https://doi.org/10.22491/2357-9730.151525

Case Report

Overlap of Hereditary Epidermolysis Bullosa and Dermatitis Herpetiformis in an Adult Woman: Case Report

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ABSTRACT

Hereditary epidermolysis bullosa (EB) is a group of genodermatoses characterized by congenital skin fragility and trauma-induced blistering, whereas dermatitis herpetiformis (DH) is an autoimmune, intensely pruritic vesiculobullous disease associated with gluten sensitivity and granular IgA deposition in the papillary dermis. We report the case of a 39-year-old woman with lifelong skin fragility and congenital abnormalities, including fused lower limbs requiring surgical reconstruction in infancy and persistent anonychia, supporting an underlying hereditary form of EB. In adulthood, she developed recurrent, highly pruritic vesicles and bullae with a symmetric distribution on the extensor forearms and lower limbs, the groin, inframammary areas, and the oral mucosa. The eruption partially improved with topical clobetasol and markedly improved after adopting a gluten-free diet. Histopathology showed epidermal hyperkeratosis and acanthosis with a superficial perivascular lymphocytic infiltrate, and direct immunofluorescence demonstrated granular IgA (3+) and IgG (1+) deposition in the papillary dermis, consistent with DH. This overlap raises the possibility that chronic tissue injury and antigen exposure in hereditary EB may predispose to secondary autoimmune blistering disease, as suggested by recent evidence of circulating autoantibodies against cutaneous structural proteins in EB patients. This case highlights the importance of integrating congenital history, clinicopathologic correlation, and immunopathology when evaluating new-onset pruritic vesiculobullous eruptions in patients with lifelong skin fragility, and it underscores the potential for evolving immune-mediated blistering processes in hereditary EB.

Keywords: *Epidermolyisis Bullosa; Dermatitis Herpetiformes; Bullous Disease; Autoimmune Diseases*

Clin Biomed Res. 2026;46:1-3

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A 39-year-old female presented with a long-standing history of skin fragility and recurrent vesiculobullous lesions. At birth, she presented with fused lower limbs and anonychia. She underwent surgical reconstruction in infancy. Throughout childhood, she had “fragile skin” with frequent erosions following minimal trauma. Approximately ten years ago, she began developing flaccid bullae that ruptured easily, leaving erosions with marked pruritus and milia cysts, primarily affecting the lower limbs, groin, inframammary regions, and ulcerations on oral and genital mucosa. Her medical history included hypertension, type 2 diabetes mellitus, obesity, hemorrhoidal disease, and chronic smoking. Medications included losartan, glibenclamide, alogliptin-metformin, simvastatin, and sibutramine. She denied drug allergies. Her family history was significant for a brother who had similar cutaneous findings at birth, though he was never diagnosed; her children were unaffected. She was lost to follow-up for eight years, reporting intermittent pruritic vesicular eruptions on her forearms. These lesions began with pruritus, followed by the formation of vesicles and crusting. She reported partial improvement with daily application of clobetasol on the forearms and face, and significant improvement after eliminating gluten from her diet. On physical examination, she presented with vesicles and crusts on the extensor surfaces of the forearms, erythematous-whitish plaques with superficial moist ulcerations in the inguinal region, and symmetric reddish papules with atrophic scars on the anteromedial legs,

some over grafted areas. The dorsal feet showed residual hypopigmentation, the halluces exhibited anonychia, and pretibial involvement with papular lesions arising over scarred skin, and she reported intense pruritus in these areas (Figure 1).

Skin biopsy from the vesicle lesion was performed, and histopathological examination revealed hyperkeratosis, hypergranulosis, acanthosis, verticalization of dermal collagen, and a superficial perivascular lymphocytic infiltrate. Direct immunofluorescence was positive for granular IgA (3+) and IgG (1+) deposition in the papillary dermis, consistent with dermatitis herpetiformis.

The combination of congenital features such as fused lower limbs and anonychia, with early-onset skin fragility, supports the diagnosis of a form of congenital dystrophic epidermolysis bullosa. Importantly, given the absence of molecular confirmation, we expanded the diagnostic rationale based on the patient's clinical phenotype: anonychia, milia over scarred areas, chronic scarring with prominent pretibial involvement, recurrent genital, oral and inframammary lesions, and intense pruritus. The pretibial papular lesions occurred over chronically scarred skin and were previously evaluated histopathologically, showing findings consistent with lichen simplex chronicus, supporting chronic itch and scratching over an EB scar background. The adult-onset pruritic vesiculobullous lesions with symmetrical distribution and granular IgA deposition are suggestive of dermatitis herpetiformis, particularly given the patient's reported improvement after initiating a gluten-free diet.

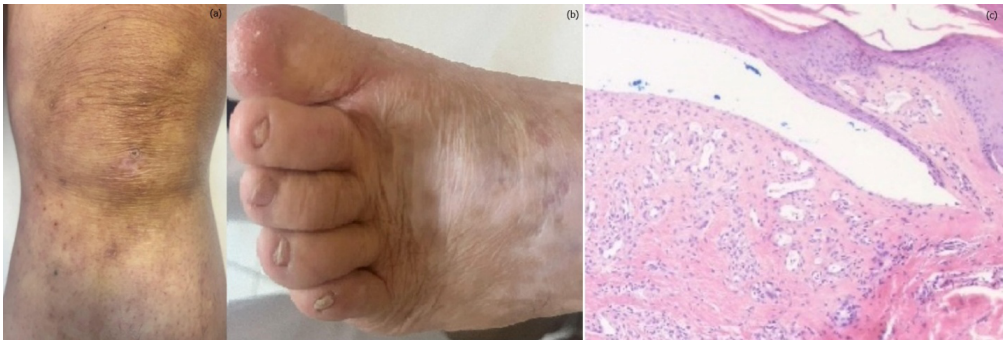

Figure 1: (a) Vesicles and crusts on the knee. (b) Anonychia of the left hallux, with residual hypochromic patch on the dorsum of the foot. (c) Hematoxylin–eosin histopathology showing subepidermal cleft, superficial dermal lymphocytic inflammatory infiltrate.

Although the definitive classification of inherited EB relies on genetic testing, in many real-world public health settings—including the Brazilian Sistema Único de Saúde (SUS)—genetic testing may not be readily available, and in individual cases it may not alter immediate clinical management. In this context, diagnosis must rely primarily on a structured clinical evaluation integrating onset, distribution of lesions, scarring pattern, milia, nail changes, mucosal involvement, extracutaneous manifestations, and family history. Clinical diagnostic matrices may increase diagnostic accuracy and guide the most likely EB subtype even in the absence of molecular confirmation. Based on the pattern of scarring, milia, nail involvement, and prominent pretibial disease, a dystrophic EB phenotype is most likely, and the distribution raises suspicion for pretibial dystrophic epidermolysis bullosa as a clinical subtype.

Although the coexistence of EB and DH is rare, recent literature suggests that patients with hereditary EB — particularly dystrophic forms—can develop circulating autoantibodies against skin structural proteins (including BP180, BP230, type VII collagen, desmoglein 1 and 3, and laminin-332), which may predispose a subset of patients to superimposed autoimmune blistering diseases[1-3]. Lehr et al. demonstrated that patients with hereditary EB may exhibit a markedly increased frequency of such autoantibodies and may be prone to secondary autoimmune blistering disease[1], and Bremer et al. confirmed this tendency in dystrophic EB in a longitudinal design[2], supporting the concept that chronic skin injury and inflammation may contribute to loss of immune tolerance and secondary autoimmunity[4-5]. In our patient, the overlapping features—both clinical and histological—raise the possibility of an autoimmune blistering component developing on the background of hereditary EB and reinforce the need for careful clinicopathologic correlation

At the same time, it is important to emphasize that pruritic inflammatory blistering eruptions may mimic DH, and clinical or histologic overlap may occur in selected contexts[6]. However, DH remains distinguished by its association with gluten sensitivity, typical distribution, and the pathognomonic granular IgA deposition in the papillary dermis on direct immunofluorescence, often accompanied by clinical response to a gluten-free diet[7-9]. Therefore, when EB and DH are both considered

in the differential diagnosis—or when patients with hereditary EB develop new pruritic vesicular eruptions—accurate differentiation requires integration of clinical history, histopathology, direct immunofluorescence on perilesional skin, relevant serology, and, when available, genetic testing. Overall, this case highlights the potential interface between hereditary and autoimmune bullous processes and underscores the importance of repeated immunopathologic evaluation if the clinical phenotype evolves.

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Received: Nov 19, 2025
Accepted: Jan 29, 2026