A Case of Possible Concurrence of Dermatitis Herpetiformis and Linear Immunoglobulin A / Immunoglobulin G Bullous Dermatosis.

Dear Editor,

Linear immunoglobulin (Ig) A bullous dermatosis (LABD), one subtype of subepidermal autoimmune bullous skin diseases (AIBDs), is characterized by linear deposit of only IgA along the basement membrane zone (BMZ) on direct immunofluorescence (DIF) (1,2). Patients showing linear deposits of both IgA and IgG are diagnosed with linear IgA/IgG bullous dermatosis (LAGBD) (3,4). Dermatitis herpetiformis (DH) is another type of subepidermal AIBD characterized by clinically pruritic erythematous skin lesions with vesicles on the elbows, knees, and buttocks with granular IgA deposits of IgA by DIF (5). In this study, we report a Japanese case of a patient who showed possible concurrence of DH and LAGBD based on clinical, histological, and immunological findings.

A 72-year-old Japanese man who had a past history of dyslipidemia and resected lung cancer but was not taking any medicines, presented with a one-year history of blistering skin lesions. Physical examination revealed erythemas and peripherally arranged vesicles and erosions on the bilateral elbows, knees, and the buttock (Figure 1, a-c). Mucous membranes were not involved. The results of all laboratory tests were within normal ranges, except for increased serum IgA level 351 mg/dL (normal ranges; 46-260 mg/dL).

Skin biopsy histopathologically showed subepidermal blisters infiltrated with neutrophils and eosinophils (Figure 1, d). DIF showed deposits of IgG, IgA, and complement component 3 along the BMZ mainly in granular but partially in a linear pattern (Figure 1, e-g).

Circulating IgG (Figure 1, h) and IgA (Figure 1, i) autoantibodies were not detected by indirect immunofluorescence (IIF) of normal skin, however, circulating IgA (Figure 1, j) but not IgG (Figure 1, k) antibodies were bound to both the epidermal and dermal sides by IIF of 1M NaCl-split normal skin. Commercially available enzyme-linked immunosorbent assays (ELISAs) for BP180 NC16a domain, BP230, and type Vll collagen (MBL, Nagoya, Japan), showed negative results

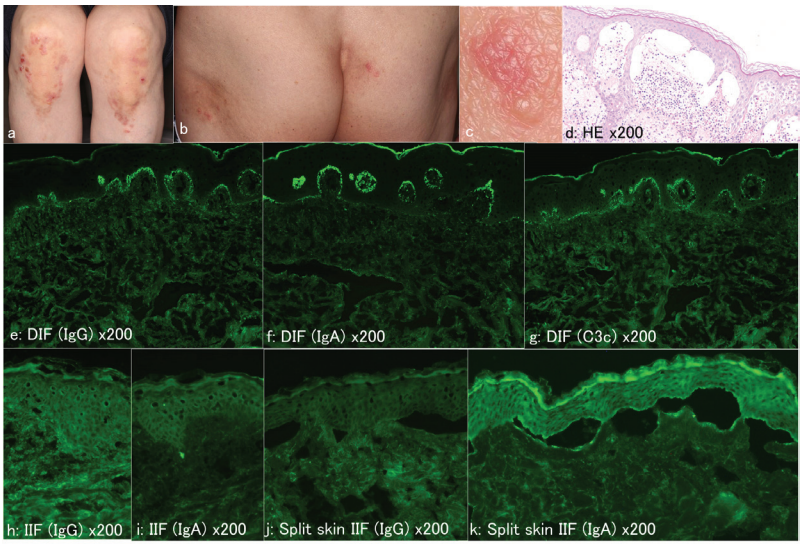

Figure 1. Clinical and histopathological manifestations and direct and indirect immunofluorescence results. (a-c) Clinical features of the skin lesions on the knee (a) and on the right buttock biopsy site (b, c). (d) Histopathological features of the skin biopsy. (e-g) Results of direct immunofluorescence for IgG (e), IgA (f), and complement component 3 (C3c) (g). (h, i) Results of indirect immunofluorescence of normal human skin for IgG (h) and IgA (i) antibodies. (j, k) Results of indirect immunofluorescence of 1M NaCl-split normal human skin for IgG (j) and IgA (k) antibodies.

for both IgG and IgA antibodies. IgG in-house ELISA for full length BP180 was also negative. IgG and IgA immunoblotting analyses of different antigen sources, including normal human epidermal and dermal extracts, recombinant proteins of NC16a, and C-terminal domains of BP180 region, BP230, purified laminin 332, and concentrated culture supernatant of HaCaT cells for LAD-1, were all negative. IgA ELISAs of tissue- and epidermal-transglutaminases were negative (1.92 AU/mL and 20.98 AU/mL, respectively; normal range <22.0 AU/mL). The patient was successfully treated with only topical corticosteroids with occasional mild local relapses.

Japanese DH is different from European DH in some respects, i.e., DH is very rare in Japan due to genetic/HLA difference, absence of celiac disease, and frequent fibrillar IgA deposition in DIF. Therefore, we believe that this case is interesting as a rare Japanese DH case with complicated conditions.

The clinical and immunochemical characteristics in the present case were compatible for both DH and LAGBD. Clinical features of vesicles on erythemas on the knees and buttock suggested DH, while histopathological features were compatible with LAGBD but also with DH, DIF results suggested both LAGBD and DH, and the results of IIF of 1M NaCl-split skin suggested LAGBD. All biochemical studies for autoantigens were negative, which suggested DH. However, autoantigens are not clearly detected in many LAGBD cases, either. IgA anti-epidermal transglutaminase antibody, a DH marker, was negative, but the titer was relatively high but within normal range.

Therefore, we considered that this case might have developed DH and LAGBD concurrently. However, there may be two other possibilities: [1] this case was DH and non-pathogenic circulating autoantibodies were secondary production, and [2] LAGBD cases may sometimes show granular-linear BMZ deposition of IgG and IgA. Future studies on similar cases are needed to clarify our speculations.

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