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Erythema With Nonscarring, Tense Blister Formation Without Circulating Anti-BP180 Antibodies

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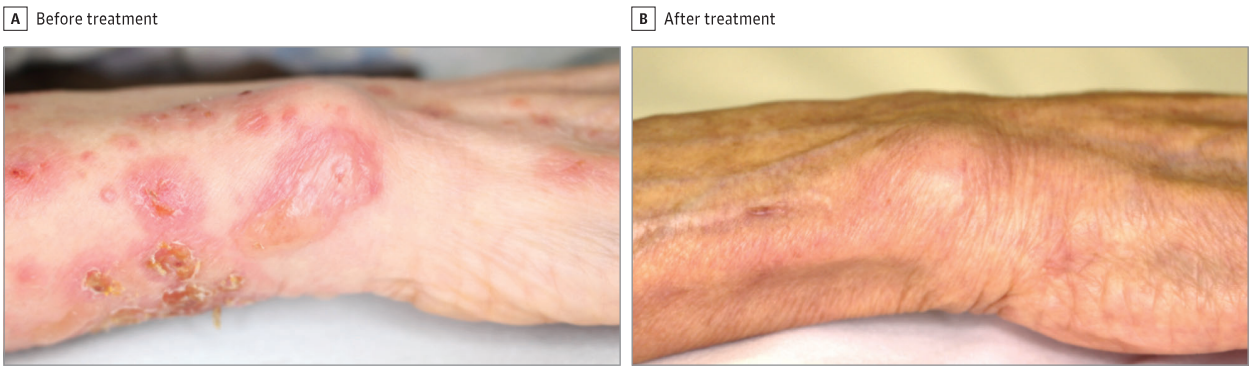

Figure 1. Clinical features before (A) and after (B) treatment with oral prednisolone, showing no scar formation.

A woman in her 80s presented with a 1-year history of pruritic erythema on the trunk and extremities. The erythema did not respond to topical corticosteroid, oral roxithromycin (300 mg/d), or narrowband UV-B phototherapy. The patient had a history of type 2 diabetes and hypertension and was treated with glimepiride, sitagliptin phosphate hydrate, and amlodipine besylate. The patient also had polymyalgia, which was treated with a low dose of prednisolone. The prednisolone therapy had been discontinued 2 months before her visit to the dermatology clinic when she had been hospitalized with pneumonia. Multiple tense blisters had subsequently appeared on the palms. Physical examination at the first visit revealed scaly erythematous plaques on the whole body and tense blisters on the arms, hands, soles, and buttocks. Neither scar formation or mucosal involvement was observed. A skin biopsy specimen was obtained from a bulla on the forearm. Histopathologic analysis revealed a subepidermal bulla with inflammatory infiltrates of neutrophils. The results of an IgG chemiluminescence enzyme immunoassay for bullous pemphigoid (BP) 180 noncollagenous (NC) 16A were negative. After treatment with oral prednisolone, 20 mg/d, the lesions healed without scar or milia formation (Figure 1).

WHAT IS YOUR DIAGNOSIS?

A. Bullous pemphigoid

B. Epidermolysis bullosa acquisita

C. Anti–laminin γ1 pemphigoid

D. Linear IgA dermatosis

Diagnosis

C. Anti-laminin γ1 pemphigoid

Microscopic Findings and Clinical Course

Direct immunofluorescence (IF) showed linear deposition of IgG and C3, but no IgA, at the basement membrane zone (BMZ). Indirect IF using 1 mol/L sodium chloride–split skin showed that the patient's IgG antibodies labeled the dermal side of the split (**Figure 2**A). Serum anti-type VII collagen IgG antibodies detected by human type VII collagen enzyme-linked immunosorbent assay were within normal range. Immunoblotting of purified human laminin 211/221 (CC085, Chemicon/Merck Millipore) identified anti-laminin γ1 IgG antibodies (Figure 2B). Prednisolone was tapered without relapse of skin lesions. One year after her initial treatment, the patient's condition was controlled with oral prednisolone, 7.5 mg/d.

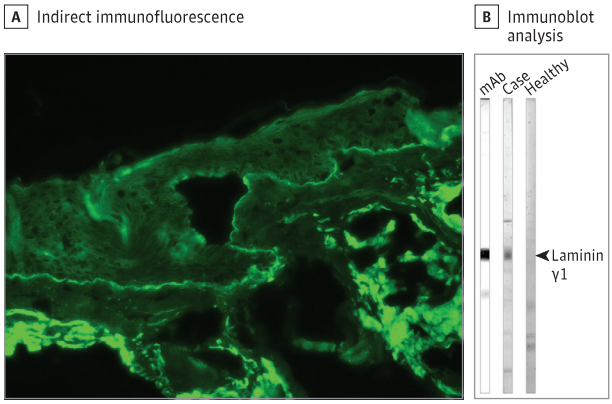

Figure 2. A, Indirect immunofluorescence using 1M sodium chloride–split skin showed reactivity of the patient's IgG antibodies to the dermal side of the basement membrane zone. B, Immunoblot analysis of purified human laminin 211/221. IgG antibodies against laminin γ1 were detected in the patient's serum but not in healthy control serum. mAb indicates mouse anti-human laminin γ1 monoclonal antibody (sc-13144, Santa Cruz Biotechnology).

Discussion

Anti-laminin γ1 pemphigoid is a rare subepidermal autoimmune blistering disease, characterized by circulating autoantibodies against a 200-kDa laminin γ1 protein at the dermal-epidermal junction. It was first described as anti-p200 pemphigoid in 1996[1,2]; in 2009, Dainichi et al[3] identified laminin γ1 as the autoantigen in 90% of cases and proposed a new name, anti-laminin γ1 pemphigoid.

The clinical presentation of anti-laminin γ1 pemphigoid can be like that of bullous pemphigoid and the inflammatory variant of epidermolysis bullosa acquisita. Most patients present with itchy urticarial plaques and tense blisters, often on the acral sites and extremities. Lesions usually heal without scar or milia formation[4] unless the disease is accompanied by other autoimmune bullous diseases that involve scar formation, such as epidermolysis bullosa acquisita or anti-laminin 332 mucous membrane pemphigoid.[5]

The diagnosis of anti-laminin γ1 pemphigoid is confirmed by histopathologic analysis, IF microscopy analyses, and detection of the specific autoantibodies. Histopathological examination shows subepidermal split formation and typically accumulation of neutrophils and/or eosinophils in the papillary dermis. Direct IF shows linear deposits of IgG and C3 along the BMZ. If serum autoantibodies bind to the dermal side of the artificial split by indirect IF microscopy on 1M sodium chloride–split skin, the differential diagnoses would include epidermolysis bullosa acquisita, anti-laminin 332 pemphigoid, and anti-laminin γ1 pemphigoid. In the present case, no circulating anti-type VII collagen IgG antibodies were detected. Anti-laminin 332 pemphigoid can usually be clinically differentiated from anti-laminin γ1 pemphigoid by the lack of mucosal lesions, although 20% of patients with anti-laminin γ1 pemphigoid develop them. The diagnosis of anti-laminin γ1 pemphigoid is definitive with detection of anti-laminin γ1 IgG antibodies by immunoblotting studies, or human laminin γ1 enzyme-linked immunosorbent assay.

The standard therapy for anti-laminin γ1 pemphigoid has not been defined. Most cases are successfully treated with mild or moderate immunosuppressive therapies such as oral corticosteroids, minocycline, dapsone, and cyclosporine.[4]

In summary, subepidermal bullous disease with circulating autoantibodies against the dermal side of the basement membrane zone and healing without scar formation are the key criteria supporting the diagnosis of anti-laminin γ1 pemphigoid. Anti-laminin γ1 pemphigoid should be considered in patients with subepidermal blister formation without anti-BP180 or type VII collagen antibodies and can be diagnosed by the detection of anti-laminin γ1 autoantibodies.

ARTICLE INFORMATION

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