A Case of Epidermolysis Bullosa Acquisita

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We report a case of epidermolysis bullosa acquisita with characteristic clinical features, subepidermal vesicles in histopathology, and deposits of IgG in basement membrane zone at routine direct immunofluorescent test.

1M NaCl-treated immunofluorescent test was performed in order to correctly diagnose our case. In this method, linear immunofluorescent deposits of IgG were found only at the dermal part of separation induced by 1M NaCl treatment to skin specimen.

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Key Words: Epidermolysis bullosa acquisita, NaCl-treated immunofluorescent test

Epidermolysis bullosa acquisita(EBA) is an immunologically distinctive subepidermal blistering disease associated with IgG autoantibody to basement membrane of squamous epithelium. The characteristic clinical features include adult-onset, skin fragility, trauma-induced blisters, erosions and healing with scars. But in some cases, EBA closely resembles other subepidermal bullous diseases, especially bullous pemphigoid(BP)[1, 2], therefore it is misdiagnosed as other bullous diseases. Although immunoelectron microscopy and immunoblotting are credible techniques to differentiate EBA from BP, they are neither easily done nor widely available until nowdays. Recently, NaCl-treated immunofluorescent method was introduced to distinguish EBA from BP[3]. We performed this method to diagnose our patient as EBA.

REPORT OF A CASE

36-year-old man was referred to our dermatology department with a two-year history of pruritic, recurrent blistering eruptions and erosions on the abdomen, the tongue and both extremities. Most of skin lesions were developed after trauma, but some other lesions were developed spontaneously on erythematous or non-erythematous bases. The skin lesions were healed leaving transient scar but no milia developed (Fig. 1, 2, 3). His past and family history were non-contributory. Physical examination and laboratory tests, including complete blood count, urinalysis, blood chemistry, liver function test and chest PA, were negative or within normal limits.

Routine histopathology of perilesional skin showed normal epidermis, subepidermal vesicles and moderate dense infiltration of mononuclear cells around papillary vessels. Routine direct immunofluorescent (DIF) test of perilesional skin showed linear IgG deposits at the basement membrane zone (BMZ).

Under the impression of EBA from his clinical features, histopathologic findings and DIF result, we performed immunofluorescent test on NaCl-treated skin to distinguish our case from other bullous diseases, especially BP. When we used 1M Nacl-splitted neonatal foreskin as substrate for indirect immunofluorescent (IIF) test, the linear IgG was deposited only at the dermal part of separation (titers of 1:20, Fig. 4), and also, in DIF test with 1M Nacl-splitted patient's perilesional skin of abdomen, linear IgG was deposit-

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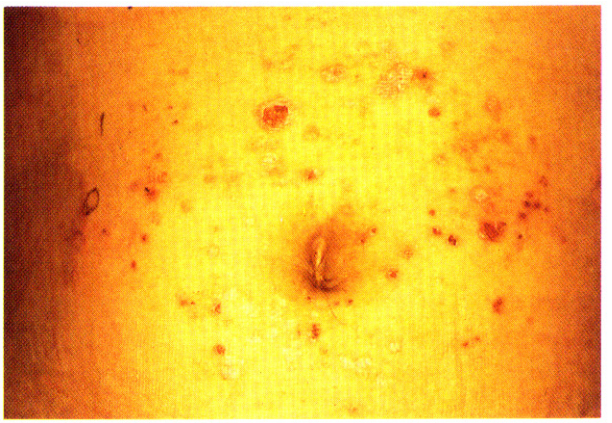

Fig. 1. Multiple skin erosions and transient healing scars on the periumbilical area.

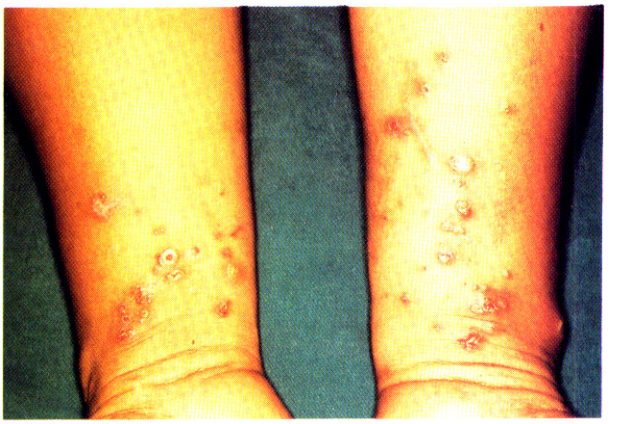

Fig. 2. Symmetrically distributed erythematous tense bullae and scars on the flexural suface of the both forearms.

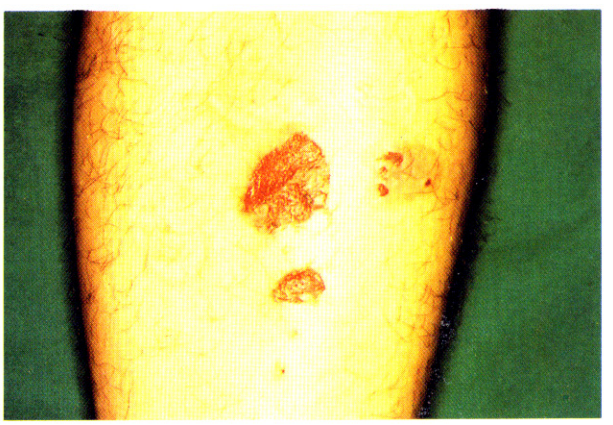

Fig. 3. Extreme skin fragility and erosion on the shin.

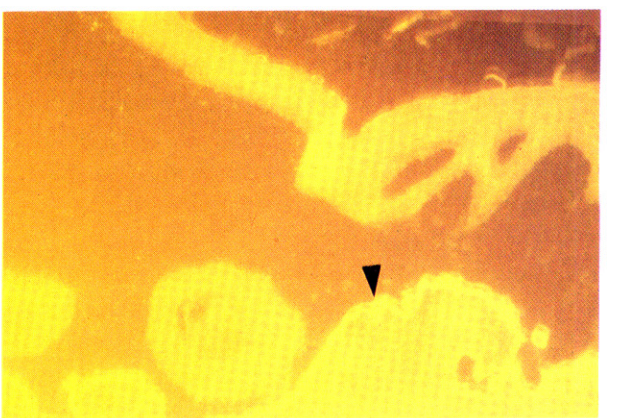

Fig. 4. The linear IgG deposit(▲) was seen only at the dermal part of separation in IIF test used NaCl-treated neonatal foreskin as substrate (×200).

Table 1. Summary of immunofluorescent results

	DIF	IIF
Routine method	BMZ	BMZ
NaCl-treated method	NPS: dermal part PPS: dermal part	foreskin: dermal part

BMZ: Basement membrane zone
NPS: Normal and non-lesional patient buttock skin
PPS: Patient perilesional skin

ed only at the dermal part of separation. In case of DIF with 1M NaCl-treated patient normal and non-lesional buttock skin, we could also find linear IgG deposits only at the dermal part of separation. The immunofluorescent results of our case were summarized in table 1.

We finally diagnosed him as EBA and treated with cyclosporine (2.5mg/kg/day) and intermittent triamcinolone acetonide (50mg) injection every 6-8 weeks. While low dose cyclosporine treatment was turned to be unsuccessful, triamcinolone injection brought about clinical improvement, but patient continued to have trauma induced erosions.

DISCUSSION

EBA is a rare but specific disease with distinc-

tive clinical and immunological features, which are sufficiently distinctive to enable EBA to be usually distinguished from other subepidermal bullous diseases. However, EBA and other subepidermal bullous diseases often have similar clinical and histologic features, so it can be misdiagnosed as other bullous diseases, especially BP. About 10% of the patients who had been diagnosed previously as having BP by clinical, histological and immunological criteria, were found to have actually[1] EBA and other study showed that incidence of EBA in patients with BMZ antibodies is 5%[4].

Recently, distinctive immunological features of EBA are characterized. EBA antigen is known to be the globular carboxyl terminus of type VII procollagen of basement membrane matrix protein[5]. In western immunoblotting of human BMZ protein extract, circulating anti-basement membrane autoantibodies in the sera of EBA bind to major 290 kD protein and minor 145 kD protein[6], while in BP, autoantibodies bind to major 230 kD and minor 160 kD BP antigen[7]. In immunoelectron microscopy, the immunoreactants are localized below the subbasal lamina anchoring fibril zone of basement membrane, thereby clearly distinguishing the immunopathology of EBA from that seen in BP (above lamina densa)[8]. Although these methods have been applied in order to distinguish EBA from BP, they are not easily done because they are expensive, technically demanding and need sophisticated apparatus. Recently, a simple and practical method was developed to diagnose EBA conveniently.

The treatment of 1M NaCl solution to normal skin specimen for 48 hours induces the separation of BMZ at the level of lamina lucida between BP antigen and laminin[9]. In this method, IIF test shows that circulating anti-BMZ IgG autoantibodies in BP and EBA bind the epidermal and dermal part, respectively[9, 10]. However, despite of its simplicity and reliability, this method has limitation to apply practically to all of these cases, because 20% and 50% of BP and EBA patients, respectively, do not possess circulating anti-BMZ antibodies. New alternative method was developed to improve availability for diagnosis of EBA and BP by Domloge-Hultsch et al.[3] and Gammon et al.[11] They performed DIF test with 1M NaCl-treated patient's normal perilesional skin. According to their reports, IgG was deposited only dermal part of separation in EBA, but in case of BP, the deposits of IgG were found at dermal, epidermal, or both sides, case by case. They also found that NaCl treatment appeared to increase the sensitivity of DIF microscopy.

In our case, IgG was found exclusively on the dermal part of NaCl-treated patient's perilesional abdominal skin in DIF test and circulating IgG anti-BMZ antibodies in the serum of patient bound also only at the dermal part of 1M NaCl-treated normal neonatal foreskin in IIF. These immunofluorescent findings were consistent with EBA. When we performed NaCl-treated another DIF test with patient's normal and non-lesional buttock skin, instead of patient's perilesional skin, we could find the same DIF results between two methods. This result is very unique finding, in that linear IgG is deposited only at the dermal part of separation in NaCl-treated DIF test with patient's normal and non-lesional skin as well as perilesional skin. The meaning of this finding should be further investigated. We also found that NaCl treatment increased the sensitivity of immunofluorescence. On routine IIF test, anti-basement membrane autoantibodies were positive at the titers of 1:10 while, on NaCl-treated IIF test, 1:20.

In conclusion, our patient showed clinical, histopathological and immunofluorescent findings of EBA. We suggest EBA can be diagnosed easily and practically with 1M NaCl-treated immunofluorescent test.

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