia), scars, and nail dystrophy
2. The mode of inheritance
3. Involvement of mucous membrane and primitive histology.

According to Shafers,[4] EB is classified into four main groups based on the mode of inheritance, anatomic

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location, distribution of the lesions, and associated morbidity. The main groups of EB that differ genotypically and phenotypically are EBS, EB dystrophic which can be dominant or recessive, junctional EB (JEB), and EB acquisita (acquired or Kindler's Syndrome). Distinct differences in the manifestation of these diseases have been given in detail by Gorlin *et al*.[3] Furthermore, these types were then delineated into distinct subgroups by phenotypic characteristics and mode of inheritance, illustrated in Table 1. Inherited EB constitutes over 30 phenotypically or genotypically distinct entities.

Historical Perspective

The term EB hereditary was first used by Koebner, in 1886, to describe multiple generations of a family with traumatic skin blistering.[4] Hallopeau became the first dermatologist after 10 years to distinguish between both the forms of the disease: EBS and dystrophic EB (DEB). Earlier, these were thought to be the two types of EB. However, in 1935, Herlitz described another distinct type of EB and referred to as JEB. JEB was observed to occur at the junction connecting the basement membrane and the basal plasma cell membrane of the skin.[5] The all different types of EB were categorized by their different clinical features in early 20th century.

The advent of electron microscopy allowed dermatologists to distinguish between EBS, JEB, and DEB based on the ultrastructural level in relation to the BMZ where split or separation occurred. Likewise, genetic research has furthered strengthened the concept of this disease by laying the foundation for understanding the cause of the disease and its potential cure. In 1991, researchers discovered that mutations in the keratin 5 and keratin 14 genes cause the majority of EBS types.[5]

Table 1: Common types and subtypes of EB

A. EBS
1. Localized EBS
• EBS-WC
2. Generalized EBS
• EBS-K
• EBS-DM
B. JEB
1. Localized JEB
2. Generalized JEB
• JEB-Herlitz (JEB-H)
• JEB-non-Herlitz (JEB-nH)
C. DEB
1. DDEB
• DDEB-CT
• DDEB-P
2. RDEB
• RDEB-HS

EB: Epidermolysis bullosa, EBS: Epidermolysis bullosa simplex, WC: Weber-Cockayne, K: Koebner, DM: Dowling-Meara, JEB: Junctional epidermolysis bullosa, DEB: Dystrophic epidermolysis bullosa, DDEB: Dominant dystrophic epidermolysis bullosa, CT: Cockayne-Touraine, P: Passini, RDEB: Recessive dystrophic epidermolysis bullosa, HS: Hallopeau-Siemens

The first report of EB was stated by von Hebra in 1870. It was seen that the pattern of inheritance may be either autosomal dominant or autosomal recessive. The recessive types of EB are more severe than the dominant types.[6]

Hereditary EB

Inherited EB is a rare skin disease that manifests as painful cutaneous erosions and blistering following minor skin trauma. Severe debilitation and pain can result when EB affects the gastro-intestinal, oral/dental, ophthalmologic, musculoskeletal, and hematologic systems, as it may in patients with recessive autosomes. In the most severe cases, infection through open wounds and overwhelming sepsis can cause death at birth or shortly thereafter. It affects males and females equally. Recessive DEB (RDEB) is characterized by severely reduced or complete lack of Type VII collagen protein production, frequently resulting from gene mutations (COL7A1).[2]

Oral and dental manifestations contribute considerably to poor nutrition and growth retardation in patients with RDEB. The oral mucosa is made up of stratified squamous epithelium, so blisters form throughout the mouth, including on the tongue and lips. Individuals with severe generalized RDEB typically have extreme fragility of their oral and perioral mucosa. The oral ulcerations can affect all areas of the oral mucosa, including the tongue. The lesions heal with scarring. The continual process of blister formation and healing with scarring results in marked changes in the oral architecture. There occurs contracture of the oral mucosa which causes obliteration of buccal sulci, microstomia along with poor dentition. The tongue loses the lingual papillae and becomes bound down to the floor of the mouth, resulting in ankyloglossia. Anatomic structures such as the palatal rugae are ablated. Obliteration of oral vestibules and restricted mouth opening follows long-term scarring of the oral mucosa.[7] Even at times, developing enamel can undergo changes in patients affected with RDEB. The tooth enamel is pitted and thin, probably caused by molecular defects in the BMZ-associated proteins in the skin.[3]

Maintaining proper dental hygiene is difficult in such patients. Individuals with a generalized recessive form of EB are associated with dental caries and are also at increased risk for developing squamous cell carcinomas.[3]

The prevalence of periodontitis and dental caries is found to be significantly greater in individuals with JEB and RDEB due to the lack of tooth brushing (Fragile oral mucosa). A change in the oral microflora has also been identified as a

possible cofactor but with limited literature. Furthermore, the immunoglobulin A secretion has been found to be greater in the RDEB group due to blistering.[8]

This case report is interesting because, besides one of the few cases reporting periodontal alterations in patients suffering from EB atropicans generalisata mitis, conventional periodontal therapy was found to be successful.

CASE REPORT

Chief Complaint

A 20-year-old female patient reported to the Department of Periodontology in MM College of Dental Sciences and Research, Mullana, Ambala, with a chief complaint of forwardly placed upper front teeth with generalized gingival bleeding and difficulty in chewing food because of mobile lower front teeth [Figure 1].

Medical History

The patient's medical history revealed that she had been suffering from several clinical problems, such as abnormalities of nails, persistent anemia, palmer-planter blistering following mild trauma. Earlier the patient had reported to the department of skin in Maharishi Markandeshwar Medical College, and the reports confirmed that she was suffering from EB, which was diagnosed at AIIMS, Delhi.

Clinical Findings

The intra-oral examination revealed high plaque index, severely inflamed gingiva, proclined upper anterior, increased overjet, and ulcers that were present on the lateral surface of the tongue with a reddish appearance of buccal mucosa [Figure 2]. Gingiva appeared red in color, soft in consistency with bulbous interdental papillae that bled easily on touch [Figure 3]; stippling was absent, generalized periodontal pockets were present ranging from 5 to 7 mm [Figure 4]. Pathological tooth migration was observed with respect to 31, 41, and 22 (FDI notation) and generalized gingival recession with mobility was seen with respect to 31, 32, 41, and 42.

On extra-oral examination, the patient reported of blisters on the hands, knees, elbows, and legs that were healed with scarring [Figure 5]. It was also observed that some nails have been completely obliterated [Figure 6]. So, together these findings suggested that the patient was suffering from EB with generalized chronic periodontitis.

Family History

The patient revealed that her brother is also suffering from the same problem which was diagnosed 5 years back.

Radiographic Features

Orthopantomogram revealed areas of horizontal bone loss. On further examination, root stumps (47, 36), multiple

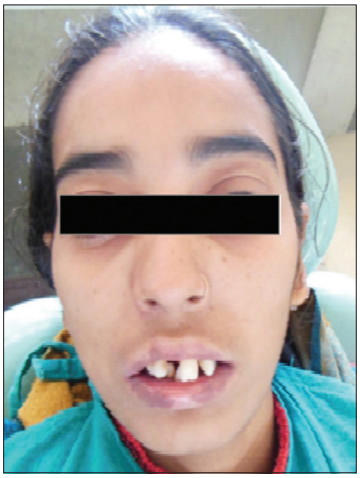

Figure 1: Patient with forwardly placed teeth

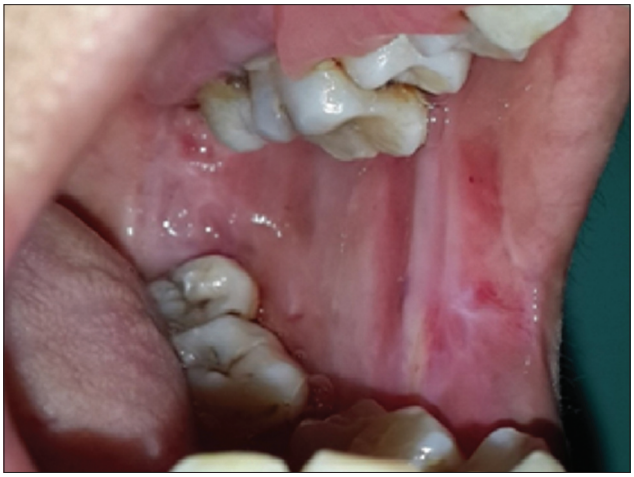

Figure 2: Blisters and reddish buccal mucosa

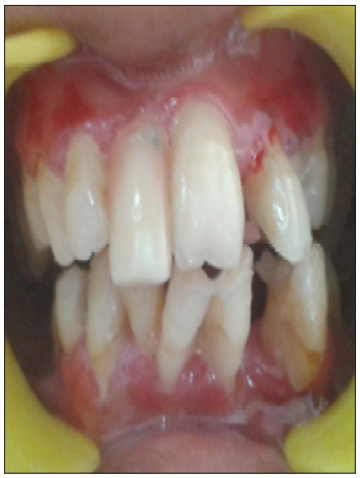

Figure 3: Pre-operative view showing inflamed gingiva and proclined upper anteriors

carious teeth, rotated teeth, and missing teeth were seen [Figure 7].

Treatment

Medical treatment

Systemic treatment consisted of medication and improvement of diet to alleviate the patient's anemia, besides complementary instructions to preclude trauma and the resultant appearance of new blisters and proper care in cleaning occasional blisters.

Dental treatment

Dental care consisted of a multidisciplinary approach. First, the patient was referred to the Department of Oral Surgery for the extraction of root stumps and teeth with a hopeless prognosis. Then, thorough oral prophylaxis was performed, i.e., quadrant by quadrant scaling and root planning was done, and instructions for maintaining oral hygiene and plaque control were given. After the non-surgical phase of treatment, the patient began the maintenance phase and returned every month for re-evaluation and prophylaxis. Followed by, the patient was sent to the department of endodontics for the restoration of decayed teeth.

At a recent re-evaluation and follow-up (i.e., after 1 month) was done [Figure 8a and b], new pocket measurements were performed. The generalized pocket reduction has occurred [Figure 9]. The patient is still kept under observation for further treatment. 0.2% chlorhexidine mouthwash has been prescribed twice daily for effective reduction in plaque index.[9]

DISCUSSION

EB is a disorder which is commonly observed in children from all ethnic origins, with no gender prediction. Its severity ranges from mild, with localized blistering of the hands and feet, to generalized blistering of the skin sometimes up to 75%, as well as of the oral cavity. As a result of chronic blistering of the skin, these patients suffer from anemia, life-threatening infection, and chronic infection. In addition, blood and serum are continuously lost through the constant bleeding and weeping of the lesions.[1]

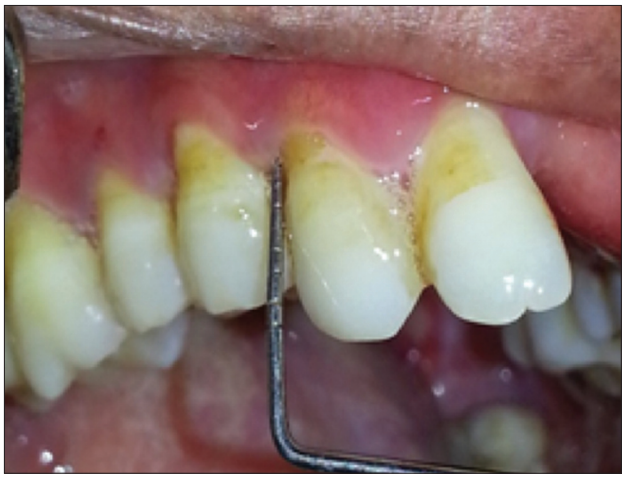

Figure 4: Pre-operative probing pocket depth

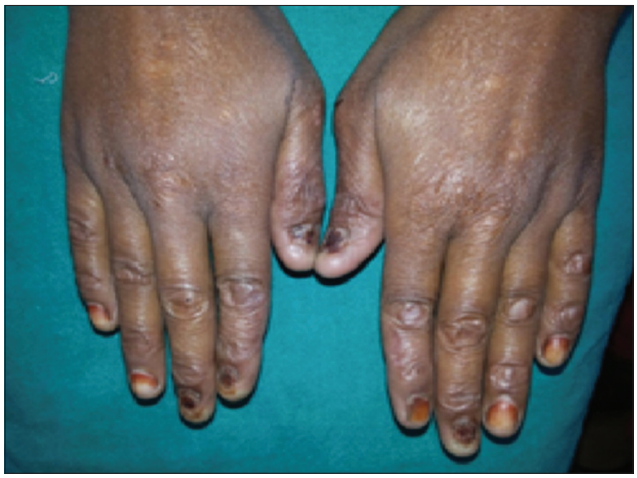

Figure 6: Obliterated nails

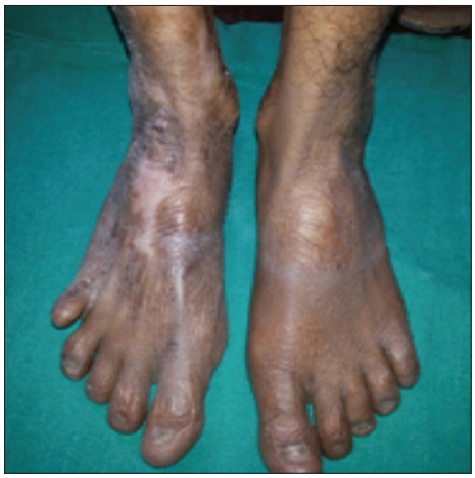

Figure 5: Blisters on feet and legs which have healed with scarring

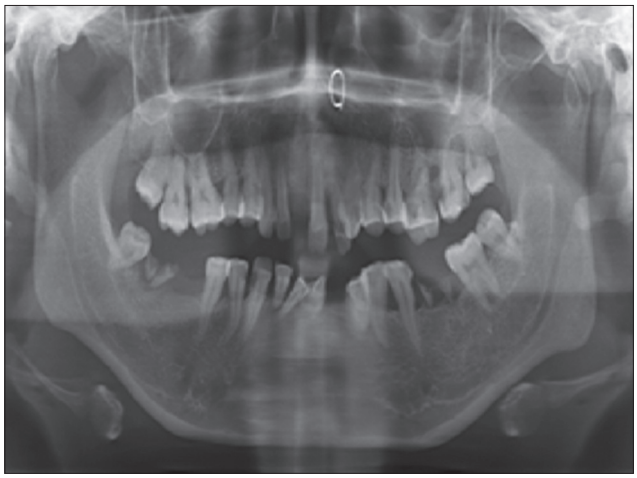

Figure 7: Orthopantomogram revealing areas of horizontal bone loss

Recessively inherited EB is a group of diseases which ranges from mild to severe in the presentation. A localized form, termed recessively inherited EB mitis, often involves acral areas and nails but shows little mucosal involvement. This subtype also demonstrates clinical manifestations similar to the dominantly inherited forms of DEB. Hallopeau–Siemens a form of RDEB, usually shows positive generalized blistering at birth and subsequent extensive dystrophic scarring that is most prominent on the acral surfaces. This can produce pseudosyndactyly (Mitten-hand deformity) of the hands and feet. Deformity of nails and teeth, as well as flexion contractures of the extremities, is increasingly common with age in RDEB. Anonychia (nail loss) caused by scarring is also common in RDEB.[10]

RDEB presents the dentist a most difficult problem and is probably more taxing of modern preventive and restorative techniques than almost any other condition.

So, preventive strategies must be aimed at plaque-related diseases of dental caries and periodontal disease. In fact, maintenance of proper oral hygiene is difficult due to the diminished oral opening and progressive obliteration of the labial sulcus. Furthermore, minor trauma from tooth brushing may cause an eruption of oral bullae thus causing discomfort and scarring. Therefore, maintaining a functional dentition reduces the potential for oral and esophageal soft-tissue damage through more efficient mastication and favors nutrition.[1]

The patient dexterity in performing oral hygiene measures is often limited by hands and fingers that have become claw-like through repeated scarring. Adequate oral hygiene should be encouraged with the gentle use of small headed soft toothbrushes and small sponge applicators. The physical removal of bacterial plaque may be supplemented with chemical inhibition by the use of 0.2% chlorhexidine gluconate solution twice daily. Chlorhexidine[9] is adsorbed to oral mucosal surfaces where it exerts an antibacterial effect for several hours. This property may also assist in reducing secondary infection of ulcerated mucosal surfaces, thereby reducing discomfort and promoting more rapid healing. However, the astringent taste may be unacceptable to some patients, and also the brown discoloration of the acquired pellicle may require professional removal every few months.[9,11]

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. So, lubrication of lips, buccal mucosa, gloves, and instruments using vaseline, petroleum jelly, and hydrocortisone ointment is recommended.[8-12]

Diet constitutes a major difficulty in caries control. Nutritional advice may be indicated as coarse foods are not well-tolerated, and a high caries rate is often the norm.[8,12-14]

Overall RDEB patients can undergo treatment without any major contraindication, illustrated in Figure 10.

The present case is remarkable not only because very few cases have been reported describing the oral manifestations of this rare disease, but also because it responded well to non-surgical periodontal therapy. From this observation, it can be speculated that the combination of bacterial plaque and dermatologic disease provoked exacerbated periodontal destruction. Despite the patient's age (20-year-old), the

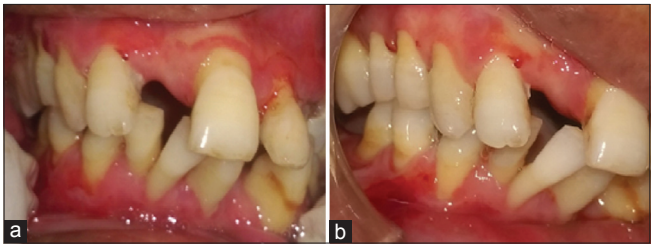

Figure 8: (a and b) Post-operative gingival condition

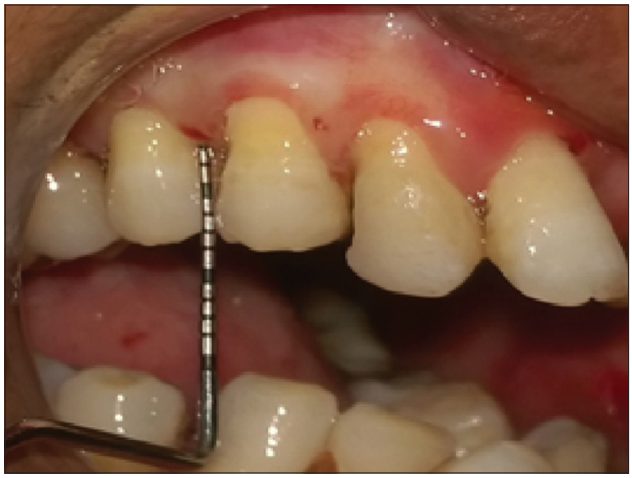

Figure 9: Post-operative view showing reduction in probing pocket depth

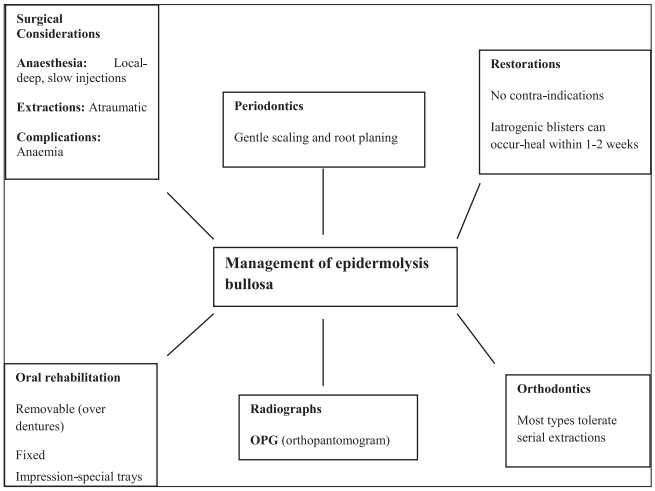

Figure 10: Oral management of recessive dystrophic epidermolysis bullosa (adapted from Kramer *et al.*[15])

prognosis appears to be favorable since she has responded well to therapy as there is a reduction in pocket depths. The patient has been seen regularly after 1 month for maintenance, and follow-up evaluations will continue to be scheduled. This case also underscores the vital importance of the physician-periodontist relationship.

A multidisciplinary approach should be involved by a team of expert health professionals. The team should involve nutritionist, dermatologist, plastic surgeon, dentist with cardiologist, pediatric surgeon, ophthalmologist, nurse, and occupational therapist.

CONCLUSION

RDEB is a very rare phenomenon. Dental surgeons need to be aware of such conditions in their patients to instigate appropriate treatment procedures. A multidisciplinary approach and priority treatment needs are set by the current working groups on EB that may guide our approach to patient management.

Cutaneous findings
- Primary Involvement of palm and soles
- Primary involvement of axilla and groin
- Reticulate hyperpigmentation
- Confluent palmoplantar keratoma.

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