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Bullous SLE with varied presentation- A Case Series

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Abstract

Bullous systemic lupus erythematosus (BSLE) is a rare autoimmune blistering disorder associated with systemic lupus erythematosus (SLE), characterized by subepidermal bullae. In this study, we analyzed four cases of BSLE in female patients aged 19–56 years, with SLE durations ranging from 1 month to 2 years. Bullous lesions predominantly involved the trunk and extremities, presenting either initially or during the course of SLE. Cutaneous manifestations included non-scarring alopecia, palatal ulcers, and diverse lupus-specific rashes (ACLE, DLE, and SCLE). Systemic features varied, including lupus nephritis (class IV), neuropsychiatric SLE (NPSLE), pancytopenia, and macrophage activation syndrome (MAS). All cases showed high ANA titers, positive anti-dsDNA, and low complement levels. Treatment involved corticosteroids, hydroxychloroquine, and additional immunosuppressants like cyclophosphamide or mycophenolate mofetil. BSLE highlights the importance of recognizing its clinical spectrum, as timely intervention is crucial to manage associated systemic complications effectively.

Key Words: American College of Rheumatology, Bullous systemic lupus erythematosus, Direct immunofluorescence

Introduction

Bullous systemic lupus erythematosus (BSLE) is a rare autoimmune blistering disorder occurring in association with systemic lupus erythematosus (SLE). It is characterized by subepidermal blisters and typically presents

after the diagnosis of SLE, though it may serve as the initial manifestation in approximately 30% of cases[1]. The bullae in BSLE usually develop on normal or erythematous skin and predominantly affect sun-exposed areas such as the face, neck, and upper extremities[1]. Mucosal involvement, though less frequent, can also be seen[2]. Importantly, these lesions typically heal without leaving scars.

The diagnosis of BSLE is based on the American College of Rheumatology (ACR) criteria, which encompass clinical, histopathological, and immunological features. These criteria include:

1. Vesicles and bullae appearing on or near sun-exposed skin.
2. Histopathology resembling dermatitis herpetiformis, characterized by subepidermal blistering and a dermal neutrophilic infiltrate, often concentrated at the papillary tips[3].
3. Direct immunofluorescence (DIF) showing deposits of immunoglobulins (IgG, IgA, and IgM) and complement components at the basement membrane zone (BMZ), in either a linear, granular, or mixed pattern[4].
4. Negative or positive indirect immunofluorescence (IIF) for circulating BMZ autoantibodies[2].

The classical histopathological hallmark of BSLE is subepidermal blistering with a predominance of neutrophils, particularly at the dermal papillary tips[3]. The immunopathological features of BSLE include immunoglobulin and complement deposition at the dermo-epidermal junction, as demonstrated by DIF[4]. While circulating autoantibodies targeting BMZ components such as type VII collagen are reported in some cases, they are not universally present[2].

BSLE is closely associated with high disease activity in SLE. Diagnostic criteria for SLE, including those defined by the Systemic Lupus International Collaborating Centre, form the foundation for identifying underlying systemic lupus[5]. Key serological markers such as ANA (≥1:320), anti-dsDNA, and anti-Sm antibodies are often elevated in BSLE patients, with frequencies of 90%, 60%, and 30%, respectively[3]. Additionally, laboratory findings such as proteinuria, low complement levels, elevated erythrocyte sedimentation rate (ESR), and hematological abnormalities are commonly observed.

Blistering in BSLE often correlates with systemic involvement, particularly lupus nephritis (commonly class III/IV) and hematological abnormalities[3]. While BSLE lesions are typically monophasic, rare cases of recurrence have been documented. Prompt recognition of BSLE, along with evaluation for systemic involvement, is critical to guide appropriate management and prevent complications.

Results

The clinical presentation and course of four cases of bullous systemic lupus erythematosus (BSLE) highlight its diverse manifestations and systemic involvement. All patients were female, aged 19 to 56 years, with varying SLE durations ranging from 1 month to 2 years. Bullous lesions were distributed across the neck, trunk, and extremities, presenting either as the initial manifestation or after the diagnosis of SLE. Non-scarring alopecia, palatal ulcers, and various cutaneous lupus features, including acute cutaneous lupus erythematosus (ACLE), discoid lupus erythematosus (DLE), and subacute cutaneous lupus erythematosus (SCLE), were observed. Systemic involvement included lupus nephritis (LN, class IV), constitutional symptoms, serositis, and hematological abnormalities, such as pancytopenia and macrophage activation syndrome (MAS). One case exhibited neuropsychiatric SLE (NPSLE) with psychosis. All cases had elevated antinuclear antibodies (ANA, 1:320), positive anti-dsDNA, and reduced complement levels (C3, C4). SLE disease activity index (SLEDAI-2K) scores ranged from 17 to 25. Treatment involved corticosteroids and hydroxychloroquine in all patients, with immunosuppressants like cyclophosphamide, mycophenolate mofetil, or tacrolimus used in select cases

based on disease severity and organ involvement. This emphasizes the importance of early diagnosis and tailored management in BSLE. (Table 1)

Table 1

Case Details	**Case 1**	**Case 2**	**Case 3**	**Case 4**
Age & Sex	19 y/F	56 y/F	37 y/F	39 y/F
SLE Duration	1 month	1 year	2 years	2 years
Bullous skin presentation & distribution	Initial Neck & Trunk Extremities	6 months after SLE diagnosis Trunk Extremities	1 year after SLE diagnosis Trunk Extremities	Initial Trunk Extremities
Other Cutaneous features	Non-scarring alopecia Palatal ulcer ACLE & SCLE	Non scarring alopecia Palatal ulcer ACLE & DLE	Non-scarring alopecia Palatal ulcer ACLE, DLE & SCLE	Non-scarring alopecia Palatal ulcer DLE
Other organ involvement	**Case 1**	**Case 2**	**Case 3**	**Case 4**
Constitutional	+	+	+	+
Polyarthritis	+	+	+	+
Serositis	+	+	_	+
Haematological	+	_ (Occult MAS) Pancytopenia ↑Ferritin	+	+
Lupus nephritis	LN class 4	_		_
NPSLE	_	_	NPSLE (psychosis)	_
ESR/CRP	75/6.8	109/1.9	60/1.3	110/18
ANA (IF)	3+,1:320, nucleus homogenous	3+,1:320, nucleus speckled	3+,1:320, nucleus speckled	3+,1:320, nucleus Speckled

LIA	Sm 3+ Nucleosome 2+	Rnp/Sm 3+ SS-A 3+	Sm 3+ RNP/Sm+	Sm 3+ dsDNA +
DCT	+	+	+	+
C3, C4 (mg/dl)	20,10	62,10	80,10	73,6
AntidsDNA (E) IU/ml	800	374	200	430
SLEDAI 2k	25	19	23	17
Treatment Steroids	**Case 1**	**Case 2**	**Case 3**	**Case 4**
Steroids	+	+	+	+
Hydroxychloroquine	+	+	+	+
Cyclophosphamide	+	_	+	_
Mycophenolate mofetil	_	+	_	+
Tacrolimus	_	_	_	+

FIG 1: Subepidermal bulla with bullous space containing RBCs and inflammatory cells, perivascular infiltrate in the upper dermis

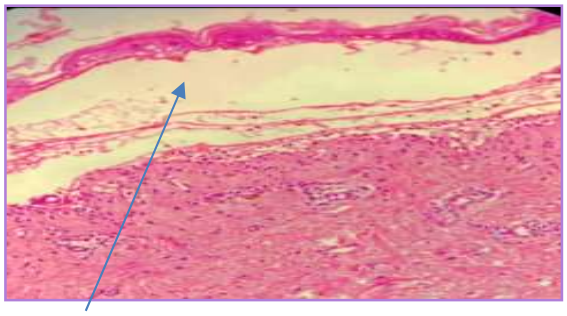

FIG 2: Bullous lesion present on extremities

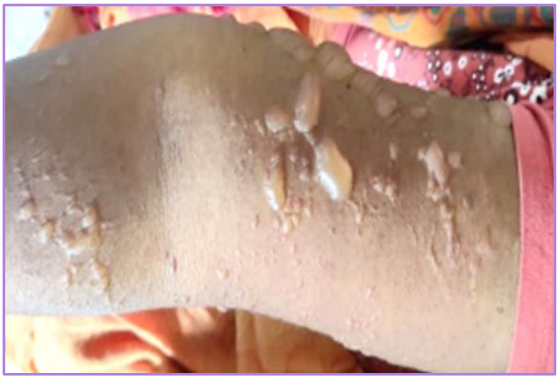

FIG 3: Bullous lesion present on extremities

FIG 4: Bullous lesion present on the dorsum Of the hand

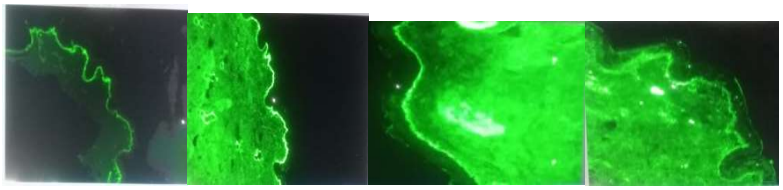

FIG 5: IgM, G, A, C3 positivity at Dermo-epidermal junction

Discussion

In our study, we discuss four cases of bullous SLE. These patients presented with bullous skin lesions and different systemic involvement. All cases were female. Three were in the second to fourth decade of life. One was presented in early adolescence. Chanprapaph et al concluded that BSLE was common in females, presenting at a young age[3].

In our study all cases presented with BSLE after SLE diagnosis which was similar to the study conducted by Chanprapaph et al. Vesiculobullous lesions were generalized in our all cases. The common sites seen in bullous SLE in our study were the trunk, extremities and neck comparable to the study conducted by Chanprapaph et al.

Histopathologically all four cases satisfied bullous SLE criteria. Indirect immunofluorescence staining for circulating BMZ autoantibodies for type VII collagen in all cases was negative in our study. Lin Qiao et al revealed that anti-BMZ autoantibodies were found in 66% [2].

The most common skin lesions apart from bullous in our study were ACLE and DLE followed by SCLE. All patients had constitutional features (fever, fatigue), haematological involvement (DCT positive), serositis and polyarthritis comparable to those conducted by Chanprapaph et al[3]. One patient was diagnosed with lupus nephritis (LN) class IV and another patient with macrophage activation syndrome. One had a history of neuropsychiatric SLE manifestation in the form of psychosis. Tullia et al concluded that mostly LN class III/IV was reported in 50% of BSLE patients and 7% had neuropsychiatric SLE. [6]

All cases had raised acute phase reactants in our study similar to the study conducted by Tullia et al. All cases had raised disease activity (low C3, C4, raised anti-ds DNA) and elevated SLEDAI-2k comparable to Tullia et al[6].

In our study, all had ANA with high titre positivity to the study conducted by Chanprapaph et al[3]. Line immune assay showed Smith positivity in all cases in our study, two had anti-RNP positive. Similarly, Chanprapaph et al commented that the most common antibody seen in BSLE was anti Sm, anti RNP followed by SS-A[3].

All cases received steroids and Hydroxychloroquine. Two patients were pulsed with Cyclophosphamide (LN, NPSLE). One patient with MAS was treated with Mycophenolate mofetil. One received Mycophenolate mofetil in addition to tacrolimus. Chanprapaph et al[3] concluded that systemic corticosteroids, immunosuppressants, antimalarials and dapsone offered a resolution of cutaneous lesions[3]. Dapsone was contraindicated in our cases due to direct Coombs positivity. There was no relapse in our study.

Patients presenting with vesiculobullous skin lesions should have a high index of suspicion for bullous SLE. Systemic involvement needs to be evaluated in cases of BSLE to prevent complications. BSLE is a marker of high disease activity.

Conclusion

Bullous systemic lupus erythematosus (BSLE) is a rare SLE association characterised by vesiculobullous skin lesions and significant systemic involvement, often reflecting high disease activity. In our study, all cases demonstrated multi-organ involvement, including lupus nephritis, neuropsychiatric lupus, and macrophage activation syndrome, with constitutional symptoms, hematological abnormalities, and high disease activity markers. Prompt diagnosis and treatment with corticosteroids, hydroxychloroquine, and immunosuppressants resulted in favorable outcomes, with no relapses observed. This highlights the importance of recognizing BSLE as a marker of severe disease activity and ensuring comprehensive systemic evaluation and timely intervention to mitigate complications.

References

1. Rutnin S, Chanprapaph K. Vesiculobullous diseases in relation to lupus erythematosus. *Clin Cosmet Investig Dermatol.* 2019; 12:653-667.
2. Qiao L, Zhang B, Zheng W, et al. Clusters of clinical and immunologic features in patients with bullous systemic lupus erythematosus: experience from a single-center cohort study in China. *Orphanet J Rare Dis.* 2022;17(1):290.
3. Chanprapaph K, Sawatwarakul S, Vachiramon V. A 12-year retrospective review of bullous systemic lupus erythematosus in cutaneous and systemic lupus erythematosus patients. *Lupus.* 2017;26(12):1278-1284.
4. Vassileva S. Bullous systemic lupus erythematosus. *Clin Dermatol.* 2004;22(2):129-138.
5. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum.* 1997;40(9):1725.
6. de Risi-Pugliese T, Cohen Aubart F, Haroche J, et al. Clinical, histological, immunological presentations and outcomes of bullous systemic lupus erythematosus: 10 New cases and a literature review of 118 cases. *Semin Arthritis Rheum.* 2018;48(1):83-89.