Extensive Extragenital Lichen Sclerosus-Like Lesions in a Patient with Junctional Epidermolysis Bullosa

Abstract

Epidermolysis bullosa (EB) is a heterogeneous group of genetic disorders characterized by the formation of blisters either spontaneously or at the sites of trauma. These heal with post-inflammatory hypopigmentation, scarring, or milia formation. We hereby present a child who presented with widespread hypopigmented atrophic areas, blistering at trauma-prone sites, and nail dystrophy. The significance of this particular case lies in the challenge of distinguishing between epidermolysis bullosa and bullous extragenital lichen sclerosus et atrophicus.

Keywords: *Hypopigmentation, junctional epidermolysis bullosa, lichen sclerosus et atrophicus, skin atrophy*

Smriti Gupta, Sanjeev Handa, Debajyoti Chatterjee[1], Dipankar De, Rahul Mahajan

Departments of Dermatology, Venereology, and Leprology, [1]Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Introduction

Epidermolysis bullosa (EB) is a diverse group of mechano-bullous genetic disorders that is caused by mutations in the genes that encode structural proteins of the skin.[1] Classically, EB is classified into four types: "EB simplex (EBS), junctional EB (JEB), dystrophic EB (DEB), and Kindler EB (KEB)."[2] JEB is inherited as an autosomal recessive disease. The plane of cleavage in JEB is in the lamina lucida of the cutaneous basement membrane zone. According to the epidemiological data available, JEB is less common than EBS and DEB. It can be associated with various extracutaneous involvement, such as pyloric atresia, urinary tract anomalies, interstitial lung abnormalities, and nephrotic syndrome.[2] Herein, we report an association of extragenital lichen sclerosus et atrophicus (LSA) with JEB due to the absence of collagen 17.

Case Report

An eight-year-old boy was brought by his parents to the outpatient department with a history of blistering on extremities since day 7 of birth, which used to heal with hypopigmentation. On examination, the child had multiple erosions, with granulation tissue predominantly over distal extremities and dystrophic nails of the lower limb [Figure 1a]. There were large areas of post-inflammatory hypopigmentation over the extremities with associated erythema. There was no cutaneous atrophy or scarring or milia formation in the healed lesions. Additionally, the patient also had atrophic hypopigmented macules, which were coalescing to form plaques over the proximal extremities, trunk, neck, and perioral areas with interspersed brown pigmentation [Figure 1b and c]. Interestingly, these lesions were not preceded by any blistering. Histopathologic examination of the skin biopsy from the atrophic hypopigmented plaque revealed focal thinning of the epidermis along with basal cell vacuolization. The upper dermis revealed superficial dermal collagenization and mild perivascular and periadnexal lymphocytic inflammatory infiltrates [Figure 2a]. Direct immunofluorescence was negative for IgG, IgA, and IgM. On immunofluorescence antigen mapping of the skin biopsy from a freshly induced blister on the thigh, there was absence of collagen XVII [Figure 2b] and the intense staining of both collagen VII [Figure 2c] and laminin 332-γ. Hence, a diagnosis of intermediate JEB with extragenital LSA was preferred.

Discussion

According to the recent consensus classification by Has *et al.*,[2] JEB can be classified into various phenotypes with corresponding genotypic correlation.

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Address for correspondence:
Dr. Rahul Mahajan, Department of Dermatology, Venereology, and Leprology, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh, India.
E-mail: drrahulpgi@yahoo.com

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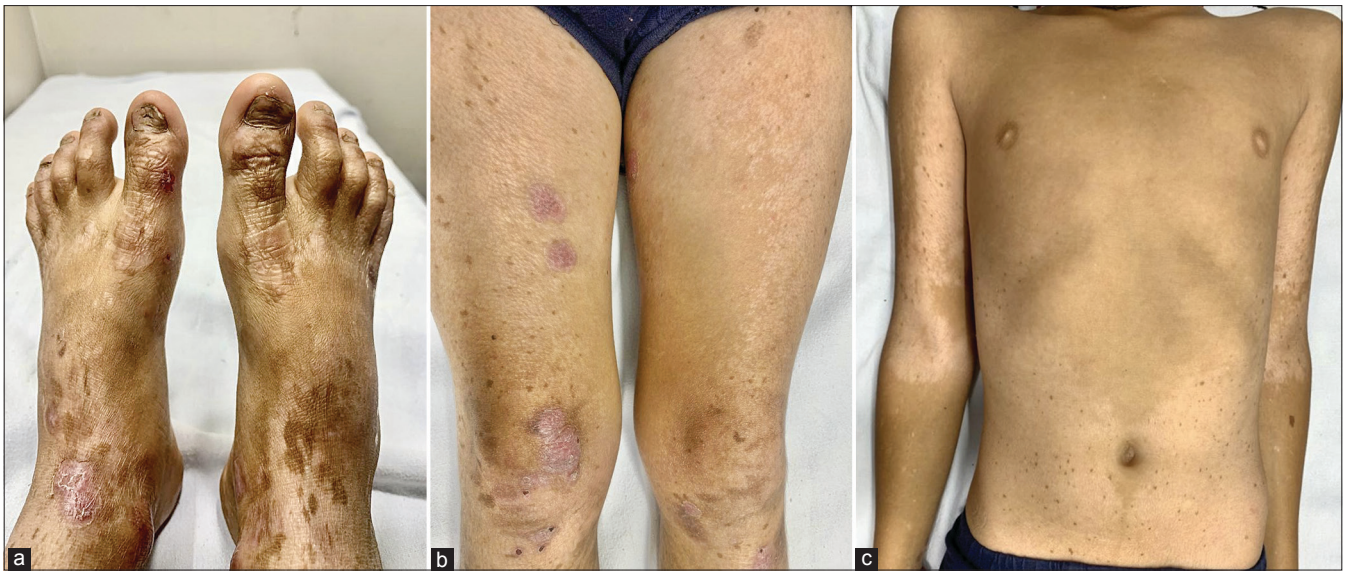

Figure 1: (a) Dystrophic toenails with erosion over the left ankle and surrounding post-inflammatory hypopigmentation. (b) Well-defined erythematous erosions over the thighs and knees and hypopigmented wrinkled depressed coalescing plaques with specks of hyperpigmentation over the proximal thighs. (c) Wrinkled hypopigmented lesions with interspersed hyperpigmented macules over the proximal arms and lower abdomen

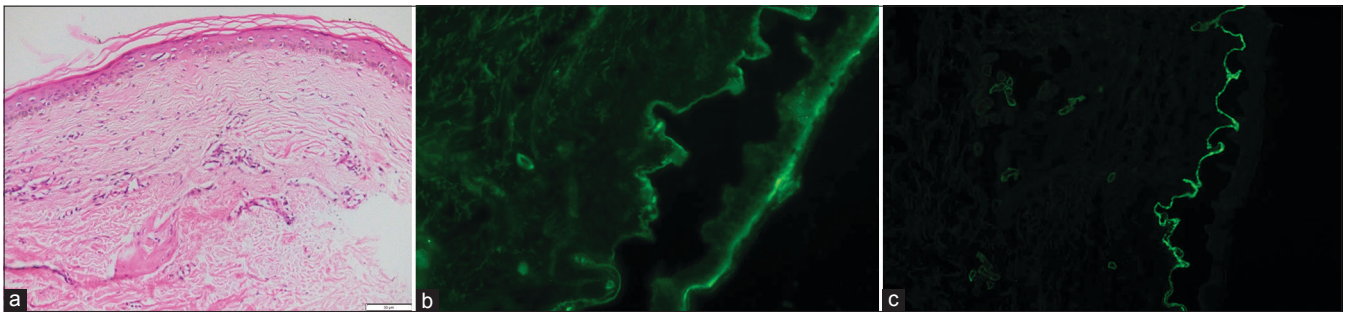

Figure 2: (a) Histopathological image showing flattening of rete ridges, collagenization in the upper dermis, and mild perivascular and periadnexal lymphocytic infiltrates (hematoxylin and eosin, 40x). (b) Immunofluorescence antigen mapping (40x) showing reduced staining of collagen XVII on the floor of the blister. (c) Immunofluorescence antigen mapping (40x) showing normal staining of collagen VII on the floor of the blister

JEB can occur due to mutations in any of the following genes: laminin genes (*LAMA3, LAMB3, LAMC2*), collagen 17 gene (*COL17A1*) and integrin genes (*ITGA6, ITGB4, ITGA6, and ITGB4*). Most mutations causing the absence of laminin or integrin are lethal, in contrast to collagen XVII absence, which usually has less severe phenotypes.[2] Kiritsi *et al*.[3] have previously observed varied phenotypes in 43 patients with collagen XVII mutation. A wide range of clinical variability was noted, ranging from localized acral blistering to severe widespread blistering, nail dystrophy, universal alopecia, and mucosal involvement. However, an LSA-like presentation has not been described till date to the best of our knowledge. LSA is a chronic inflammatory dermatosis characterized by ivory-white atrophic and sclerotic plaques, which can be genital or extragenital in location. Extragenital LSA can have various morphologies, such as ulcerative, annular, desquamative, verrucous, telangiectatic, and bullous. The bullous variant presents as flaccid blisters and is sometimes associated with hemorrhage, ulceration, and crusting.[4] Extragenital LSA is most commonly present on proximal extremities and trunk[5] as was seen in our case. The presence of nail dystrophy, blistering at trauma-prone sites, and the absence of white sclerotic plaque and atrophy at the healed site of the blister in the patient favored the diagnosis of EB, and the presence of white atrophic plaques with specks of hyperpigmentation over the trunk and proximal extremities and historically the absence of blister at these sites favored the diagnosis of extragenital LSA. The hyperpigmented macules over the LSA were differentiated from the eruptive nevi associated with the inherited EB and generalized lentiginosis syndrome. The eruptive nevi occurred at the previous sites of blistering and not on the uninvolved area,[4] and the pigmentation was limited to the sites of hypopigmentation and atrophy and did not involve the surrounding normal skin; hence, it was considered part of LSA rather than generalized lentiginosis syndrome. Furthermore, previous studies have shown that LSA shows melanocytic proliferation.[6] It may be emphasized that clinically it needs to be differentiated from the albopapuloid lesions of DEB, which are classically described as small, usually less than 1 cm, atrophic wrinkled depressed scars, and/or ivory-white papules.[7]

The co-occurrence of these two rare dermatoses may be a chance occurrence or may have resulted from a shared pathogenesis. Although the pathogenesis of LSA is not fully elucidated, autoantibodies against the extracellular matrix protein 1 and BP230 and BP180 have been seen in patients of LSA and are implicated in the pathogenesis. One of the probable mechanisms of the overlap seen in our patient could be the abnormal collagen 17 (BP180), which triggered the extensive LSA.[8]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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