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Case Report

An unusual case of bullae and scars

Tanvi P. Vaidya*, Ramesh M. Bhat, Sukumar Dandekeri

Department of Dermatology, Father Muller Medical College, Mangalore, Karnataka, India

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***Correspondence:**
Dr. Tanvi P. Vaidya,
E-mail: dr.tanvivaidya@gmail.com

ABSTRACT

The term epidermolysis bullosa (EB) encompasses a group of inherited mechano-bullous disorders, clinically characterized by blisters over skin and mucosae following minor frictional trauma. The diagnosis is predominantly clinical, but further classification is carried out by defining the histological level of the split. Histopathology tends to be ambiguous, as it was in this case. Our case is of a twelve-year-old male child who came with complaints of recurrent painful fluid filled lesions all over the body since 10 days of birth, aggravated by trauma, with exacerbations in the summer, and with a history of similar lesions in the mother and maternal uncle. On examination, there were multiple flaccid bullae, crusted erosions, scars and milia over trauma prone sites, such as the elbows, back, knees, shins and knuckles, with nail dystrophy and pitting of the teeth. The clinical impression as well as histopathology suggested a dominant dystrophic or a junctional EB, but immunofluorescence antigen mapping revealed it to be a case of EB simplex. We must thus bear in mind that histopathology is not definitive in EB, and immunofluorescence antigen mapping or transmission electron microscopy is imperative to correctly diagnose it.

Keywords: EB, Basement membrane antigens, Immunofluorescence antigen mapping

INTRODUCTION

Epidermolysis bullosa (EB) encompass a group of inherited mechano-bullous disorders, clinically characterized by blisters over skin and mucosae following minor frictional trauma.[1]

Based on the ultrastructural site of cleavage, EB can be classified into four types as follows epidermolysis bullosa simplex (EBS), junctional epidermolysis bullosa (JEB), dystrophic epidermolysis bullosa (DEB), and Kindler syndrome.[2]

EBS has an intra-epidermal cleavage plane, JEB has its cleavage plane at the lamina lucida, and DEB has a sub-epidermal cleavage plane. Kindler syndrome is a mixed type, exhibiting multiple cleavage planes which may be intra-epidermal, in the lamina lucida or sub-epidermal.[3]

CASE REPORT

Our case is of a twelve-year old male child, residing at Karwar, Karnataka who presented to us with the complaints of multiple fluid filled lesions and raw areas all over the body since ten days of birth. The lesions ruptured to leave reddish raw areas which eventually healed with scarring. The lesions tended to appear over areas of trauma or over pressure bearing sites, and they aggravated in the summer. There was a history of discoloration and thickening of nails, as well as dental caries. The patient's mother and maternal uncle reported similar complaints. There was no history of consanguinity in the parents.

On examination, the boy was poorly built with a body mass index of 16.1. There were multiple flaccid blisters, scars and milia over the back, elbows, dorsa of the hands, knees, shins and feet (Figures 1a and b).

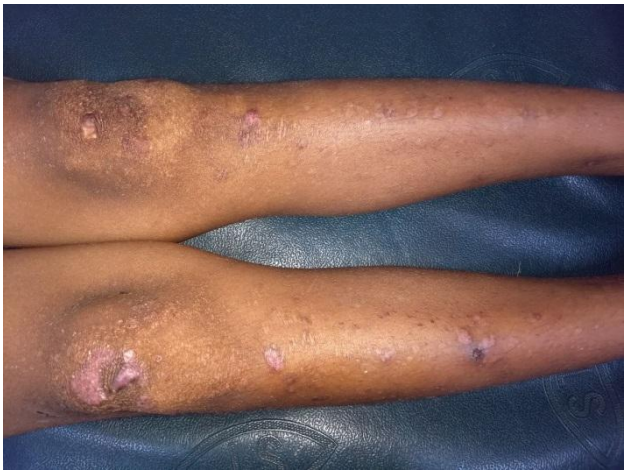

Figure 1 (a): Multiple hypopigmented and atrophic scars, and milia over bilateral shins.

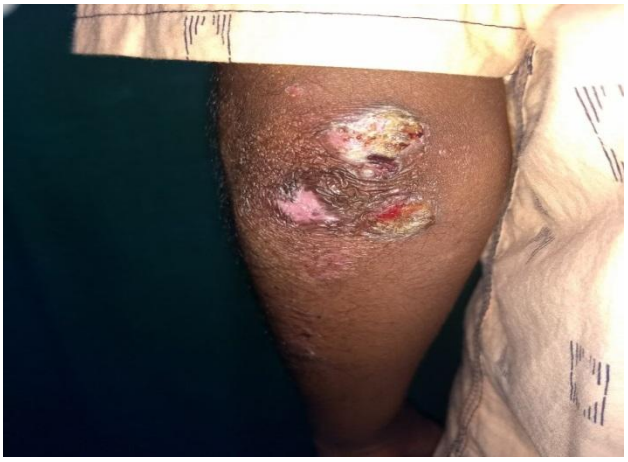

Figure 1 (b): Flaccid blisters and depigmented scars over sites prone to trauma such as the elbows.

The lesions were seen predominantly over extensors and trauma prone sites. Nikolsky sign was negative, while the Sheklakov sign was positive. Nail plate discolouration, nail dystrophy and onycholysis were seen in nails of bilateral upper and lower limbs (Figures 2a-c).

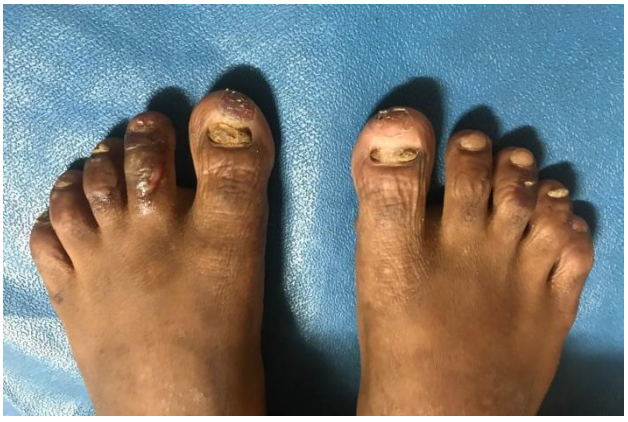

Figure 2 (a): Nail plate discoloration, dystrophy and onycholysis seen in the toenails.

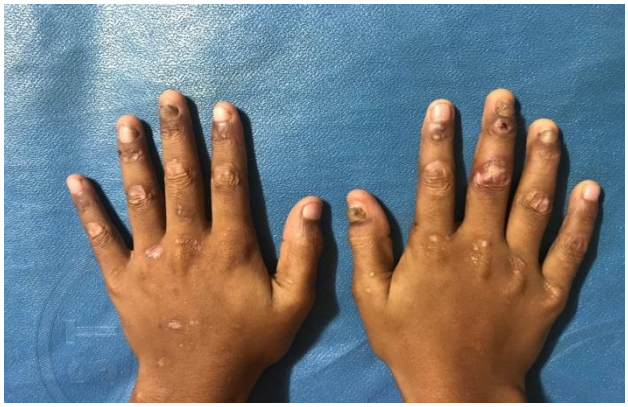

Figure 2 (b): Multiple flaccid blisters, scars and milia seen over the knuckles and dorsum of the hands.

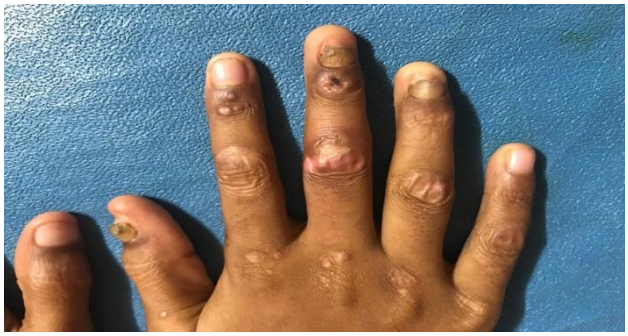

Figure 2 (c): Flaccid blisters, scars and milia over the knuckles, and nail dystrophy seen over the fingernails.

Multiple scars were seen over the hard palate (Figure 3).

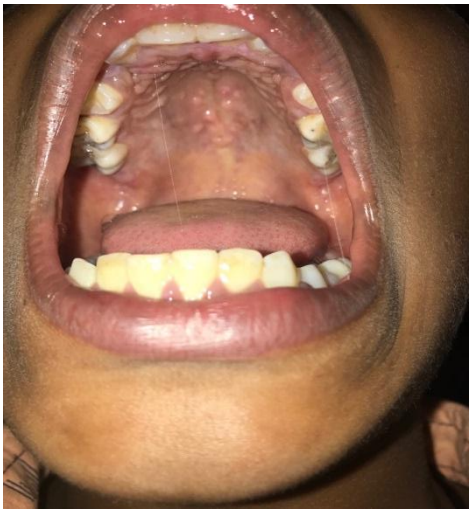

Figure 3: Multiple scars seen over the hard palate, and enamel pitting seen over the teeth.

Pitting and discoloration, along with dental caries were visible in the teeth.

The extent of scarring and milia formation, severe nail dystrophy and enamel pitting, without palmoplantar keratoderma, were in favor of dominant dystrophic

epidermolysis bullosa (DDEB) or JEB. The presence of lesions in the patient's mother and maternal uncle, with no consanguinity in the parents suggested a possible autosomal dominant inheritance. This is uncommon in JEB. EBS was considered as a possibility, as autosomal dominant inheritance with blisters and scarring is also seen in EBS. Despite this, it was considered less likely due to the sparing of the palms and soles and presence of enamel pitting. Also, in this case the scarring was more extensive than would have been expected in EBS. We thus came to a provisional clinical diagnosis of DDEB.

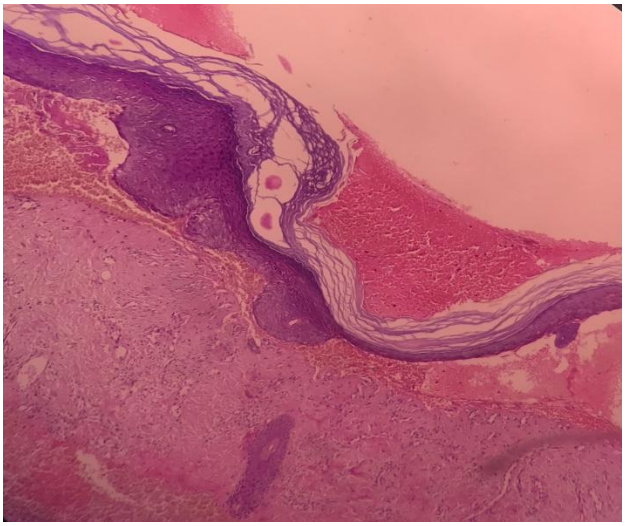

Figure 4 (a): Histopathological image of subepidermal blister seen on 400x (high power) magnification using H and E stain.

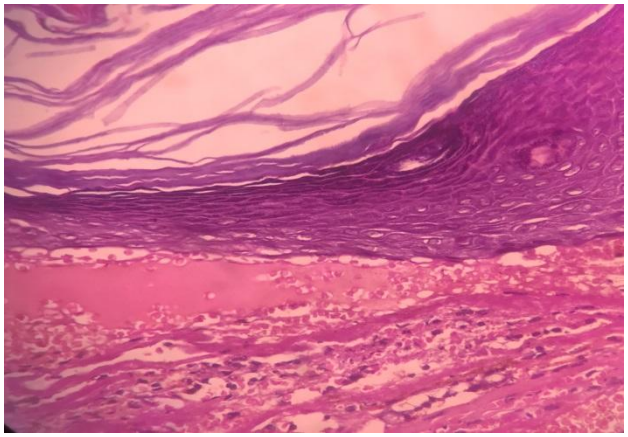

Figure 4 (b): Histopathological image of subepidermal blister seen on 400x (high power) magnification using H and E stain.

A Tzanck smear was done from one of the newer blisters, but it was negative for giant cells or acantholytic cells. Shave biopsies from freshly induced blisters were sent for histopathology. Histopathology showed a sub-epidermal blister (Figures 4 a-b), further contributing to our diagnosis of DEB.

For further classification and prognostication, immunofluorescence antigen mapping (IFM) was performed. This revealed an intraepidermal blister, with laminin-332, collagen IV as well as collagen VII, all staining in the floor of the blister (Figure 5). IFM for collagen XVII was not available at the laboratory. TEM could not be performed due to non-availability of resources.

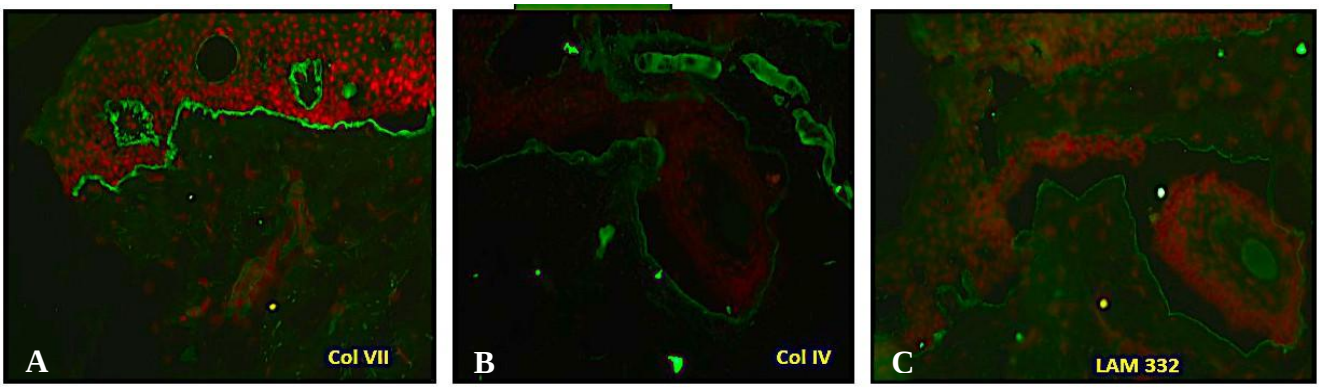

Figure 5: (A) Collagen VII, (B) collagen IV as well as (C) laminin 332 all staining in the floor of the blister on IFM, suggesting a diagnosis of EBS.

With this, a final diagnosis of EBS was made. The patient was treated with antibiotics post biopsy, and counselling and psychological support was provided to the patient.

DISCUSSION

EB is a wide group of disorders, with mutations involving various proteins of the basement membrane zone. Each of these sub types has varied presentations and inheritance patterns. It is therefore essential to be able to accurately classify the disease into the correct sub type.

The latest consensus classification is based on the "onion skinning" approach that classifies EB on the basis of the level of skin cleavage, phenotypic characteristics, mode of inheritance, targeted protein and gene mutations.[3]

Histopathology may be employed for the diagnosis of EB, although the skin biopsy must be taken by a shave biopsy, preferably from a freshly induced blister.[4]

It must be noted that histopathological examination is not ideally recommended in the diagnosis and classification of EB. This is because it often tends to be ambiguous, and light microscopy may not be able to tell apart a lower intra-epidermal cleavage plane from a sub epidermal cleavage plane. Thus, routine histopathological examination cannot reliably distinguish the cleavage planes of EBS, JEB and DEB.[5]

This classification is imperative, as each subtype of EB proceeds with a different course and carries a significantly different prognosis. This is why higher diagnostic tests like IFM or Transmission electron microscopy (TEM) are the need of the hour, as they provide a much-needed confirmatory diagnosis.[6]

TEM was the earliest test for confirmatory testing and classification and is the gold standard laboratory test in the diagnosis of EB for several years now.[7] IFM, however has now taken precedence over TEM, owing to its cost effectiveness, easy transportation of samples, lower reporting time and less requirement of expertise in performing the test and interpreting results.[5] Hence in our case, due to financial constraints and lack of availability, only IFM and not TEM was performed.

Using an extended panel of antibodies and observing the various staining patterns has paved the way to rapid and easy sub-classification of EB, with identification of mutated proteins, and clear visualization of blister cleavage planes.[7]

IFM has not only helped us understand the pathophysiology of EB better, but has also helped us with molecular testing to identify newer genetic mutations by mutational analysis, understand their mechanisms and identify revertant mosaicism.[8]

CONCLUSION

It is imperative to perform IFM or TEM in every case of EB, as the histopathological picture may not be able to truly reveal the location of the blister. Further sub classification of EB will not be possible without these vital investigations.

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