

# Epidermolysis bullosa pruriginosa: Report Of A Rare Case

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## Abstract

Epidermolysis bullosa pruriginosa is an extremely rare variant of dystrophic epidermolysis bullosa in which combination of intense pruritus and skin fragility lead to hypertrophic, lichenified nodules and plaques and show scarring, milia and nail dystrophy. Histologically, features of hyperkeratosis, acanthosis and minimal blistering at dermal-epidermal-sublamina level are characteristic. Most cases are inherited as autosomal recessive, dominant or sporadic. Its onset is often late, the clinical course is unpredictable and various factors leading to intense pruritus remain speculative. Diagnosis is from characteristic clinicopathologic features. The defect in anchoring fibrils has been attributed to mutations in COL7A1 gene mapped to 3p21.3 locus but glycine substitution within triple helical collagen domain of type VII molecule may not be exclusive to this variant. There is no satisfactory treatment and it is not known whether treatment of pruritus would prevent development of other manifestations of the disorder. Genetic counseling, future clinical surveillance and prenatal diagnosis perhaps remain useful. This paper describes a case of this rare disorder revisiting its various aspects.

## INTRODUCTION

Dystrophic epidermolysis bullosa (EB) comprises a heterogeneous group of inherited mechanobullous disorders characterized by trauma induced blistering, scarring associated with milia formation, and nail dystrophy. Both recessive and dominant forms of dystrophic EB are caused by mutations in the COL7A1 gene that encodes type VII collagen, the major component of anchoring fibrils at the dermal-epidermal junction, and result in impaired anchoring fibril formation/function. Ultrastructurally, there is blister formation at sublamina densa level and quantitative or qualitative changes in the anchoring fibrils at dermal-epidermal junction. However, phenotypic variations occur in affected individuals and at least 10 distinct clinical variants of dystrophic EB have been recognized till date<sup>1</sup>. With cases of autosomal recessive or dominant inheritance and localized or generalized cutaneous manifestations it may sometimes be difficult to classify many types of dystrophic EB into one particular type suggesting existence of heterogeneity within a given subtype as well. Epidermolysis bullosa pruriginosa (EBP) is a rare and distinct clinical subtype of dystrophic EB described for the first time in 1994<sup>2</sup>. It is characterized by skin fragility, blistering and scarring, often with milia formation, nodular prurigo-like lichenified lesions, nail dystrophy, and variable presence of allopapuloid lesions. Clinically, these features may also overlap with pretibial form of dystrophic EB. However, the

reported cases collectively suggest the distinct nature and clinical spectrum of this disorder. Furthermore, the lesions in EBP are more widespread, always associated with intense pruritus, and the onset of the disorder is often late during adulthood. Other closely mimicking acquired non-bullous dermatoses, such as nodular prurigo, lichen simplex chronicus, dermatitis artefacta, lichen planus hypertrophicus, Neekam's disease, lichen amyloidosis and hypertrophic scars, have distinct clinicopathologic features and will not show subepidermal cleft formation on histology. In this communication we report a case of this rare variant with an idea of its documentation and also revisit various aspects of EBP.

## CASE REPORT

A 40-year-old male, born to non-consanguineous parents after an uneventful pregnancy and birth, presented with symmetrical, itchy, moist, prurigo-like hypertrophic lesions over extremities and back since childhood. The intense pruritus was socially embarrassing and often disturbing sleep. History revealed that he has been developing small blisters over extremities following minor trauma since childhood. These blisters used to rupture and the erosions would heal with scarring. The severity and frequency of blistering decreased with age but he had developed persistent pruritic nodulo-plaques. Historically his severe pruritus could not be attributed to atopy, food or drug allergy,

cutaneous or any systemic disorder. His parents and other siblings were reportedly healthy. Topical or systemic steroids and antihistamines had provided temporary relief in the past.

Cutaneous examination showed numerous excoriated and lichenified papules coalescing to form plaques in a linear configuration over extensor aspects of shins and lower back (Figs 1 & 2)

**Figure 1**

Figure 1: Lichenified papulo-plaques over extensor aspects of shins. Note linear configuration and excoriated blisters at places



**Figure 2**

Figure 2: Excoriated and lichenified plaques, scarring and milia formation seen over back.



Few isolated lesions were present over forearms but face and flexures were spared completely. Scarring, milia, excoriations and freshly eroded lesions were observed interspersing these lesions. There were minimal intact flaccid bullae which when pricked exuded clear or hemorrhagic fluid. There were no albopapuloid lesions. All his finger- and toenails were dystrophic or partially lost (Fig3)

**Figure 3**

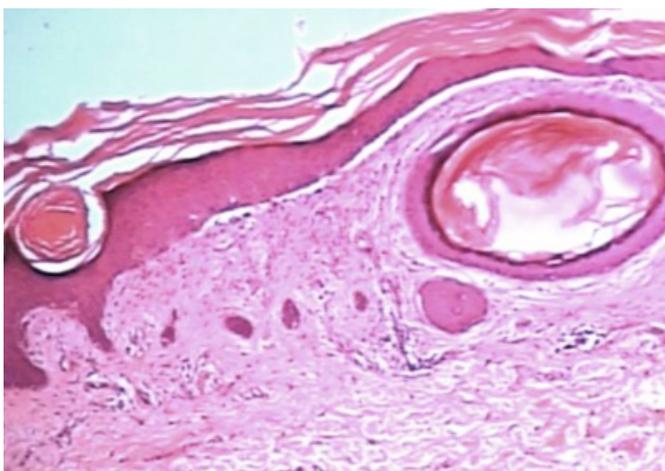
Figure 3: Finger nail and toenail dystrophy.



Hair, mucosae and other systemic examination showed no abnormality. Routine laboratory investigations including complete blood counts, serum biochemistry, urinalysis, chest x-rays were essentially normal. Histopathologic examination (Fig 4) of skin biopsy specimen from a shin lesion showed

**Figure 4**

Figure 4: Hyperkeratosis, mild acanthosis, intact basal cells, a subepithelial cleft and milia as seen in a histologic section (H & E, x10).



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(Fig 4) of skin biopsy specimen from a shin lesion showed hyperkeratosis, mild acanthosis, intact basal cells and sub-basal cleft. There was mild interstitial and perivascular polymorpho-lymphocytic infiltrate in the upper and mid-dermis. Milia were also observed in few sections. He could not afford the cost of immunofluorescence or molecular studies. Based on the characteristic clinical and histologic features a diagnosis of EBP was made and the patient was counseled for genetic and prognostic implications of the disorder. He was prescribed oral cetirizine (10mg x b.i.d.) and twice daily application of topical Fucibet® cream. When seen after 6 months his clinical condition improved significantly and new blistering had decreased.

### **DISCUSSION**

Epidermolysis bullosa pruriginosa is a rare type of dystrophic EB and both autosomal dominant and recessive patterns of inheritance have been described<sup>3</sup>. Many sporadic cases have also been reported<sup>2</sup>. The clinical presentation is characterized by intensely pruritic linear lichenified or nodular prurigo-like lesions over extremities, occasional trauma induced blistering, excoriations, milia, nail dystrophy and in some cases albopapuloid lesions over trunk. Age of onset for skin lesions in EBP is very variable. Its onset at birth or during infancy/childhood is usually with mild acral blistering, however, developing first clinical signs in adulthood is not uncommon and can be as late as 40 years of age<sup>3</sup>. The reasons for the delayed presentation in comparison to that of other forms of dystrophic EB are not known. Symptoms in some patients with onset at birth or infancy may also ameliorate to an extent during childhood or adolescence<sup>4</sup>. However, predicting its clinical course is rather difficult as additional genetic, environmental, metabolic, immunologic, hormonal, or other cutaneous or systemic factors which initiate EBP are not well understood. Histologically, hyperkeratosis, mild acanthosis, a cleft/blister at the dermal-epidermal junction and mild to moderate dermal lymphohistiocytic infiltrate are usual but frank blisters are rarely seen. Our patient more or less had all these clinico-pathologic features and apparently inherited the disorder sporadically. The intense pruritus associated with the disorder has been attributed to atopy, iron deficiency, thyroid dysfunction, hyper IgE, abnormal dermal reactivity or COL7A1 mutation, but no universal abnormality has been found to link all cases of EBP<sup>2,5</sup>. As in other forms of dystrophic and junctional EB<sup>2</sup>, pruritus is perhaps an integral feature of EBP.

Like other forms of dystrophic epidermolysis bullosa, EBP

is also caused by mutations in COL7A1 gene (Gene map locus 3p21.3) with a similar defect in anchoring fibrils<sup>6</sup>. Recent molecular analysis studies have shown a glycine substitution within the triple helical collagenous domain of the type VII molecule exclusively associated with EB pruriginosa<sup>6,7</sup>. Although this may have possible implication for diagnosis in pre-symptomatic patients, the diagnosis in majority is usually based on clinico-pathologic features; direct immunofluorescence findings are variable<sup>8</sup> and electron microscopy or molecular studies are prohibitory expensive. Moreover, immunohistochemical staining with type VII collagen monoclonal antibody (LH 7:2) producing bright, linear band along the dermo-epidermal junction or blister roof is not different from similar findings in other forms of dystrophic EB<sup>2</sup>.

As no specific therapies are known, clinical management of EBP is often difficult. Nevertheless, some helpful interventions include topical tacrolimus<sup>9</sup>, systemic cyclosporine<sup>10</sup>, thalidomide<sup>11</sup> or etretinate<sup>2</sup>, cryotherapy<sup>8</sup> and surgical treatment in the form of dermabrasion or excision-grafting<sup>12</sup>. However, new lesions would usually continue to appear. UVB phototherapy tried in one patient had worsened generalized pruritus<sup>2</sup>. Although symptomatic management of pruritus with oral antihistamines or topical/systemic or intralesional corticosteroids, and antibiotics for secondary infection at best seems palliative, treating pruritus aggressively appears to prevent development of other manifestations of the disorder.

Genetic counseling 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.

### **DRUGS USED**

Fucibet® cream of Leo Pharmaceutical Products Ltd.

Denmark, contains fucidic acid (2%) and betamethasone valerate (1 %).

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