

Case Reports

Bullous Systemic Lupus Erythematosus

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Abstract

Bullous systemic lupus erythematosus (BSLE) is extremely rare but distinct disease, characterized by vesicobullous skin eruptions in systemic lupus erythematosus (SLE). It can develop either before or after a diagnosis of SLE has been established. BSLE is characterized by a dermatitis herpetiformis-like histology and an autoimmunity to type VII collagen. It must be differentiated from other autoimmune vesicobullous diseases such as epidermolysis bullosa acquisita, dermatitis herpetiformis, linear IgA disease, and bullous pemphigoid. Its important to combine clinical, histological, and immunofluorescence findings to establish a diagnosis of BSLE. We report a case of BSLE to illustrate and emphasize the need for an integrative diagnostic approach.

Key words: Bullous systemic lupus erythematosus, systemic lupus erythematosus, autoimmune disease.

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Introduction:

Bullous systemic lupus erythematosus (BSLE) is a rare autoimmune blistering disorder that typically manifests as an acute vesicobullous eruption in a patient with known systemic lupus erythematosus (SLE). It is a rare but distinctive presentation of SLE occurring in less than 5% of lupus cases.¹ Single study conducted in 3 regions of France reported an incidence of 0.2 cases per million inhabitants.² Rarely; BSLE is the initial clinical manifestation of SLE. The differential diagnosis of blistering in patients with SLE is broad; careful assessment is necessary to confirm the diagnosis. The classic histologic and immunofluorescence findings of BSLE are separation within the dermal-epidermal junction, a neutrophilic infiltrate in the superficial dermis, immunoglobulin G (IgG) deposition at the dermal-epidermal junction, and antibody deposition on the dermal side of basement membrane zone-split skin. Anti-collagen VII

autoantibodies are the serologic marker of BSLE. A rapid response to Dapsone therapy is characteristic. Here, we present a case of BSLE to illustrate and emphasize the need for an integrative diagnostic approach, to include clinical, histological and immunofluorescence findings.

Case summary:

A 20 years old female, married presented with multiple painful non pruritic tense blister on her face, neck, front and back of the trunk, both upper & lower extremities. These lesions were eventually ruptured and healed up spontaneously without scarring leaving multiple hypopigmented & hyperpigmented patches (Figure 1). She also complained of oral ulceration but no difficulty in swallowing. Her parents and siblings have no similar disease. She has no history of trauma induced blistering. Photosensitive rash, joint pain or swelling was absent. She did not provide any history of drug exposure before appearance of rash. No history of rash before & after appearance of blister. Redness or ulceration on eye or in vagina, digital ulceration was absent. There was no preceding history of similar type of illness. Her menstruation was regular. She did not give any history of abortion & tampon use. She was anaemic. We found that blisters were tense with well-defined border having thick wall & erythematous base. Nikolsky sign was negative. All other systemic examination was unremarkable. Investigation revealed low Hb (7.2g/dl) with high ESR (84mm in 1st hour). WBC count showed only lymphopenia (463 cell/mm³). PBF revealed normocytic normochromic anaemia with lymphopenia. Her urinalysis, liver & renal function test were

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Figure 1: *Non pruritic tense blisters on different parts of body.*

normal. Her S. Ferritin was high (409ng/ml). ANA (9.9IU/ml) & Anti ds-DNA (33.9IU/ml) were strongly positive. However, her 24 hour UTP was normal (0.20 g/day). Chest X ray, ECG & USG of whole abdomen appeared normal. We performed skin biopsy from the lesion that showed sub-epidermal blister. The dermis shows mild perivascular infiltrates of chronic inflammatory cell. Direct Immunofluorescence (DIF) of cryostat section showed linear deposition of IgG (+) and C3 (trace) along the dermo-epidermal junction. No deposition of IgA, IgM or fibrinogen is seen. However, Indirect Immunofluorescence with salt slit skin smear was not done due to unavailability. As initial therapy we maintained adequate hydration followed by high dose Prednisolone (80mg/day), Hydroxychloroquine (400 mg/day), Azathioprine (100 mg/day). As blister appeared persistently we add Dapsone (50mg/day) that made striking response.

Discussion:

In 1973, Pedro and Dahl³ described the first case of BSLE. After this, several cases with similar characteristics were reported. BSLE patients produce autoantibodies that recognize type VII collagen, a major component of anchoring fibrils, which play an important role in dermo-epidermal adhesion. Chan and colleagues⁴ identified further autoantibodies reacting to multiple basement membrane components including bullous pemphigoid antigen 1, laminin-5 and laminin-6 in patients with BSLE. This hyper-immune state seems to be associated with the gene for major histocompatibility complex HLA-DR2.³ Patients with SLE rarely (in less than 1%) develop widespread vesicobullous eruptions that cannot be classified as either of the primary bullous dermatoses and are not merely a manifestation of extreme basal cell hydropic degeneration and the resulting epidermal-dermal separation. In such cases, it is referred to

as BSLE, a unique dermatosis that is regarded as a distinct variant of SLE.⁵⁻⁷ Similarly to SLE, BSLE most often affects young patients, predominantly female, in the second to fourth decades of life. Although any sun-exposed or non-sun-exposed areas can be affected, the upper trunk, neck, supraclavicular areas, and proximal extremities are predilection sites.^{5,6} The skin eruption comprises bullae arising either from areas affected by diffuse erythema or on an urticarial base resembling bullous pemphigoid, or as grouped vesicular lesions mimicking dermatitis herpetiformis.^{6,7} The onset of vesicobullous cutaneous lesions can precede, coincide with, or follow the diagnosis of SLE, as defined by the revised American Rheumatism Association criteria for classification of SLE.^{3,7} Camisa & Sharma⁸ proposed criteria for the diagnosis of bullous SLE, as follows: (a) a diagnosis of SLE by criteria of the American Rheumatism Association, (b) a wide spread, non-scarring vesicobullous eruption, (c) a sub epidermal blister with dermal inflammation characterized by neutrophilic papillary micro abscess like those seen in dermatitis herpetiformis, (d) negative indirect IF for circulating basement membrane zone antibodies (later, they suggested that the criteria be modified to include: negative or positive indirect IF for circulating basement membrane zone antibodies using separated human skin as substrate), (e) direct IF of lesional & non lesional skin always reveals linear or granular IgG and/or IgM or often BMZ antibodies.

Our patient satisfied most of these criteria like oral ulcer, alopecia, strongly positive ANA & Anti dsDNA. Bullous SLE may be confused with bullous pemphigoid, Epidermolysis bullosa acquisita, dermatitis herpetiformis or linear IgA dermatitis. In our patient her blister was not associated with trauma or rash; that is compatible with BSLE

rather Epidermolysis bullosa acquisita, dermatitis herpetiformis. Direct IF may be helpful to exclude dermatitis herpetiformis & linear IgA dermatitis.³ Direct IF of our patient showed no granular IgA deposition & linear IgA deposits concomitant with linear IgG & C3 at the dermo epidermal junction. This finding is in favour of Bullous SLE compared with dermatitis herpetiformis & linear IgA dermatitis. Bullous pemphigoid antibody binds the roof of split skin whereas the binding is observed at the base of the split skin in Bullous SLE.⁹ By using 1M NaCl split skin as a substrate for indirect IF, it is possible to distinguish between bullous pemphigoid & bullous SLE.¹⁰ However; we could not perform Indirect IF due to technical difficulty & unavailability.

Conclusion:

BSLE responds well to treatment with Dapsone, which differs from EBA. In cases that do not respond to Dapsone, the use of Prednisone and Azathioprine is suggested. BSLE may regress completely and independently of systemic involvement without recurrence.

Conflict of interest: None.

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