CASE REPORT

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Skin: The Mirror of Internal Disease

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Abstract

Systemic lupus erythematosus (SLE) is associated with diverse mucocutaneous manifestations. Bullous SLE (BSLE) is associated with sub-epidermal blisters with profuse neutrophilic infiltration. Other bullous lesions in SLE include bullous pemphigoid (BP), dermatitis herpetiformis (DH), and epidermolysis bullosa acquisita (EBA). Histopathology is essential to clinch the diagnosis, on the backdrop of SLE. We report a case of isolated BSLE, which was not associated with SLE flare, or with systemic involvement like lupus nephritis (LN).

Key words: Bullous SLE, SLE flare, lupus nephritis.

Introduction

Mucocutaneous manifestations of systemic lupus erythematosus (SLE) range from discrete oral ulcers, malar rash or discoid lupus erythematosus (DLE), to little-known variants like hypertrophic LE, chilblain LE and lupus panniculitis. Bullous skin lesions are relatively rare in SLE, with a reported prevalence of around 5% among SLE patients[1]. LE-nonspecific skin disease includes skin changes that are frequently associated with LE but are not specific to the disease itself. Among these, bullous SLE is associated with sub-epidermal blisters with profuse neutrophilic infiltration, in contrast to the lymphocytic predominance seen in classical cutaneous lesions of SLE[2].

Case report

A 30-year-old lady, was admitted under our care with multiple joints pain for six months and multiple, blistering, fluid filled lesions for last two months. The joint pain was insidious in onset, boring in character, migrating, symmetrical, was associated with morning stiffness, and involved wrists, proximal interphalangeal joints, elbows, and knees. The pain worsened with rest and improved with activity, was initially associated with surrounding soft tissue swelling, and was not associated with weakness or wasting of surrounding muscles. The joint pains were accompanied with a low grade fever, malaise and unintentional weight loss, without any history of cough, headache, bleeding manifestations, night sweats or photophobia.

The lady developed bullous lesions 2 months back, which were acute in onset, initially involving the trunk and spreading to the extensor surfaces of limbs, mildly itchy and not painful or tender. Individual lesions appeared as small vesicles, progressed to the size of bullae, and eventually ruptured, leaving an area of crusting, without any feature of pustule formation. She had associated hair loss and a single, painless oro-mucosal ulcer on the hard palate (Fig. 1). There was no history of muscle weakness, frothy urine, oliguria, facial rash, chest pain or heaviness, sensation of pins and needles, numbness or discoloration of fingertips, purpura, pain abdomen, seizure or decline in cognitive function. She had no pre-existing co-morbidities, no similar past history, no addictions, and an uneventful obstetric history with a single full term normal delivery. She was using intramuscular (IM) depot medroxyprogesterone acetate 150 mg every three months as contraception for the last five years.

The general examination was significant for severe pallor. Musculo-skeletal system examination revealed inflammatory arthritis predominantly involving the proximal interphalangeal, wrist and knee joints. Overall, the patient had a swollen joint count of 2 and a tender joint count of 10, without any joint deformity.

Skin examination was significant for multiple flaccid bullous vesicles on an erythematous base, with crust formation and negative Nikolsky sign. A single painless ulcer with erythematous base was noted on the hard palate. There were no genital ulcers, purpura, livedo reticularis or digital gangrene. Examination of chest, cardiovascular and neurological systems was unremarkable.

Investigations showed Hb 5.6 g/dL, MCV 77 fL, ESR 85 mm in 1st hour, normal fasting blood glucose, TSH, LFT and renal function tests. Rheumatoid factor, ASO titer, viral markers were all negative. ANA by IIF method was positive (2+) with nuclear speckled and cytoplasmic pattern, and

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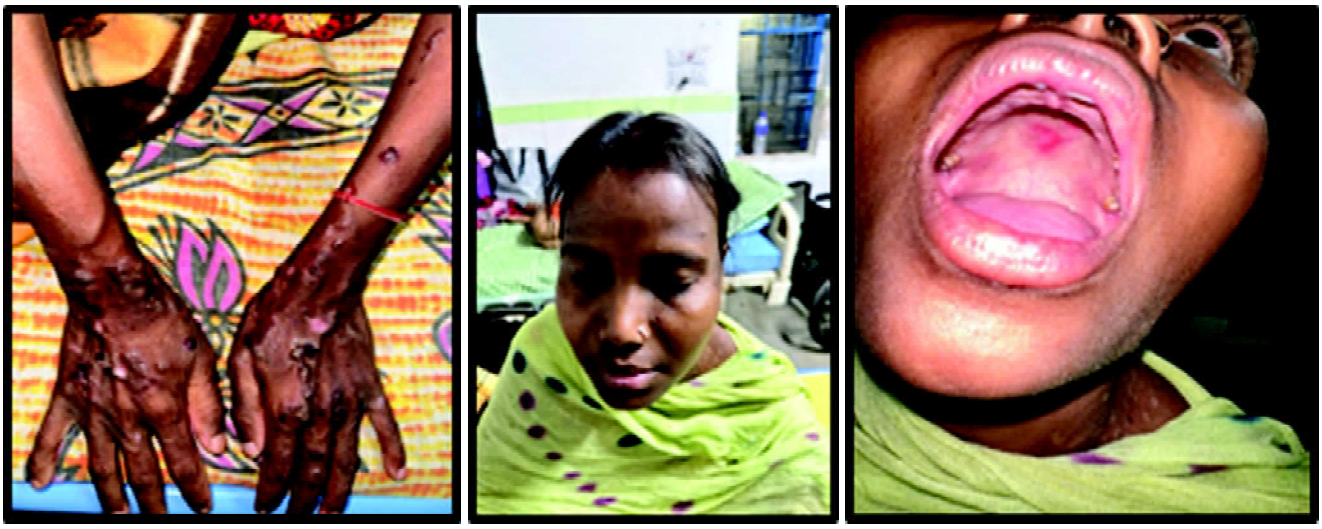

Fig. 1: *Mucocutaneous manifestations showing bullous lesions with crusting (1A), non-scarring alopecia (1B) and oral ulcer (1C).*

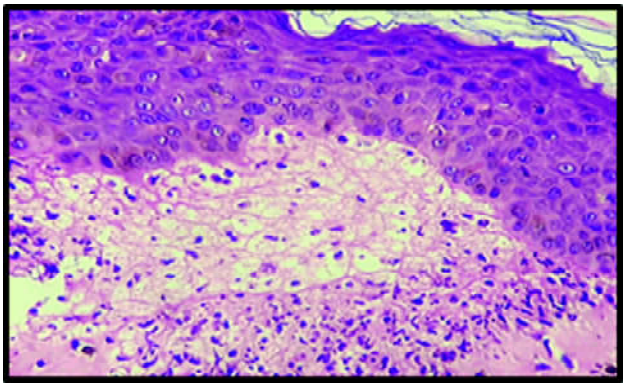

Fig. 2: *Histopathology of skin showing superficial vesiculobullous lesions with subepidermal neutrophilic infiltration.*

reduced C3 (49.50 mg/dL, normal 90 - 180 mg/dL), and C4 (6.80 mg/dL, normal 10 - 40 mg/dL) levels. Routine examination of urine and urinary ACR were non-contributory. The 24-hour urinary protein was 53 mg and quantitative anti-dsDNA was below the cut-off, essentially ruling out a disease flare. Skin histopathology revealed subepidermal vesiculobullous lesions harbouring predominantly neutrophils, along with dermal perivascular inflammation (Fig. 2). DIF showed linear deposits of immune complexes of IgA, IgG and C3 (Fig. 3).

The patient fulfilled the 2019 EULAR classification criteria of SLE[3]. In view of her clinical and laboratory findings, we entertained a diagnosis of BSLE and managed the patient with tablet Hydroxychloroquine 5 mg/kg daily, tablet Prednisolone 40 mg/day in tapering dose over 6 weeks, and tablet Dapsone 50 mg daily for 2 weeks followed by 100 mg daily to continue. We noticed significant clinical improvement with resolution of the bullous lesions with hypopigmentation but without residual scarring (Fig. 4). She is currently asymptomatic on follow-up over the past 4 months.

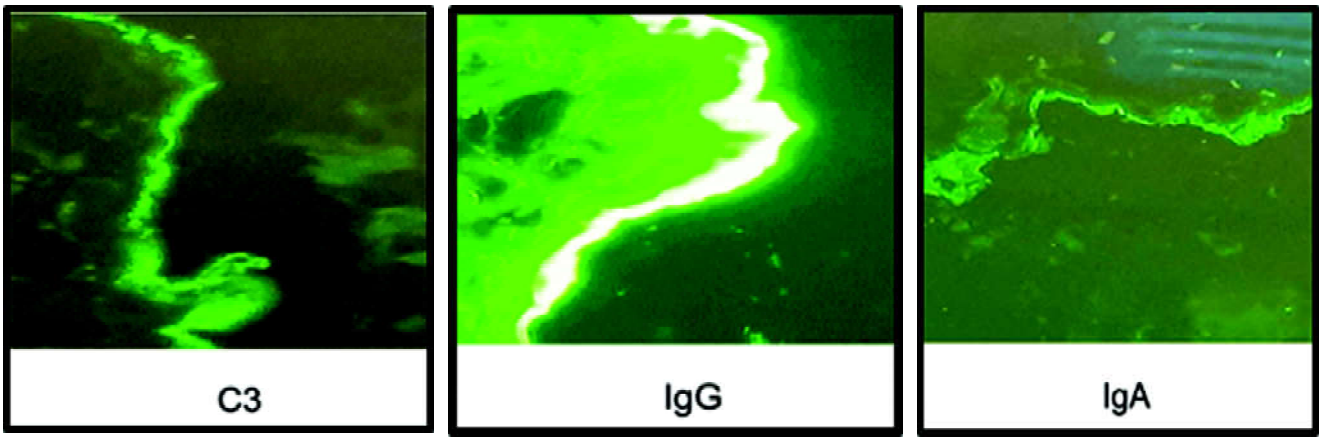

Fig. 3: *Direct immunofluorescence (DIF) of skin biopsy showing linear deposition along the basement membrane of C3 (3A), IgG (3B) and IgA (3C).*

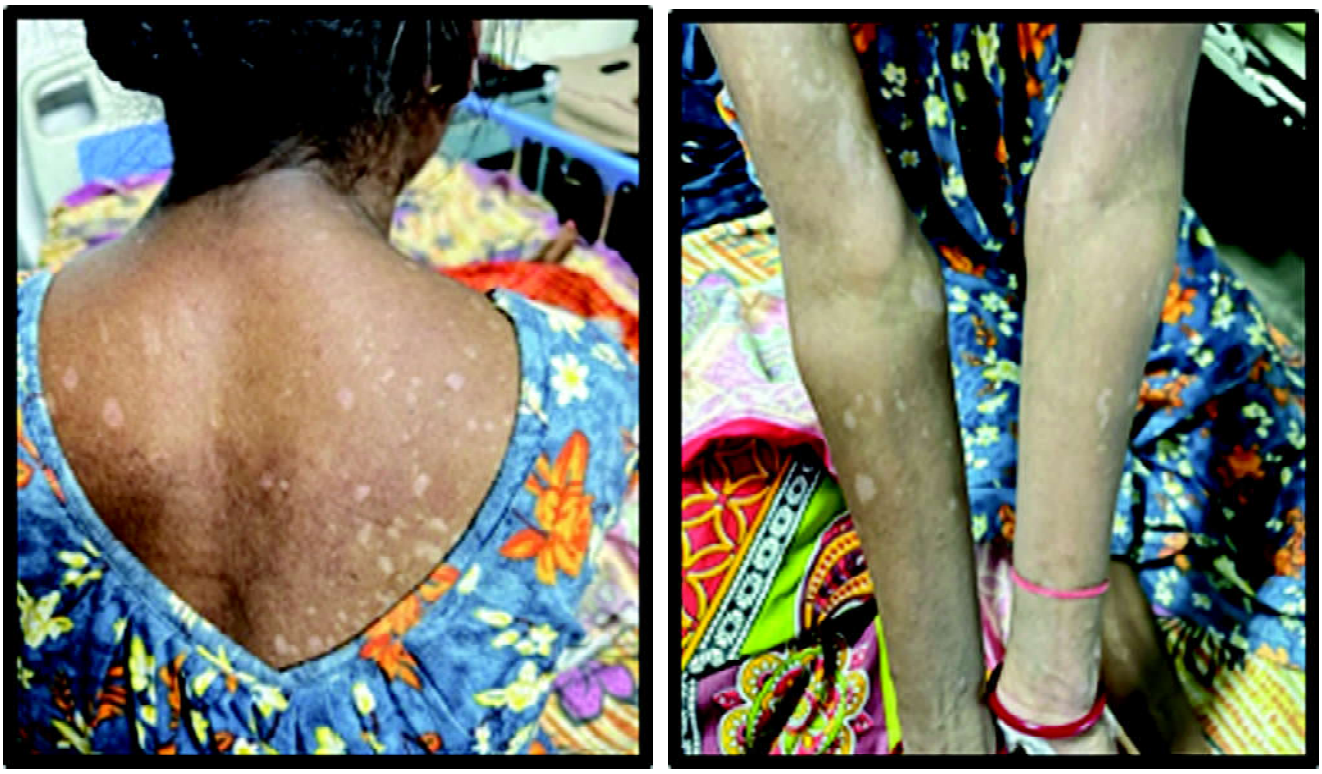

Fig. 4: *Patient after 24 weeks of Dapsone initiation showing no fresh vesiculobullous lesion and resolution of previous lesions with hypopigmentation.*

Discussion

Subepidermal blister formation in the course of severe SLE can occur due to extensive interface inflammation and basal cell vacuolation, presenting as polycyclic erosions with advancing blistering border, predominantly on sun-exposed areas[4]. However, BSLE is a distinctive bullous eruption occurring in patients with SLE, presenting with typical clinical and pathological findings including circulating antibodies primarily directed against type VII collagen {NC1 (noncollagenous domain 1) domain}, or sometimes against laminin 5, laminin 6, and BP230 (bullous pemphigoid antigen)[5].

Differentials to be considered for vesiculobullous lesions in lupus include bullous pemphigoid (BP), dermatitis herpetiformis (DH), and epidermolysis bullosa acquisita (EBA)[6]. BP is characterised by tense blisters, more intense pruritus and a densely eosinophilic infiltrate, in contrast to the neutrophilic predominance of BSLE lesions[7]. DH is a chronic, autoimmune, blistering disease that causes an extremely pruritic rash, sometimes associated with blister formation, and demonstrating granular IgA deposits within the dermal papilla[8]. Lastly, both inflammatory EBA and mechanobullous EBA emerge as differentials of BSLE[9]. However, EBA is associated with more severe scarring and poorer response to dapsone. Above all, a diagnosis of BSLE must satisfy the criteria of SLE.

Our case satisfied the 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus[3]. The following criteria for the diagnosis of bullous SLE have been proposed: (1) a diagnosis of SLE; (2) vesicles and bullae arising upon but not limited to sun-exposed skin; (3) histopathology compatible with DH; (4) negative indirect immunofluorescence for circulating basement membrane zone (BMZ) antibodies; (5) direct immunofluorescence positive for IgG and/or IgM and often IgA at the BMZ[10].

Blistering eruptions are rare cutaneous manifestations of SLE that can result from two distinct mechanisms: vesicles arising from a subepidermal blistering disease with an acute neutrophil-predominant infiltrate in the upper dermis, known as BSLE, or blisters developing from hydropic degeneration of the basal layer and severe oedema in the upper dermis, also referred to as SLE with blisters[11]. BSLE is a rare, transient autoimmune bullous disease which is closely associated with lupus nephritis (LN). In contrast, SLE with blisters has not been associated with systemic manifestations of SLE. Our case belongs to the former category, and remains unique in being a case of BSLE without associated LN, or any other organ – system involvement. The resolution of skin lesions in our case with hypopigmentation and no residual scarring is supported by the world literature[12].

Conclusion

SLE is associated with diverse mucocutaneous manifestations. Among these, BSLE is a rare entity, usually seen during SLE flares, in association with extra-cutaneous involvement like lupus nephritis (LN). Our case appears unique in neither presenting as an episode of SLE flare, nor being associated with other organ – system involvement. The fact that our patient remained undiagnosed for more than six months highlights the need to identify such uncommon dermatological manifestations in resource restricted settings, where both the diagnosis and the treatment of SLE are often delayed.

References

1. Saez-de-Ocariz M, Espinosa-Rosales F, Lopez-Corella E. Bullous lesions as a manifestation of systemic lupus erythematosus in two Mexican teenagers. *Pediatr Rheumatol Online J* 2010; 8: 19-24.
2. Stull C, Sprow G, Werth VP. Cutaneous Involvement in Systemic Lupus Erythematosus: A Review for the Rheumatologist. *J Rheumatolo* 2023; 50: 27-35.
3. Aringer M, Costenbader K, Daikh D. *Ann Rheum Dis* 2019; 78: 1151-9.
4. Yung A, Oakley A. Bullous systemic lupus erythematosus. *Australas J Dermatol* 2000; 41: 234-7.
5. Chan LS, Lapiere JC, Chen M. Bullous systemic lupus erythematosus with antibodies recognizing multiple basement membrane components, bullous pemphigoid antigen1, lamini-5, laminin-6, and type VII collagen. *Arch Dermatol* 1999; 135: 569-73.
6. Giri G, Bagheri S. Bullous Systemic Lupus Erythematosus: A Case Report. *Cureus* 2023; 15 (6): e40002.
7. Yossy V, Akhyar G, Tofrizal A. Bullous Systemic Lupus Erythematosus Mimicking Bullous Pemphigoid: A Case Report. *Health and Med J* 2021; 3 (2): 51-8.
8. Mirza HA, Gharbi A, Bhutta BS. Dermatitis Herpetiformis. (Updated 2023 Aug 17). In: StatPearls (Internet). Treasure Island (FL): StatPearls Publishing; 2024 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493163/.
9. Odonwodo A, Vashisht P. Bullous Systemic Lupus Erythematosus. StatPearls Publishing, Treasure Island, FL, USA; 2023. https://pubmed.ncbi.nlm.nih.gov/32491377/.
10. Camisa C, Sharma HM. Vesiculobullous systemic lupus erythematosus. *J Amer Academy of Dermatolo* 1983; 9 (6): 924-33.
11. Dhir R, Desylva PLK, Gehi N. Pericardial effusion with vesiculobullous lesions in a young female. Bullous systemic lupus erythematosus (bullous SLE). *Ind J Dermatol Venereol Leprol* 2006; 72: 175-7.
12. 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): 1278-84.