Epidermolysis bullosa pruriginosa: A report of two cases

Varadraj Vasant Pai, Tukaram Sori[1], Kikkeri Narayanshetty Naveen[2], Sharatchandra Bhimrao Athanikar[2], Vijetha Rai[2], Dinesh Udupi Shastry[3]

Department of Dermatology, Goa Medical College Bambolim, Goa, [2]Dermatology, [3]Pathology, SDM College of Medical Sciences and Hospital, Sattur, Dharwad, [1]Consultant Dermatologist, Gadag, Karnataka, India

Access this article online

Website: www.idoj.in

DOI: 10.4103/2229-5178.126030

Quick Response Code:

Address for correspondence:
Dr. Varadraj V Pai, DepartmentofDermatology, Goa Medical College, Bambolim, Goa - 580 009, India.
E-mail: docpai@rediffmail.com

ABSTRACT

Epidermolysis bullosa (EB) pruriginosa is a very rare pattern of dystrophic EB caused by type VII collagen gene mutation, with distinctive clinico-pathological features. It is characterized by nodular prurigo-like lichenified lesions, nail dystrophy, and variable presence of albopapuloid lesions. We report two such cases.

Key words: Bullosa, epidermolysis, pruriginosa

INTRODUCTION

Epidermolysis bullosa (EB) refers to a group of inherited disorders that involve the formation of blisters following trivial trauma.[1] EB pruriginosa is a type of dystrophic EB caused by type VII collagen gene mutation, with distinctive clinico-pathological features. It is characterized by nodular prurigo-like lichenified lesions, nail dystrophy, and variable presence of albopapuloid lesions.[2] Most cases are sporadic, but a few show autosomal dominant or autosomal recessive pattern of inheritance.[2,3] In India, very few cases of EB pruriginosa have been reported. Here we present two cases of EB pruriginosa.

CASE REPORTS

Case 1

A 52-year-old lady presented to our outpatient department with complaints of itching and blackish discoloration of skin of both the lower limbs for more than 35 years and fluid filled lesions over the lower limbs since two years. Lesions were extremely pruritic without any diurnal variation. There was no history of drug intake before the onset of lesions nor any seasonal exacerbation. There was no history of similar complaints in other family members. Patient was a known case of diabetes since five years and on regular treatment. On examination, multiple lichenified papules to nodules were present over the lower limbs extending from the knee to the ankle joint. Depigmentation at the center with scarring was seen over the larger nodules. Few pus filled lesions were also seen [Figure 1]. There was no associated nail involvement. Routine investigations were normal. Based on the clinical picture, EB pruriginosa was suspected. Skin biopsy and immunohistochemistry was done to confirm the diagnosis.

On histopathological examination, epidermis showed subepidermal and intraepidermal bulla with degeneration of keratinocytes. Foci of cellular infiltrate consisting of fragmented neutrophils with occasional mononuclear cells and hemorrhage [Figures 2 and 6]. Direct immunofluorescence was negative. Patient was admitted for four days and was given parenteral steroids and antibiotics. Itching subsided and lesions began to heal. On discharge patient was started on tab dapsone 100 mg once a day with good response. Hematological parameters and lipid profile were monitored.

Case 2

A 34-year-old female patient came to the outpatient department with complaints of skin lesion over both the lower limbs associated with intense itching was noted since 15 years. No seasonal variation in lesions. There were no lesions in the oral cavity. None of the family members had similar lesions. The patient was non-diabetic and normotensive. Cutaneous examination revealed lichenoid papules over both shins extending on to the knee [Figures 3 and 7]. Papules were non tender associated with mild scaling. There was no associated nail or mucosal

involvement. Lab investigations were normal. Skin biopsy showed subepidermal bulla filled with fibrin and RBCs. Dermis showed perivascular mixed inflammatory cell infiltrate and cyst lined by stratified squamous epithelium [Figures 4 and 5]. Direct immunofluorescence was negative.

The patient was started on topical steroids with systemic antihistamines with minimal response after one month.

DISCUSSION

EB pruriginosa is a type of dystrophic EB termed by McGrath in 1994,[2] though a number reports of similar condition have appeared in literature since 1946.[4] In the one original series of eight cases reported by McGrath, three had family history of similar skin disease, with two showing an autosomal dominant and the other an autosomal recessive pattern of inheritance.[2] In our cases there was no family history of similar complaints indicating a sporadic inheritance.

Genetic linkage studies in families with dominant and recessive dystrophic EB have confirmed tight linkage to the type VII collagen gene. Structural protein abnormalities of type VII collagen either in the helical portion or the globular end domains suggesting the possible influence of type VII collagen gene, along with some other factor, might be responsible for causing a variety of abnormalities in the collagen helix assembly dimer formation or lateral aggregation, thus resulting in a diversity of clinical features.[5,6] Recent molecular analysis studies have revealed a glycine substitution within the triple helical collagenous domain of the type VII molecule, to be exclusively associated with the dominant dystrophic EB, and EB pruirigunosa.[7]

EB pruriginosa presents either at birth with mild acral

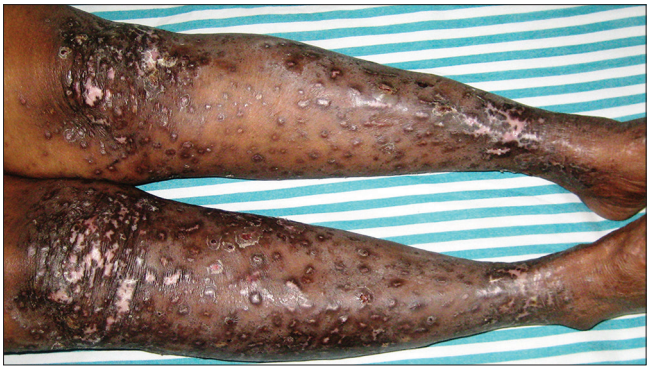

Figure 1: Lichenified papules to nodules over the shin with depigmentation and scarring

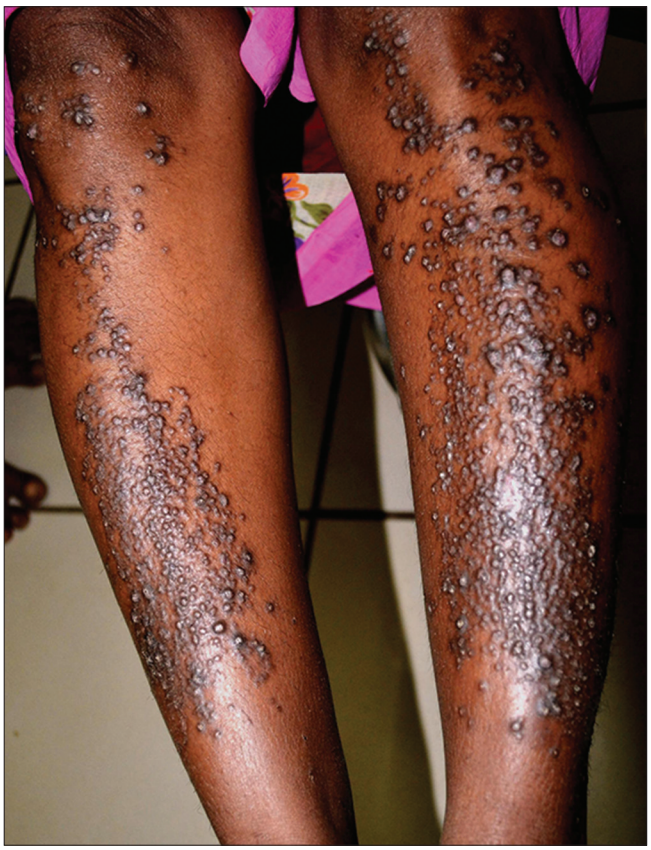

Figure 3: Lichenoid papules over both shins extending on to the knee

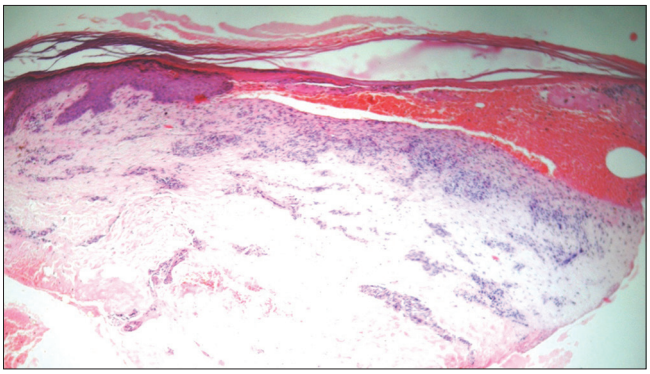

Figure 2: Epidermis showed subepidermal bulla with degeneration of keratinocytes. Foci of cellular infiltrate consisting of fragmented neutrophils. H and E, ×40

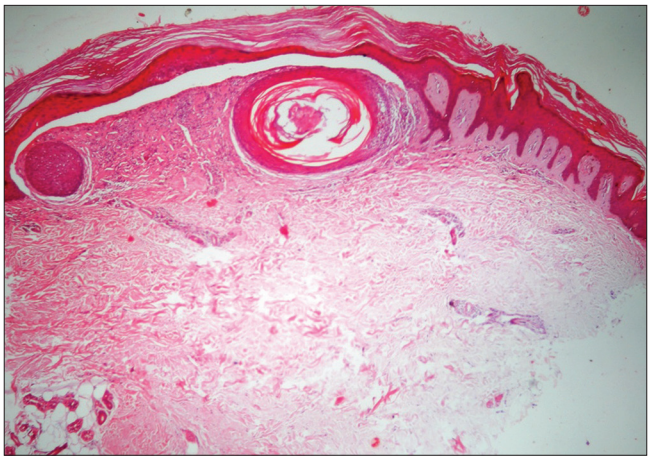

Figure 4: Subepidermal bulla filled with fibrin and RBCs. Dermis shows mixed inflammatory infiltrate with keratin cysts. H and E, ×40

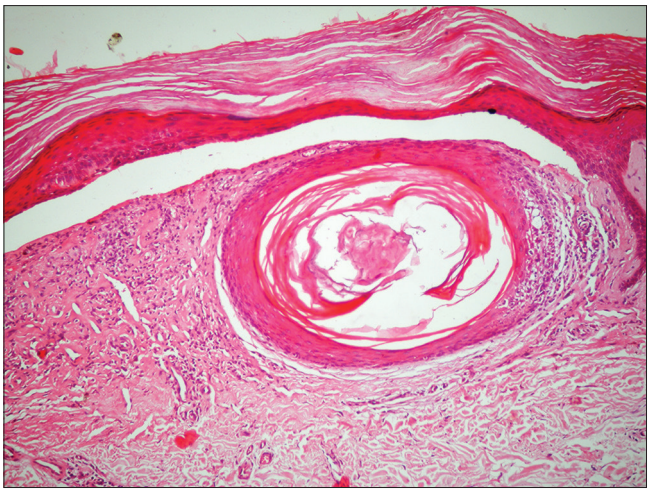

Figure 5: Close up photomicrograph of the second patient

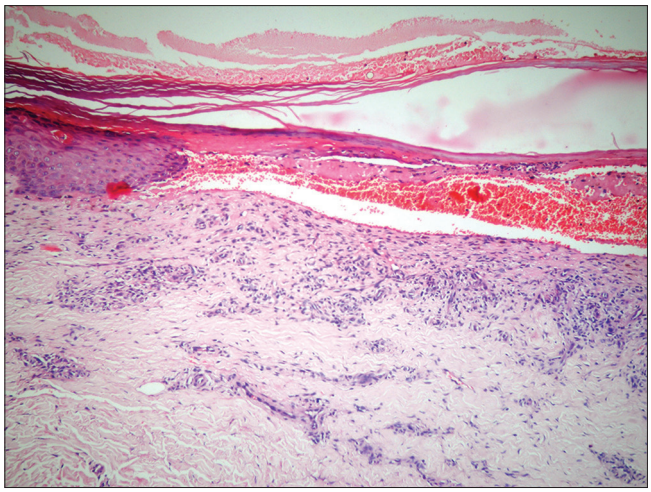

Figure 6: Close up photomicrograph of first patient

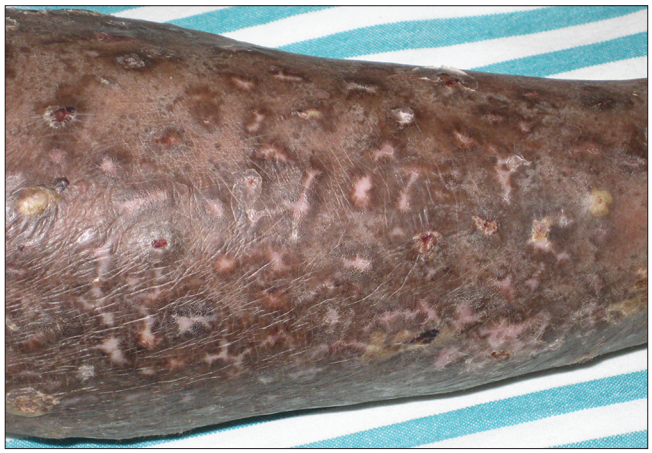

Figure 7: Close up of first patient

blistering and erosions, or during infancy or childhood. In adults, the lesions are chiefly lichenified plaques.[3] In both of our cases the lesions presented in early adolescence. The condition is characterized by extremely pruritic linear lichenified or nodular prurigo-like lesions predominantly over legs, occasional trauma-induced blistering, excoriations, milia, nail dystrophy and in some case albopapuloid lesions on the trunk. The exact cause of pruritus in this condition is unknown. Possibly, the exposure of type VII collagen is known to trigger the activation of the kinin cascade. Bradykinin possibly interacting with other mediators might be responsible for the severe pruritus.[8]

Histopathology of the lesion of the original series showed hyperkeratosis, mild acanthosis, disruption of the dermoepidermal junction and frank subepidermal blister formation in some areas. Moderate perivascular lympho histiocytic inflammatory infiltrate was seen. Milia were observed in several sections. Ultrastructurally, there were alterations in the number and structure of anchoring fibrils in the lesional and perilesional skin consistent with a diagnosis of dystrophic epidermolysis bullosa.[9]

Treatment is symptomatic and is aimed at controlling pruritus and halting the progression of cutaneous lesions. Potent topical steroids and intralesional triamcinolone have been reported to reduce the pruritus in some cases, but do not produce sustained improvement. Systemic therapy with H1 antihistamines, corticosteroids, or etidronate had no sustained effect. However, successful results have been achieved with topical tacrolimus and thalidomide, as well as cyclosporine. Oral administration of cyclosporine has been reported in one case as controlling the cutaneous lesions and decreasing the pruritus.[10-12]

Genetic counselling and gene therapy probably remain the most promising approaches. As in other forms of dystrophic EB, a prenatal diagnosis is possible by finding a cleft/blister formation at dermo-epidermal junction by light microscopy or more precisely by electron microscopy in fetal skin biopsy taken at 15 to 18 weeks of gestation. Similarly, rapid prenatal diagnosis may be possible by using LH 7:2 monoclonal antibody staining of skin samples obtained from 18 weeks fetus at risk.[13]

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Cite this article as: Pai VV, Sori T, Naveen KN, Athanikar SB, Rai V, Shastry DU. Epidermolysis bullosa pruriginosa: A report of two cases. Indian Dermatol Online J 2014;5:44-7.

Source of Support: Nil, **Conflict of Interest:** Nil.