

# A Case of Bullous Systemic Lupus Erythematosus: Clustered Tense Bullae Localized on the Face

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A 21-year-old woman, who had a one-year history of pancytopenia with histiocytic necrotizing lymphadenitis and hepatosplenomegaly, presented with a 5 day history of tense bullae, which were localized on the face. These clusters of tense bullae occurred on clinically normal skin, she did not have other skin lesions. A diagnosis of bullous systemic lupus erythematosus (BSLE) was established based on clinical, laboratory, histological, and immunological findings. The bullae showed good responses to dapsone (100mg, daily) and resolved within 10 days without scarring. Bullous lesions of SLE may be the first cutaneous manifestation in some patients with SLE and should be considered in the differential diagnosis of the other subepidermal bullous disorders. (*Ann Dermatol* 11(2) 82~85, 1999).

*Key Words* : Bullous systemic lupus erythematosus

## INTRODUCTION

Bullous systemic lupus erythematosus (BSLE) is a distinct clinicopathological entity<sup>1</sup>. A number of criteria have been suggested<sup>1,2</sup>: SLE meeting the criteria of the American Rheumatism Association (ARA)<sup>3</sup>, non-scarring blistering eruptions, subepidermal blisters with acute neutrophil-predominant inflammation in the upper dermis without any histological evidence of LE, immunoglobulin and complement deposition at the basement membrane zone (BMZ) on direct immunofluorescence (DIF), and immune deposits ultrastructurally localized on or beneath the lamina densa. A number of patients fulfilling these criteria have circulating antibodies to type VII collagen<sup>2,4</sup>.

We report a case of BSLE, the tense bullae of

which were localized on the face before any other cutaneous manifestations

## CASE REPORT

In October 1997, a 21-year-old woman was referred for a dermatologic consultation because of some tense bullae on both cheeks that had been present for with 5 days. She visited the department of internal medicine because of malaise and fever.

Her past history revealed that she had been admitted to the department of internal medicine because of fever and abdominal pain one year previously. At that time, a physical examination revealed that her liver was palpable at 2 finger breadths. The patient's leukocyte count, hemoglobin and hematocrit levels and platelet count were decreased to 1,500/mm<sup>3</sup>, 8.8 gm/dl, 25.0%, 98,000/mm<sup>3</sup> respectively. Typhoid O, H antibodies, antinuclear and anti-dsDNA antibodies, and rheumatic factors were negative. Her hematological diagnosis was pancytopenia with an infectious process based on the peripheral blood smear that showed pancytopenia, and toxic granula-

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**Fig. 1.** 0.5 × 0.5 cm-sized or smaller and 1 × 1.5-cm sized, yellowish fluid-filled, tense, clusters of bullae on both cheeks.

tion of neutrophils and the bone marrow aspiration that showed myeloid hyperplasia. Her Abdominal CT finding was hepatosplenomegaly and lymphadenopathy. Splenic lymph node and liver biopsies were taken and the results were suggestive of histiocytic (subacute) necrotizing lymphadenitis of unknown cause and previous toxic injury or an inflammatory process of the liver. She was discharged after conservative treatment with antibiotics and NSAID.

On physical examination, she had 0.5 X 0.5 cm-sized or smaller and 1.5 X 2.0-cm sized, multiple, yellowish fluid filled, tense, clusters of bullae on both cheeks (Fig. 1). Laboratory findings revealed a reduced leukocyte count, hemoglobin value and hematocrit level of 2500/mm<sup>3</sup>, 10 gm/dl, and 30.8%, respectively. Platelet, creatinine, urea, total protein, and blood glucose levels were normal. Nothing abnormal was detected on urinalysis. Antinuclear antibodies (ANA) were detected in the titer of 1:160 in a homogenous pattern. Anti-dsDNA antibodies were detected also in the concentration of 28.79 IU/ml. The C3 level was decreased to 21 mg/dL. Anti-platelet, smooth muscle, Ro and La antibodies were negative. A Histopathological examination showed a subepidermal blister with polymorphonuclear cells and

**Fig. 2. A:** A subepidermal blister, containing some inflammatory cells (H&E, × 200).

**B:** Inflammatory cells in blisters are composed of polymorphnuclears and eosinophils. (H&E, × 400).

**Fig. 3.** Indirect IgG immunofluorescent microscopy on 1.0 M NaCl-split skin using patient's serum showed a linear deposition of IgG on the dermal side of the split.

Deposits of IgG(ANA) the nuclei of keratinocytes are seen. (× 40).

eosinophils. An inflammatory infiltration was not prominent (Fig. 2). Direct immunofluorescence (DIF) of perilesional skin from the face showed homogenous linear deposits of IgG at the basement membrane zone (BMZ); DIF from non-sun-exposed normal skin demonstrated no immune deposits. Indirect immunofluorescent (IIF) microscopy on 1.0 M NaCl-split skin using serum from the patients revealed that a linear band of IgG was deposited on the dermal side of the split skin at a titer of 1:20; deposits of IgG on the nuclei of keratinocytes were also seen (Fig. 3).

An Administration of dapsone 100mg / day was

commenced in addition to prednisolone with a dose of 40mg / day. The blisters were resolved within 10 days without leaving any scars. After withdrawal of dapsone one month later, remission of the cutaneous lesions could be maintained with 10mg of prednisolone on alternative days.

## DISCUSSION

Seventy six percent of SLE patients will have skin changes at some stage in the course of the disease. Less than 5% of these patients will have chronic vesicobullous lesions<sup>4</sup>. The clinical features of blisters include widespread, non-scarring vesicles and / or bullae commonly arising upon sun exposed skin, although involvement of unexposed skin and mucosa is not uncommon. Blisters usually occur on preceding erythematous macules and plaques, but may occur on clinically normal skin<sup>1,2</sup>.

Gammon et al<sup>1,2</sup> have divided blisterings in systemic lupus erythematosus into three groups. Among them a specific subgroup of bullous systemic lupus erythematosus (BSLE)<sup>1</sup> have been defined on the base of a number of criteria. The criteria include 1) a diagnosis of SLE by ARA; 2) an acquired, non-scarring bullous eruption; 3) a subepidermal blister with acute neutrophilic-predominant inflammation in the dermis and at the BMZ and 4) IgG/IgA/IgM deposits in perilesional skin, and the Ig deposits must be on or beneath the lamina densa to exclude other primary subepidermal bullous diseases which have autoantibodies to hemidesmosomal or lamina lucida such as bullous pemphigoid, dermatitis herpetiformis, linear IgA dermatosis<sup>5,6</sup>. Gammon et al<sup>2</sup> also suggested a subdivision of BSLE into two types. Patients with circulating autoantibodies to type VII collagen, confirmed by IIF on 1.0 M NaCl split skin or immunoblotting / immunoprecipitation have been designated BSLE type 1. Patients fulfilling the criteria without autoantibodies to type VII collagen are BSLE type 2.

Our patient fulfilled four of those ARA criteria<sup>3</sup> for the diagnosis of SLE (positive findings of antinuclear antibodies, anti-ds-DNA antibodies, and hypocomplementemia, proteinuria, leukopenia and anemia on more than 2 occasions). In addition, she also covered the postulated criteria for BSLE type 1. A differential diagnosis with the

other subepidermal bullous diseases such as dermatitis herpetiformis, porphyria cutanea tarda, linear IgA dermatosis could be excluded by DIF<sup>5,6</sup>. The main differential diagnosis of BSLE is epidermolysis bullosa acquisita (EBA), because they share the characteristics of collagen VII autoimmunity<sup>10,12</sup>. In spite of these similarities, there are disease-specific clinical features. Epidermolysis bullosa acquisita shows a poor response to treatment, whereas a rapid improvement after dapsone therapy is often seen in patients with BSLE. The clinical features of our patient were in favor of BSLE.

We consider that our patient demonstrated some notable features. Firstly, the tense bullae occurred on clinically normal skin, and they were limited to both sides of the cheeks. Secondly, histologically, infiltration of inflammatory cells were not prominent. Thirdly, bullous lesions initially developed without other cutaneous manifestations. A precise diagnosis could be made after developing facial multiple bullae, since she had not fulfilled the ARA criteria on her first admission. It can be considered that facial blisters may be an early manifestation of BSLE.

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