Case Report

Bullous Systemic Lupus Erythematosus Induced by UVB: Report a Case

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Bullous systemic lupus erythematosus (BSLE) is a rare blistering disease that dramatically responds to dapsone administration without leaving any scar. Generally, those patients with BSLE meet the criteria for systemic lupus erythematosus, but some have a widespread vesiculobullous eruption only as an initial manifestation without any specific clinical or laboratory findings that fulfill the American College of Rheumatology diagnostic criteria for SLE. The authors report here a middle-aged female patient, whose diagnosis of BSLE was suspected at first from the characteristic vesiculobullous eruption, histopathology, immunofluorescent pattern, and positive antinuclear antibody, who was later confirmed to have UVB photosensitivity that induced the typical skin lesions.

Keywords: *Bullous systemic lupus erythematosus, Phototest, UVB, Dapsone*

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Bullous systemic lupus erythematosus (BSLE) is a rare but distinct generalized blistering disease that presents widespread tense blisters, which show a dramatic clinical response to dapsone, subsiding without leaving any scar formation. Its histopathologic findings resemble those of dermatitis herpetiformis. However, its immunohistologic findings are composed of a linear, granular, or mixed linear and granular pattern of immunoglobulin (IgG, IgA, IgM) deposition along the basement membrane zone, whereas the circulating immunoglobulins bind the dermal side of salt-split normal human skin, which is further demonstrable to react with type VII collagen with Western immunoblotting and enzyme-linked immunosorbent assay. Generally, the clinical and laboratory findings in patients with BSLE meet the criteria for systemic lupus erythematosus, but some may exhibit only a widespread vesiculobullous eruptions as an initial manifestation without any clinical or laboratory findings fulfilling the American College of Rheumatology diagnostic criteria for SLE. The authors describe here a Thai middle-aged female patient presenting typical blistering lesions of BSLE, in whom we could produce successfully her characteristic skin lesions only with UVB irradiation test.

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Case Report

A 51-year-old Thai female presented with the abrupt onset of generalized non-pruritic blisters without any mucosal involvement. Physical examination revealed the presence of multiple tense bullae existing on the erythematous urticarial lesions that involved the trunk and upper extremities (Fig. 1A). Her previous history did not reveal any clear evidence of photosensitivity or any of such symptoms as arthritis, oral ulceration, fever, or recurrent episodes of the skin eruption suggesting the presence of underlying SLE. From her history of intake of amoxycillin and acyclovir just prior to the appearance of the skin lesions, the authors even suspected the possibility of overlapping erythema multiforme and toxic epidermal necrolysis. However, the biopsy specimen taken from the intact vesicle revealed a subepidermal blister with papillary neutrophilic microabscess formation compatible with the feature of dermatitis herpetiformis (DH). There was no evidence of basal vacuolar degeneration, basement membrane (BM) thickening, thinning of the epidermis or leukocytoclastic vasculitis. Direct immunofluorescence (DIF) at the perilesional skin revealed linear deposition of IgG,

IgA, IgM, and C3 at the basement membrane zone (BMZ). Indirect immunofluorescence (IIF) by using a salt split skin revealed the deposition of immunoglobulins at the dermal side (Fig. 2). FANA was positive, showing a speckled and nucleolar pattern at a titer 1:160. Other laboratory investigations revealed negative results for anti-DNA antibody, leucopenia, lymphopenia, or thrombocytopenia, and negative results for urinalysis, renal and liver function tests. The authors could not perform further immunoblotting or immunoelectron microscopic study because of the lack of the available facilities.

After her admission, the authors treated her initially with oral prednisone starting at 40 mg daily, which induced quick resolution of the lesions without leaving any scarring or milia formation after two weeks (Fig. 1B). Thereafter, she was discharged with a daily dose of prednisone 30 mg given as a home remedy. One week later when she was still on prednisone 30 mg per day, the authors conducted photo-testing. At 24-hour post-irradiation, her irradiated sites showed a decrease in MED for UVB (at 30 mJ/cm^2) and MPD for UVA (at 50 J/cm^2). However, none of the irradiated site of double-dose UVA (at 100 J/cm^2) or visible light induced neither blistering nor other abnormal reactions. By contrast, the blisters started to develop at the UVB irradiated sites at 50 mJ/cm^2 and higher doses (Fig. 3A, B). Moreover, after 48 hours the blistering reaction rapidly spread beyond the irradiated area marking (Fig. 3C). Eventually such new crops of blisters involved more than 10% of the body surface area (Fig. 3D). Therefore, the second provocative test of UVA was cancelled and the authors re-admitted her to the Institute of Dermatology, Bangkok.

The histopathological and immunopathological findings of the UVB-induced bullae showed the features similar to those of the original spontaneously developing bulla. Therefore, the authors confirmed that these bullae were reproducible with UVB irradiation. On her second hospitalization, dapsone 50 mg per day was added to her treatment. Thereafter, her skin lesions promptly improved, leaving erythematous patches. After seven days, she was discharged with home medication of dapsone 50 mg per day and prednisone 30 mg per day. Later, her prednisone dosage was gradually reduced successfully only with the dapsone intake and avoidance of sunlight exposure.

Discussion

The present patient with BSLE developed the typical blistering lesions, showing the characteristic

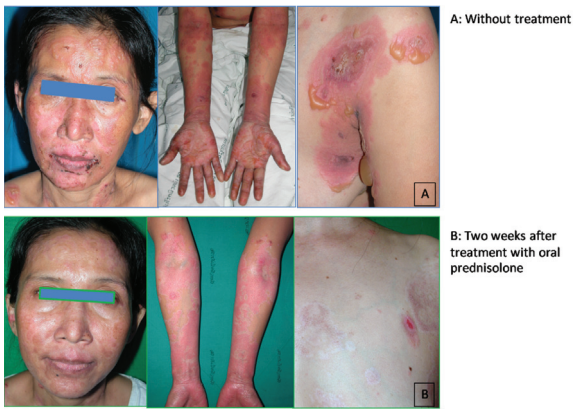

Fig. 1 Shows the clinical manifestation before and after being treated with oral steroid

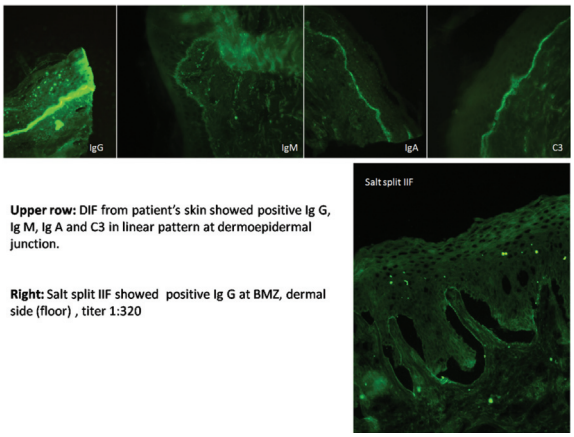

Fig. 2 Shows positive DIF staining on patient's skin and salt split skin IIF staining to patient's serum

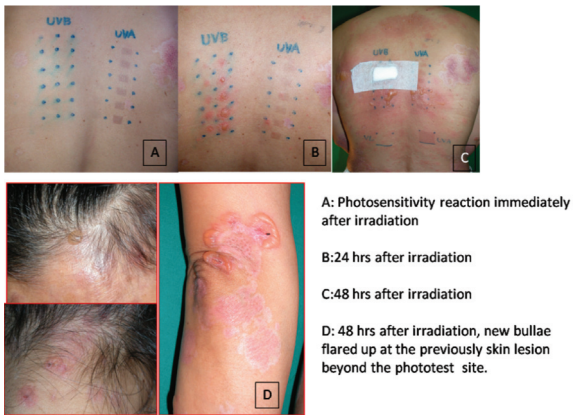

Fig. 3 Shows the photosensitivity reaction at the test site and that induced at the previously involved sites after a phototest immediately (A), 24 hours (B) and 48 hours (C) respectively

clinical, histopathologic, and immunopathologic findings, which were successfully treated with oral dapsone administration as reported before. It is of interest that the authors could reproduce her characteristic skin lesions artificially only with UVB irradiation that induced even wide development of the blistering lesions even in the neighboring non-irradiated skin areas.

Approximately 5% of patients with SLE develop such vesiculobullous lesions. They have been classified into three categories: 1) SLE with blisters due to severe vacuolar degeneration of the dermoepidermal junction, 2) BSLE due to autoantibody to type VII collagen and 3) SLE with primary blistering disease such as epidermolysis bullosa acquisita (EBA), bullous pemphigoid (BP), dermatitis herpetiformis (DH). According to the recent study from France[1], until now, approximately 70 cases with BSLE have been reported, or with the incidence of 0.2 per million revealed by.

The diagnostic criteria for BSLE have been first proposed by Camisa and Sharma (1983), and have been later revised after the introduction of split-skin immunofluorescence technique. Until now, there are five diagnostic criteria that the authors used for the diagnosis of the present case as shown below.

1. A diagnosis of SLE based upon American Rheumatism Association criteria.

2. Vesicles or bullae developing upon but not limited to sun-exposed skin.

3. Histopathologic features of the lesional skin compatible with subepidermal blisters containing predominantly a neutrophil infiltration, similar to that of DH or inflammatory EBA.

4. Negative or positive IIF for circulating BMZ antibodies using split–skin technique.

5. DIF of the lesional or non-lesional skin reveals linear or granular deposits of IgG and/or IgM and often IgA at the BMZ in case of the linear pattern deposition.

An immunoelectron microscopy should be done if available, in order to demonstrate the immune reactants below the basal lamina[2]. BSLE typically affect young adults in the second to fourth decade of life without any racial predilection. Thus, the presented patient a little bit older as that of BSLE. Women are found more often than men but this may reflects the general female preponderance of SLE. The clinical presentation of BSLE is characterized generally by an acute onset of a widespread eruption of tense blisters arising on clinically normal or inflamed skin. The eruption can appear at any sites, but the sun-exposed skin seems to be more often affected. Occasionally they tend to run a chronic course consisting of the periods of remission and exacerbation, without the development of fragile skin that leads to the development of mechanobullous lesions, scar and milia formation, characteristically observed in classical variant of EBA[3]. In addition to the blistering eruption, patients with BSLE may exhibit any of the symptoms of SLE especially lupus nephritis according to its activity. However, the onset and course of the cutaneous lesions do not necessarily parallel the onset and activity of the systemic involvement, as previously reported in a few cases of BSLE whose blistering eruption is an initial manifestation several months before the development of clinical and serologic features that fulfill the ACR criteria for SLE[4,5].

To the authors' knowledge, the results of phototest and photoprovocative test carried out in a BSLE patient have never been published before. In the presented patient, expecting that her skin would exhibit a photosensitivity feature as in other variants of cutaneous LE, the authors performed phototesting on the patient's uninvolved skin. As a result, the authors could demonstrate photosensitivity reaction to UVB, without any hypersensitivity to UVA or visible light. The patient showed a lowered MED than the normal range in Thais who have the same skin type as she has. To the authors' knowledge, there was only one report published on a case EBA with photosensitivity but it mentioned no specification of the wavelength[6]. Therefore, there has been no study on the wavelength that has succeeded in the production of the blistering eruption in BSLE patients except for the presented patient. The histopathologic feature of the early stage of the blisters in the presented patient showed sub-epidermal vesicle and papillary-tip neutrophil microabscesses, indistinguishable from those of DH. The authors found the deposition of immunoreactants along the BMZ, the most consistent immunopathologic feature in BSLE by DIF on the perilesional and clinically uninvolved skin together with complement. These deposits contained all major classes of immunoglobulins (Igs), IgG, IgA, and IgM. In BSLE, IgA is encountered more than twice as often than in the cases of SLE without blistering lesions, while IgM is detected in about a half of the patients. Complement components are frequently detected in biopsies from the skin lesions but much more rarely in clinically uninvolved skin. Like in most BSLE patients, the presented patient responded well to dapsone, which

Table 1. Comparison of the present case to inflammatory epidermolysis bullosa acquisita and bullous systemic lupus erythematosus[7]

Clinical	The present case	Bullous SLE
Cutaneous lesions	Generalized tense blisters	Generalized tense blisters
Mucous membranes involvement	No involvement	Rare
Scarring & milia	None	Rare (only one case report)
Photosensitivity	Yes (photosensitivity to UVB with abnormal MED & antinuclear antibody +ve)	Yes, not necessarily parallel the onset of blistering eruption
Histology	Subepidermal blister with papillary neutrophilic microabscess compatible with DH	Subepidermal blister mainly with neutrophil infiltration, similar to DH or inflammatory EBA
DIF	Linear deposit of IgG, IgA, IgM, C3 at the BMZ	40% linear, 60% granular deposit of IgG and/or IgM and often IgA at the BMZ
IIF on salt-split skin	Deposit of immunoglobulins on dermal side of salt-split skin	Same as inflammatory EBA
Response to dapsone	Good	Good

SLE = systemic lupus erythematosus; DIF = direct immunofluorescence; IIF = indirect immunofluorescence; DH = dermatitis herpetiformis; BMZ = basement membrane zone; EBA = epidermolysis bullosa acquisita

helped to differentiate BSLE from EBA especially its inflammatory subtype. Although the clinical and immunologic findings in the present patient did not fulfill the strict diagnostic criteria for SLE, the authors have been unable to rule out BSLE in the present case because there were many cases of the BSLE reported so far that initially presented only the skin lesions who subsequently began to develop the other features of SLE after a follow up period for a while. As the authors mentioned, similar to a reported case of EBA who also presented photosensitivity, a diagnosis of EBA might have been also a possible diagnosis for the presented patient. However, the presented patient revealed the photosensivity to UVB and positive FANA together with a good clinical response to dapsone, all of which are in favor of the diagnosis of BSLE. Here below, the authors presented the comparison of the clinical features and laboratory investigation data between the presented case and the most similar clinical entities, *i.e.*, the prototype of bullous SLE and inflammatory EBA (Table 1).

In conclusion, the authors reported here a unique case of bullous SLE who showed FANA positive and the blistering lesion exacerbated by UVB phototest. The skin lesion of the case responded well to a combination of oral prednisone and dapsone.

Potential conflicts of interest

None.

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รายงานผู้ป่วย: ผู้ป่วย bullous systemic lupus erythematosus ที่มีภาวะผิวหนังไวต่อแสง UVB

โปรดปราน ณ สงขลา, วลัยอร ปรัชญพฤทธิ์, Hachiro Tagami

Bullous systemic lupus erythematosus เป็นโรคที่พบน้อย ตอบสนองดีมากต่อการรักษาด้วย dapsone ไม่ทิ้งรอยแผลเป็นหลังการหาย โดยทั่วไปผู้ป่วยมักมีอาการอื่นตามเกณฑ์การวินิจฉัยโรค systemic lupus erythematosus ร่วมด้วย อย่างไรก็ตามผู้ป่วยบางรายอาจมาด้วยการมีตุ่มน้ำพองกระจายทั่วตัวเป็นอาการนำเพียงอย่างเดียวในช่วงแรกได้ ทำให้ยากต่อการวินิจฉัย ผู้นิพนธ์ได้รายงานผู้ป่วยหญิง อายุ 51 ปี ที่ได้รับการวิจฉัยเบื้องต้นว่าเป็น bullous systemic lupus erythematosus จากลักษณะตุ่มน้ำ ผลการตรวจทางพยาธิวิทยา อิมมูโนวิทยา ผลการตรวจความไวแสง รวมถึงการที่ผู้ป่วยตอบสนองอย่างรวดเร็วต่อการรักษาด้วย dapsone