A Case of Linear IgA Bullous Dermatosis

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This paper deals with a case of linear IgA bullous dermatosis (LABD).

The patient was a 58-year-old woman who had multiple pruritic vesicles on the trunk, buttocks, thighs, tongue and buccal mucosa.

A biopsy of a lesion revealed subepidermal vesicles. Direct immunofluorescence examination of the perilesional skin showed a linear deposition of IgA along the basement membrane zone (BMZ). Indirect immunofluorescence examination, using NaCl split skin as substrate, showed antiBMZ IgA antibodies bound only to the epidermal side.

The skin lesions responded well to oral dapsone therapy.

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Key Words: Linear IgA bullous dermatosis

Linear IgA bullous dermatosis is a vesiculobullous eruption characterized in part by the presence of linear deposition of IgA at the basement membrane zone[1-6]. Although the pathogenesis of LABD is unknown, this disorder is believed to be autoantibody mediated[2].

Prior to the use of immunofluorescence techniques, both LABD and chronic bullous dermatosis of childhood (CBDC) were considered to be uncommon variants of dermatitis herpetiformis (DH) or bullous pemphigoid. However, further investigations of these diseases using immunofluorescence techniques and immunoelectronmicroscopy have strengthened the idea that they are distinct categories[1,5,7,8,9,10,11].

We report a case of LABD diagnosed by immunofluorescence study.

REPORT OF A CASE

A 58-year-old female patient visited Eulji General Hospital with intensely pruritic vesicles, crusted lesions and erythema measuring from match-head size to walnut size on the trunk, buttocks and thighs. She had had diabetes mellitus for 7 years and hypertension for 15 years, but they had been under control.

The skin lesions appeared on the trunk as vesicles on an erythematous base 25 days prior to her visit (Fig. 1). The number of the lesions gradually increased and spread over the buttocks and thighs, accompanied by severe itching. Owing to scratching, vesicles ruptured and crusts formed. Blisters were also observed on the tongue and buccal mucosa (Fig. 2). Other physical examinations were not remarkable.

A skin biopsy of an immature lesion showed subepidermal vesicles and inflammatory cell infiltrates composed chiefly of neutrophils and eosinophils (Fig. 3).

Direct immunofluorescence examination of the perilesional skin showed a linear deposition of IgA along the BMZ (Fig. 4). In indirect immunofluorescence examination, using human normal abdominal skin as substrate, which was incubated in 1M NaCl to induce separation of the tissue through the lamina lucida, IgA BMZ antibodies were shown to be bound only to the epidermal side of the lamina lucida (Fig. 5).

Laboratory findings were as follows: hemoglobin level, 10.3g/dl; hematocrit, 31%; white blood cell count, 8,000/m^3 with 62.5% neutrophils, 28.0% lymphocytes, 5.1% monocytes, 3.3% eosinophils, 1.1% basophils; ESR, 4mm/hr; methemoglobin

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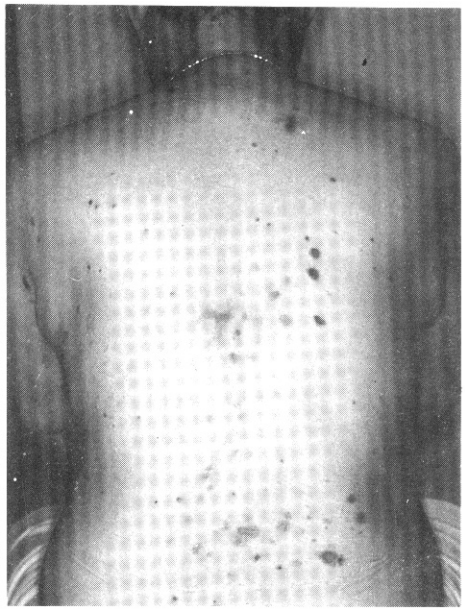

Fig. 1. Erythematous plaques and a few vesicles on the back.

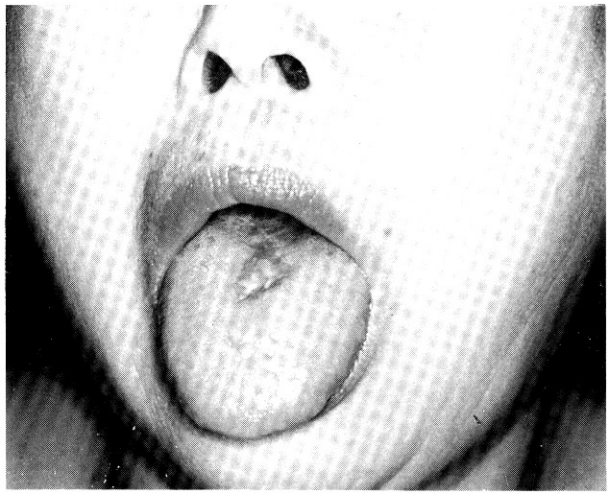

Fig. 2. Eroded patches on the tongue.

Fig. 3. Subepidermal bulla (H & E stain, ×40).

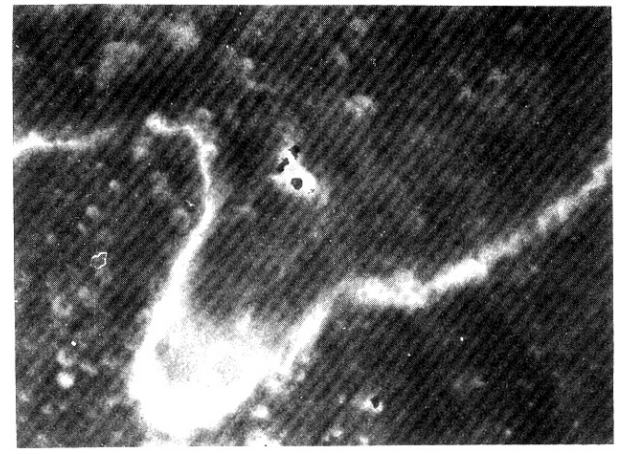

Fig. 4. Linear deposits of IgA along the basement membrane zone (DIF, ×200).

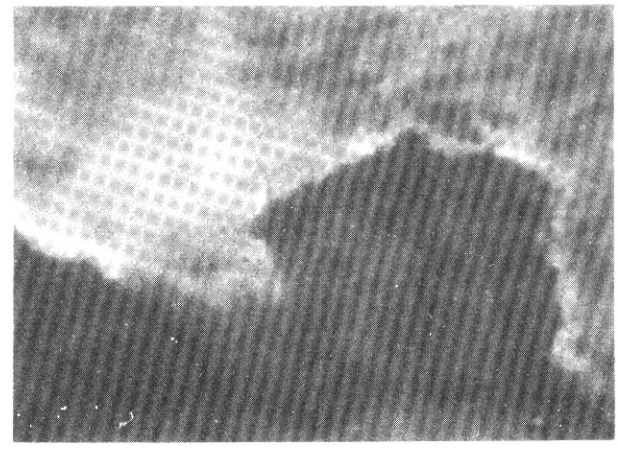

Fig. 5. IgA antiBMZ antibodies are seen to be bound only to the epidermal side (IIF: NaCl split skin substrate, ×200).

level, 0.1%; urinalysis, liver function test, serum protein electrophoresis, immunoglobulin quantitation, complement profile, rheumatoid factor, antithyroglobulin antibody, antimicrosome antibody, and antinuclear antibody were within normal limits or negative.

Theatment was initiated with dapsone 50mg/D, PO, and the dosage was gradually increased to 150mg/D, PO in 20 days. The skin lesions improved in 2 months. She has been almost free of the symptoms and signs for 1 year while receiving depsone therapy (50mg/D, PO) and no complication was observed.

DISCUSSION

LABD is a subepidermal blistering disease characterized in part by the presence of the linear deposition of IgA at the BMZ.

Tense vesicles, bullae or erythematous papules developed on the scalp, back, buttocks and extremities which resemble the lesions of DH or bullous pemphigoid. the sex ratio is equal and age at onset is usually over 40[1-6].

The pathogenesis Of LABD is unknown and this disorder is believed to be autoantibody mediated. Several authors reported cases of LABD in association with the administration of vancomycin, lithium, diclophenac or glibenclamide[2]. However, this case does not seem to be related with any antihypertensive agents or the antidiabetic agent she had taken because the lesions persisted even after she stopped taking the antihypertensive agents and antidiabetic agent at the onset of itching.

The role of IgA deposition in several inflammatory disease is not known. However, several studies suggest that IgA deposits in LABD and DH may contribute to the accumulation of neutrophils at the basement membrane and tips of dermal papillae respectively, by functioning as adherence ligands[3].

CBDC is also rare subepidermal blistering disease characterized by the linear deposition of IgA at the BMZ, clinically characterized by the predilection of the lesions for the pelvis, perineum and perioral sites in preschool children[1-6].

CBDC was initially considered a variant of DH. It has now been differentiated from DH by the lack of gluten-sensitive enteropathy and the lower incidence of HLA B8 among patients[1,5,6].

LABD and CBDC have immunologic differences. IgA autoantibody using conventional substrates in an indirect immunoflourescence method is found in the majority of sera from the patients with CBDC, but infrequently detected in those with LABD. When antibodies are detected, titers are generally low and do not correlate with disease activity[1,3,4].

There is also a difference in the immunogenetics. In patients with CBDC 75% are HLA B8 positive, whereas this serotype is of normal incidence or is only slightly raised in patients with LABD[1,5].

LABD can be distinguished from the other subepidermal blistering diseases: bullous pemphigoid (BP), cicatricial pemphigoid (CP), pemphigoid gestationis (PG), and epidermolysis bullosa acquisita (EBA) by the class of immunoreactant, the localization of the antibody binding site and the tissue distribution of the antigen. The presence of IgA autoantibodies is an unusual finding in bullous pemphigoid and if IgA autoantibodies are found, they always coexist with other immunoreactants or antibodies. Chorzelski et al[12] suggested that the absence of C_3 deposits and circulating anit-BMZ antibodies is important in differentiating LABD from bullous pemphigoid with linear IgA deposit. In addition, BP antigen is present in transitional as well as stratified squamous epithelia, wherease the LABD antigen is absent from transitional epithelia. Split-skin studies have demonstrated dermal as well as epidermal binding of antibodies in LABD/CBDC[7,8]. The majority of immunoelectron microscopy studies have shown a deposition of IgA in LABD/CBDC in the sublamina densa or a combined sublamina densa and lamina lucida pattern, whereas in BP, PG and CP, the binding is generally accepted within the lamina lucida and in DH it is accepted in the sublamina densa[7-11].

Immunoblotting and immunoprecipitation techniques have clearly defined the major bullous pemphigoid antigen as an epidermal glycoprotein of 220-240 kDa, which has recently been cloned and sequenced. A further 180 kDa epidermal antigen has been identified in BP and PG. The antigens in CP remain controversal. The EBA antigen has been identified as the carboxy terminal of type VII collagen in dermal extracts of human skin. The LABD/CBDC antigen is identical with a molecular weight of 285 kDa, detected only in dermal not in epidermal extracts of human skin, which accords well with the binding of these antisera to the sublamina densa on immunoelectron microscopy[1-9].

The patients with CBDC/LABD are ordinarily treated with dapsone or sulfapyridine[6], but Aram[13] reported a case in which hemolysis occurred with the use of dapsone and a switch to colchicine proved completely successful. Systemic

Table 1. Summary of the reported cases in Korea

Reference	Park et al. A case of CBDC KJD, 1981	Park et al. A Case of LABD KJD, 1986	Kim et al. LABD KJD. 1987	Lee et al. A case of CBDC KJD, 1988	Cho et al. A case of CBDC KJD, 1990	Yoon et al. A case of LABD KJD (suppl.), 1992	Present case
Age/Sex	12/M	29/M	32/M	8/M	3/M	58/F	58/F
Cutaneous lesions	vesicles & erythema	papulovesicles & hyperpigmented macules	erythematous maculopapules & vesicles	papules, vesicles & bullae	vesicles & bullae	vesicles, denuded or crusted patches	vesicles, denuded or crusted patches
Distribution	ear, face, hands, scapulae, wrists, knees, elbows, feet	back, buttocks, extensor surface of extremities	face, chest, buttocks, extremities	face, chest, buttocks, extremities	neck, trunk, pelvic region, extremities	trunk, head upper extremities	trunk, buttocks, thighs
Mucosal lesion	+	+	+	+	+	+ (oral mucosa)	+ (tongue & buccal mucosa)
Subepidermal bulla	+	+	+	+	+	+	+
DIF	linear IgA	linear IgA	linear IgA	linear IgA	linear IgA	linear IgA	linear IgA
IIF	Negative	ND	ND	ND	Negative	Negative	Positive (1:10), split skin subst.)
Tx & Course	dapsone, 150mg/D Excellent	depsone, 100mg/D Excellent	dapsone, 150mg/D Excellent	dapsone, 4mg/kg Excellent	dapsone, 2mg/kg Excellent	dapsone, 100mg Excellent	dapsone, 150mg Excellent

*CBDC: chronic bullous dermatosis of childhood
LABD: linear IgA bullous dermatosis
DIF: direct immunoflourescence
*IIF: indirect immunofluorescence
ND: not done
KJD: Korean Journal of Dermatology

corticosteroids are at times necessary and effective[6].

There have been seven cases of LABD/CBDC reported in Korea including the present case. Three cases are CBDC, and four cases are LABD. All CBDC patients are male and they are 3, 8, and 12 years old. In LABD patients, two of them are male and the remainder are female, the age of the patients being 29, 32, 58 and 58. All seven cases showed the deposition of linear IgA at the BMZ. Only the present case showed circulating IgA by indirect immunoflourescence examination. All patients showed a clinical response to the use of dapsone (Table 1)[14-19].

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