This open-access article is distributed under Creative Commons licence CC-BY-NC 4.0.

Refractory bullous systemic lupus erythematosus in a 14-year-old girl successfully treated with low-dose rituximab: A case report

N K P Sari,[1] MD; **M Fitriah,**[2] MD; **N K Mulyantari,**[3] MD, PhD

[1] *Clinical Pathology Sub-Specialisation Programme, Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo Hospital, Surabaya, Indonesia*
[2] *Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo Hospital, Surabaya, Indonesia*
[3] *Department of Clinical Pathology, Faculty of Medicine, Udayana University, Indonesia; Prof. IGNG Ngoerah General Hospital, Denpasar-Bali, Indonesia*

Corresponding author: *M Fitriah (fitriah.munawaroh@gmail.com)*

Background. Bullous systemic lupus erythematosus (BSLE) is a rare vesiculobullous manifestation of systemic lupus erythematosus and is uncommon in paediatric patients.
Case presentation. A 14-year-old girl presented with pruritic vesiculobullous lesions involving the lips, neck, trunk, axillae and groin, accompanied by oral ulcers. Laboratory tests showed leukopenia, anaemia, elevated transaminases, low complement C3 and a high-titre antinuclear antibody (1:10 000). Histopathology revealed a subepidermal blister, and direct immunofluorescence demonstrated linear deposition of IgG, IgA, C3 and C1q along the dermoepidermal junction, confirming BSLE. After inadequate response to initial therapy, low-dose rituximab (100 mg) was administered, resulting in marked clinical improvement.
Discussion. Low-dose rituximab may provide effective disease control in refractory paediatric BSLE when conventional therapy is insufficient.
Conclusion. Low-dose rituximab can be considered an alternative therapeutic option for refractory paediatric BSLE.

Keywords: systemic lupus erythematosus, bullous, autoimmune, rituximab, blisters

S Afr J Child Health 2026;20(2):e4594. https://doi.org/10.7196/SAJCH.2026.v20i2.4594

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterised by multisystem involvement, with cutaneous manifestations occurring in approximately 72 - 85% of patients.[1,2] Among these manifestations, vesiculobullous eruptions known as bullous systemic lupus erythematosus (BSLE) are rare and account for <1% of SLE cases.[3,4] BSLE is characterised by the rapid development of tense subepidermal blisters that may arise on erythematous or normal-appearing skin and are frequently distributed on sun-exposed areas.[2,3]

BSLE predominantly affects young adult women and is rarely reported in paediatric populations, making early recognition and appropriate management challenging.[1,2] Although conventional therapies such as systemic corticosteroids, immunosuppressants, and dapsone are commonly used, refractory cases requiring alternative therapeutic approaches may occur.[3,5]

Here, we report a paediatric case of refractory BSLE successfully treated with low-dose rituximab, highlighting its potential role as an alternative therapeutic option.

Case presentation

A 14-year-old female patient presented to the hospital with complaints of redness and fluid-filled blisters on the lips, lower abdomen, neck, axillae, bilateral groin, calves and palms. The symptoms began with oral ulceration resembling aphthous stomatitis on the lips, which appeared 4 days prior to admission. On the following day, the patient developed erythematous patches and bullae on the lips, which gradually spread to the neck, trunk, groin and axillary folds. These lesions were accompanied by chills, pain and persistent pruritus, significantly disrupting sleep. The patient also reported bilateral eyelid swelling, beginning 1 week prior to admission, and facial erythema, particularly on the cheeks, which had been present for approximately 2 weeks. Additionally, she experienced hair loss over the previous 3 months, and a reduced appetite and fluid intake since the onset of oral lesions. Lesion location can be seen on Fig. 1.

Physical examination

On physical examination, the patient appeared mildly pale with positive alopecia characterised by easily pluckable hair. No jaundice was observed and vital signs were within normal limits. Anthropometric assessment showed a body weight of 75 kg and a height of 160 cm, resulting in a body mass index of 29.3 kg/m^2, consistent with overweight status. The waist-to-height ratio was 1.81 and the calculated ideal body weight was 51.4 kg.



Fig. 1. Lesion location.

Dermatological examination revealed multiple vesicles and bullae involving the lips, neck, axillae, inguinal region and left eyelid. The lesions were round to oval in shape with diameters ranging from 0.5 cm to 1.2 cm. The blisters had tense walls filled with serous fluid and were generally distributed on an erythematous background without crusting or purulent discharge.

Additional cutaneous findings included multiple urticarial lesions located over the anterior and posterior thoracoabdominal regions, bilateral lower legs and left thigh. These lesions were sharply demarcated, geographical in configuration, measured approximately 0.7 cm to 1 cm in diameter, and were discretely distributed in a generalised pattern.

Laboratory examination

Complete blood count revealed leukopenia with a white blood cell count of 2.93 × 10^3/µL (reference range 4.0 to 10.0 × 10^3/µL), anaemia with haemoglobin level of 11.8 g/dL (reference range 12.0 to 16.0 g/dL), and an elevated erythrocyte sedimentation rate of 67 mm/hour (reference range <20 mm/hour), suggesting an ongoing inflammatory process.

Parameter	Titer	Pattern	Reference
ANA-IF	1:10.000	*Fine speckled*	Negative

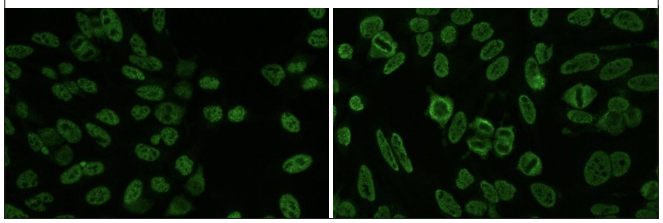


Fig. 2. Antinuclear antibody testing (ANA-IF) using HEp-2 cell indirect immunofluorescence assay showing a fine speckled pattern at an endpoint titre of 1:10 000 (laboratory reference: negative <1:80).

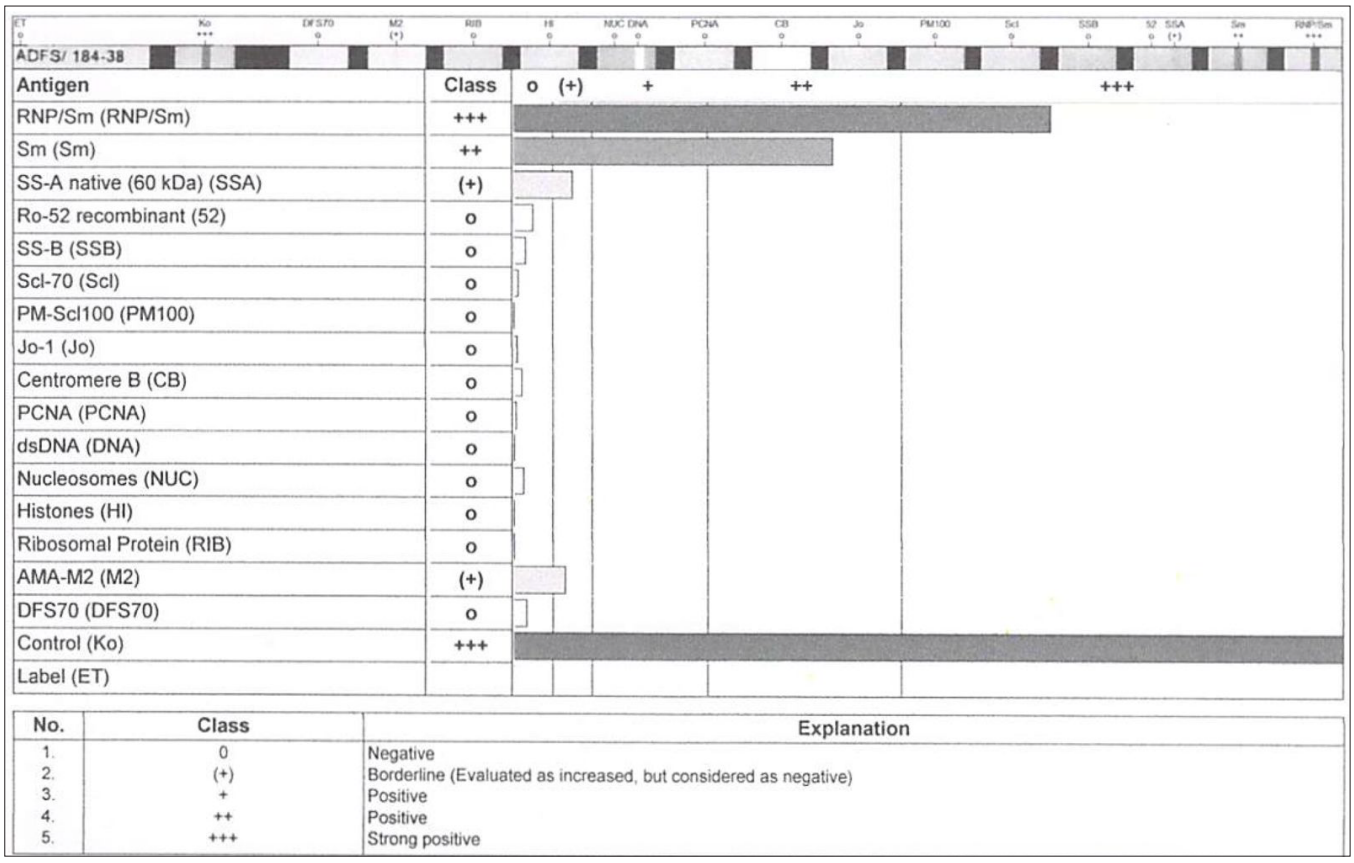
Serum chemistry demonstrated elevated aspartate aminotransferase of 85 U/L (reference range <40 U/L), alanine aminotransferase of 92 U/L (reference range <41 U/L) and lactate dehydrogenase of 273 U/L (reference range 140 - 280 U/L), accompanied by decreased serum calcium of 8.4 mg/dL (reference range 8.6 - 10.2 mg/dL) and albumin level of 3.0 g/dL (reference range 3.5 - 5.0 g/dL). These findings suggested possible hepatic involvement and impaired nutritional status.

Immunological examination showed decreased complement C3 level of 37.6 mg/dL (reference range 90 - 180 mg/dL) and vitamin D level of 25.0 ng/mL (reference range 30 to 100 ng/mL).

Antinuclear antibody testing

Antinuclear antibody (ANA) testing using indirect immunofluorescence assay on HEp-2 cells demonstrated a high titre of 1:10 000 with a fine speckled pattern (reference value negative at titres <1:80). In our laboratory, ANA titres are reported using serial dilutions up to 1:10 000, representing the endpoint dilution at which fluorescence remains detectable, indicating markedly elevated ANA levels consistent with active systemic autoimmune disease. The fine speckled pattern is shown in Fig. 2. This pattern may be observed in conditions such as SLE, mixed connective tissue disease (MCTD), Sjögren's syndrome, neonatal lupus, dermatomyositis, progressive systemic sclerosis (PSS), scleroderma, chronic hepatitis and cancer-associated dermatomyositis.

The ANA profile showed positive results for anti-RNP/Sm, anti-Sm, SS-A (Ro) native, and AMA-M2 antibodies. Based on the ANA



No.	Class	Explanation
1.	0	Negative
2.	(+)	Borderline (Evaluated as increased, but considered as negative)
3.	+	Positive
4.	++	Positive
5.	+++	Strong positive

Fig. 3. ANA profile results.

screening and detailed ANA profile, the findings are supportive of a diagnosis of SLE. The ANA profile result can be seen on Fig. 3.

Histopathology examination

The type of histopathological examination was biopsy of skin specimen. The examination demonstrated basket weave orthokeratosis of the epidermis with focal vacuolar degeneration at the dermoepidermal junction. A subepidermal blister was identified, accompanied by a mild inflammatory infiltrate consisting predominantly of neutrophils and lymphocytes in the superficial dermis. These histopathological findings are consistent with autoimmune subepidermal blistering disorders and support the diagnosis of BSLE when correlated with clinical and immunofluorescence findings.[3,4] The differential diagnosis was considered consistent with lupus erythematosus.

Direct immunofluorescence

Direct immunofluorescence findings (Table 1) were consistent with SLE.

Radiology examination: Impression

Chest radiography (Fig. 4) demonstrated cardiomegaly with a configuration suggestive of left atrial enlargement and left ventricular hypertrophy, while no pulmonary abnormalities were identified. These findings may reflect possible cardiac involvement associated with SLE, although no acute cardiopulmonary complications related to the bullous eruption were observed at the time of evaluation.

Diagnosis

The diagnosis made was BSLE, comorbid with obesity.

Table 1. Differential diagnosis of bullous systemic lupus erythematosus[2-4]

Disease	Clinical presentation	Histology	Direct immunofluorescence	Indirect immunofluorescence/ split skin substrate
Cutaneous lupus erythematosus (CLE)	Acute: malar or diffuse rash, macular, erythematous Subacute: annular, psoriasis-like lesion, scaly Chronic: (mostly discoid lupus) scaly, round or annular plaques that scar	Lichenoid tissue pattern with epidermal atrophy, hydropic changes, apoptotic keratinocytes, and dermal mononuclear infiltrate at the dermoepidermal junction, mucin deposits in dermis	Positive lupus band test, granular IgG, IgM and C3 at BMZ	May show ANA or ds-DNA antibodies in granular pattern
Bullous systemic lupus erythematosus (BSLE)	Patient meets ACR or SLICC criteria for SLE, tense blisters on inflamed or normal skin, typically trunk, upper extremities, face, lips, and oral mucosal involvement; non-scarring, classically without milia	Subepidermal blisters, neutrophilic microabscesses in papillary dermis, abundant mucin deposits in dermis, absence of eosinophils	Linear or granular of IgG, IgA, IgM and C3 at the BMZ	Circulating IgG anti-BMZ antibodies – dermal pattern or negative (some with epidermal)
Bullous pemphigoid (BP)	Tense blisters on inflamed or normal skin, and urticarial plaques, typically on the flexor surfaces of the arms and legs, lateral trunk; no mucosal involvement; more common in elderly patients	Subepidermal bulla with inflammatory eosinophil-predominant infiltrate, also containing lymphocytes and neutrophils	Linear deposits of IgG and/or C3 at the BMZ	Circulating IgG anti-BMZ antibodies – epidermal pattern and within lamina lucida
Epidermolysis bullosa acquisita (EBA)	Skin fragility, trauma-induced blisters healing with scarring and milia, typically on extensor surfaces, mucous membranes commonly involved; middle-aged patients	Classic: subepidermal bulla with sparse mononuclear cell infiltrate Inflammatory: subepidermal bulla with mixed, neutrophilic infiltrate	Linear deposits of IgG and C3 at the BMZ, rarely IgA and IgM	Circulating IgG anti-BMZ antibodies – dermal pattern
Linear IgA bullous dermatosis	Tense blisters on erythematous skin, pruritic plaques with blisters at the border of healing lesions, most common on flexor surfaces, trunk, perineum, face, oral mucosa	Subepidermal bulla with inflammatory, neutrophil- or eosinophil-predominant infiltrate	Linear deposits of IgA and C3 at the BMZ	Circulating IgA anti-BMZ antibodies – epidermal, dermal or mixed pattern
Dermatitis herpetiformis (DH)	Intensely pruritic erythematous papules and small vesicles in herpetiform arrangement, typically on elbows, knees, buttocks, back, shoulders, face, and scalp; associated GSE; young adults and children affected	Subepidermal bulla with neutrophil microabscesses in dermal papillae	Granular deposits of IgA and C3 at the tips of the dermal papillae only	Negative

BMZ = basement membrane zone; SLICC = Systemic Lupus International Collaborating Clinics; GSE = gluten-sensitive enteropathy.

Therapeutic management

Therapeutic management of the patient was as follows:

- Fluid requirement: 2 600 mL/day
- Intravenous fluid: dextrose 5% in half normal saline at 25 mL/hour
- Methylprednisolone: 0.5 mg/kg body weight
- Ranitidine: 1 - 2 mg/kg body weight
- Folic acid: 1 mg orally every 12 hours
- Mycophenolate sodium: 180 mg every 12 hours
- Sodium fusidate 2% cream: topically every 12 hours
- Cetirizine: 10 mg once daily
- Rituximab: 100 mg in 500 mL normal saline

The patient initially received systemic corticosteroids and mycophenolate sodium. However, new blister formation persisted, indicating an inadequate therapeutic response. Dapsone, which is commonly considered first-line therapy for BSLE, was not administered because the patient had pre-existing anaemia and radiographic evidence of cardiomegaly. Considering the potential haematological adverse effects of dapsone, including haemolytic anaemia and methaemoglobinaemia that may worsen oxygen delivery and cardiopulmonary status, alternative therapy was preferred.

In our institution, the standard rituximab regimen consists of 750 mg per infusion (maximum 1000 mg) diluted in 500 mL normal saline and administered twice at a 2-week interval. However, in this case, a low-dose regimen of 100 mg diluted in 500 mL normal saline was administered due to clinical considerations. Following rituximab administration, the patient demonstrated progressive clinical improvement with cessation of new blister formation and gradual healing of existing lesions during hospitalisation.

Clinical course during hospitalisation

The patient was hospitalised for 45 days. At the time of discharge, most of the blisters had dried up, and the patient was able to eat and drink well. The patient was advised to attend regular outpatient clinic follow-ups.

Discussion

BSLE is a rare autoimmune blistering manifestation of SLE characterised by the formation of subepidermal blisters mediated by autoantibodies directed against type VII collagen at the dermoepidermal junction.[3,4] Binding of these autoantibodies activates complement pathways and recruits neutrophils, resulting in inflammatory damage and blister formation. Clinically, BSLE may resemble other autoimmune subepidermal blistering disorders such as epidermolysis bullosa acquisita, dermatitis herpetiformis, and linear IgA bullous dermatosis; therefore, histopathological and direct immunofluorescence findings are essential for accurate diagnosis.[2-4]

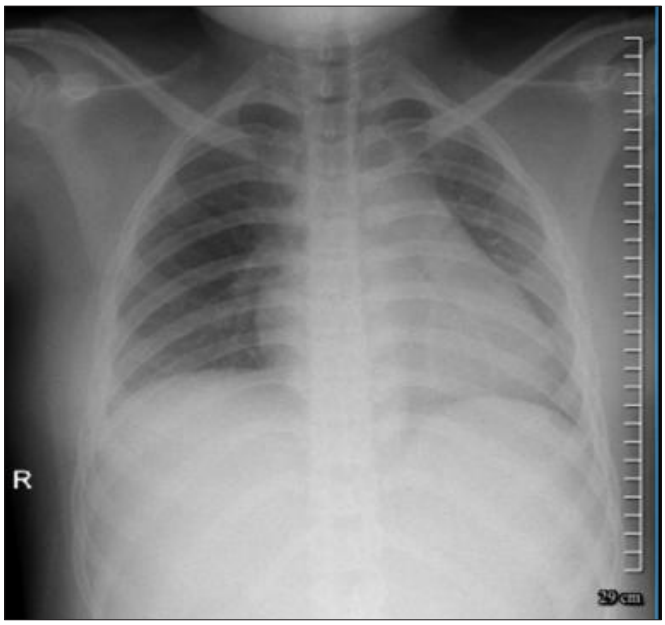


Fig. 4. Chest radiography.

In the present case, the diagnosis of BSLE was established based on compatible clinical findings of generalised tense vesiculobullous eruptions, laboratory evidence of active SLE, histopathological identification of a subepidermal blister with neutrophilic infiltration and linear deposition of IgG, IgA, C3 and C1q along the dermoepidermal junction on direct immunofluorescence. These findings fulfilled the diagnostic features of BSLE and supported the diagnosis in correlation with the 2019 the European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) classification criteria for SLE.

Systemic corticosteroids and immunosuppressive agents remain the mainstay of therapy for BSLE, while dapsone is frequently considered first-line treatment because of its rapid clinical response.[3,5] However, some patients demonstrate inadequate response or clinical contraindications, necessitating alternative therapeutic approaches. Rituximab, a monoclonal antibody targeting CD20+ B cells, has increasingly been reported as an effective treatment for refractory BSLE, leading to rapid lesion resolution and prolonged remission in several case reports and small series.[1,5]

In this case, administration of low-dose rituximab resulted in marked clinical improvement with cessation of new blister formation and progressive healing of existing lesions. This observation supports previous reports suggesting that rituximab may serve as an effective therapeutic option for refractory BSLE, particularly when conventional therapy is insufficient.

Several autoimmune subepidermal blistering disorders should be considered in the differential diagnosis of BSLE, including epidermolysis bullosa acquisita, dermatitis herpetiformis and linear IgA bullous dermatosis.[2-4] Differential diagnosis of BSLE can be seen in Table 2.

Conclusion

BSLE is a rare vesiculobullous manifestation of SLE that requires careful clinicopathological and immunofluorescence correlation for accurate diagnosis, particularly in paediatric patients. Although conventional therapies remain the primary treatment, refractory cases may require alternative therapeutic approaches. This case demonstrates that low-dose rituximab may represent an effective therapeutic option for refractory BSLE, resulting in significant clinical improvement and cessation of new blister formation.

Table 2. Direct immunofluorescence findings

Parameter	Result
IgG	Positive, linear deposition along the dermoepidermal junction
IgA	Positive, focal deposition at the dermoepidermal junction
IgM	Negative
C3	Positive, focal deposition at the dermoepidermal junction
C1q	Positive, linear deposition along the dermoepidermal junction

Data availability statement. None.

Declaration. Artificial intelligence (AI) tools (ChatGPT, OpenAI) were used only to assist in improving the clarity and structure of the discussion section. All clinical interpretations, diagnostic reasoning, data analysis and conclusions were developed entirely by the authors without reliance on AI.

Acknowledgements. None.

Author contributions. NKPS: data collection, analysis, histopathology interpretation, manuscript drafting. MF: clinical evaluation, supervision, histopathology interpretation, manuscript review. NKM: histopathology interpretation, manuscript editing. All authors read and approved the final manuscript.

Funding. None.

Conflicts of interest. None.

1. Akpabio AA, Otike-Odibi BI. Severe bullous systemic lupus erythematosus successfully treated with low dose rituximab: A case report from sub-Saharan Africa. Reumatismo 2020;72(2):115-119. https://doi.org/10.4081/reumatismo.2020.1274
2. Sprow G, Afarideh M, Dan J, Hedberg ML, Werth VP. Bullous systemic lupus erythematosus in females. Int J Womens Dermatol 2022;8(3):e034. https://doi.org/10.1097/JW9.0000000000000003
3. Contestable JJ, Edhegard KD, Meyerle JH. Bullous systemic lupus erythematosus: a review and update to diagnosis and treatment. Am J Clin Dermatol 2014 Dec;15(6):517-524.
4. Odonwodo A, Vashisht P. Bullous systemic lupus erythematosus. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK557445/ (accessed 8 November 2025).
5. Ratanapokasatit Y, Aphinan C, Chanpraph K. Refractory bullous systemic lupus erythematosus successfully treated with rituximab: A case report and literature review. Clin Cosmet Investig Dermatol 2023:16:883-890.

Received 8 December 2025. Accepted 19 February 2026.