Epidermolysis bullosa pruriginosa - Report of three cases

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ABSTRACT

Epidermolysis bullosa pruriginosa, a genetic mechanobullous disease, is characterized by pruritus, lichenified or nodular prurigo-like lesions, occasional trauma-induced blistering, excoriations, milia, nail dystrophy and albopapuloid lesions, appearing at birth or later. Scarring and prurigo are most prominent on the shins. Treatment is unsatisfactory. We report three such cases: two of them first cousins, are described with history of blisters since childhood, followed by intensely pruritic lesions predominantly on the shins, and dystrophy of toenails, but no albopapuloid lesions or milia. Intact blisters were present in one case, and excoriations were seen in the other two. All of them showed encouraging response to cryotherapy.

Key Words: Dystrophic epidermolysis bullosa, Cryotherapy

INTRODUCTION

Epidermolysis bullosa (EB) refers to a group of inherited disorders that involve the formation of blisters following trivial trauma.[1] Epidermolysis bullosa pruriginosa is a recently described variant, caused by Type VII collagen gene mutation, with distinctive clinicopathological features.[2] Most cases are sporadic,[3] but a few show autosomal dominant or autosomal recessive pattern of inheritance.[2] Microscopic studies of EB pruriginosa show typical findings of dystrophic EB,[4] and it has been postulated that itching lesions of EB pruriginosa could represent an abnormal dermal reactivity of some subjects to their inherited bullous disorder. The study of the molecular basis of dominant dystrophic EB (classical) and EB pruriginosa shows that both diseases are caused by a missense glycine substitution mutation by different amino acids in the same codon of COL 7A (G2028R and G2028A).[5]

CASE REPORT

Case 1: A 14-year-old boy presented with blisters since the age of one year on both the lower extremities and also on the elbows. The blisters appeared on mild trauma and healed as severely pruritic papules (Figure 1). Most of them eventually healed leaving behind scars, but a few gave rise to pruritic papules. The frequency of new lesions had decreased over the last 4 to 5 years, and the new blisters gave rise to prurigo-like lesions. No family member of the patient had a similar disease. On examination, many prurigo-like lesions were seen on the shins, dorsal aspect of the feet, above the medial
malleoli, knees, and elbows. A few small tense vesicles were seen at the base of the toes and both the great toenails were dystrophic.

Case 2: A 22-year-old unmarried female presented with blisters that used to come up mainly over the extensors of the extremities since the age of 3 years, on mild trauma, and heal as severely pruritic papules. There was history of similar rash in her first cousin, but all other family members were free from similar skin lesions. With age, the number of new blisters reduced, but the pruritic papules persisted. On examination, multiple prurigo-like lesions and excoriations were seen on the shins, dorsal aspect of both feet and both forearms, and also on a localized area on the lower back. All the toenails except the third ones on both feet were dystrophic.

Case 3: A 20-year-old unmarried female, first cousin of Case 2, presented with history of itchy rashes over the extensor surface of the extremities since 2 years of age. As she grew up the number of new lesions decreased, but the itchy eruption persisted. On examination, multiple small prurigo-like lesions and excoriations were seen on the shins, dorsal aspect of both feet and both forearms. Both the great toenails were dystrophic.

All three patients were born of non-consanguineous marriages. Their mucosae, hair, scalp, and palms and soles were free from any lesions, and the teeth were normal. There were no albopapuloid lesions or milia-like lesions. There were no signs of atopy or any other significant skin disease to account for the pruritus. Systemic examination was unremarkable. Routine blood and urine examinations were within normal limits. No fungus was found in the nail clippings of the clinically dystrophic nails. Histopathology showed hyperkeratosis, acanthosis, a mild lymphohistiocytic inflammatory infiltrate in the dermis in all the cases, and a subepidermal bulla in Case 1. Direct immunofluorescence testing failed to show any deposit of IgG, IgM, or C3. Electron microscopy and gene mutation studies could not be done due to lack of facility.

Topical steroids, with or without occlusion, along with systemic antihistamines, were tried in all three cases, but failed to bring any relief. Multiple sittings of cryotherapy with liquid nitrogen spray on the prurigo-like lesions, was done on an experimental basis, under local anesthesia achieved by topical application of cream containing EMLA (eutectic mixture of lidocaine and prilocaine 1:1 by weight) under occlusion for 1 hour. The swelling and pain that followed was adequately treated with elevation of the legs, and oral aspirin 300 mg 8 hourly for 3-5 days. The resultant blisters healed by themselves in about 10 days. This procedure resulted in the alleviation of symptoms and disappearance of pruritic papules to a great extent in Cases 2 and 3, and to some extent in Case 1. New lesions that continued to come up also responded to cryotherapy during the follow-up period of 12 months for Case 1, and 6 months for Case 2 and Case 3. A few small soft depigmented scars that resulted from the procedure were acceptable to the patients.

DISCUSSION

EB pruriginosa is a newly characterized variant of dystrophic EB. In the original series of eight cases reported in 1994, patients had multiple papular and nodular prurigo-like lesions, mostly on the shins, and also on other parts of the legs, forearms, elbows, dorsal aspect of the hands, shoulders, and lower back, developing since birth in some cases, and between 6
months to 10 years of age in others. The face and flexures were always spared, and nail dystrophy, altopapuloid lesions, blisters, and milia were other common but not invariable features. Out of the eight cases of the original series, three had family history of similar skin disease, with two showing an autosomal dominant and the other an autosomal recessive pattern of inheritance. Histopathology showed hyperkeratosis, mild acanthosis, dermal lymphohistiocytic infiltrate, and also subepidermal bullae in some areas. Ultrastructural studies showed a reduction of anchoring fibrils in lesional, perilesional, and non-lesional skin, similar to dominant dystrophic or localized recessive EB, and morphometry of anchoring fibrils alone could not distinguish between different subtypes of dominant dystrophic or localized recessive EB and EB pruriginosa.

In the three cases reported from India so far, the clinical and histopathological findings were very similar. In our patients, pruritus was the most oppressive symptom. Clinical presentation and histopathology were consistent with the diagnosis of EB pruriginosa, however, there were no altopapuloid lesions or milia. The occurrence of the condition in two cousins points strongly towards a genetic origin, but the exact mode of inheritance is hard to specify.

The response of our cases to cryotherapy is encouraging. This mode of treatment was not tried in the original series, and many other therapies that were tried failed to yield desirable results. Treatment with potent topical steroids under occlusions, or intralesional triamcinolone reduced pruritus in some cases but failed to produce sustained improvement. Antihistamines, systemic steroids, or etretinate produced no sustained effect, and UVB therapy worsened the condition.

Our previous experience in successfully treating prurigo nodularis with liquid nitrogen cryotherapy served as the backdrop for our venture in these cases. Cryotherapy is certainly not curative for any genetic disorder like EB pruriginosa, but the extremely pruritic papules responded well to it.

REFERENCES