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CASE REPORT

A Rare Case of Extensive Oral Involvement in Bullous Systemic Lupus Erythematosus: Diagnostic and Therapeutic Challenges

Tiara Resmi[1], Oki Suwarsa[2], Irna Sufiawati[3]

[1]Oral Medicine Residency Programme, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia; [2]Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia; [3]Department of Oral Medicine, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia

Correspondence: Irna Sufiawati, Department of Oral Medicine, Faculty of Dentistry, Universitas Padjadjaran, Jalan Sekeloa Selatan I, Bandung, 40132, Indonesia, Email irna.sufiawati@unpad.ac.id

Abstract: Bullous systemic lupus erythematosus (BSLE) is a rare autoantibody-mediated subepidermal blistering disease that affects fewer than 5% of systemic lupus erythematosus (SLE) patients. While oral involvement is generally mild, extensive oral lesions as the predominant manifestation are exceptionally uncommon and present significant diagnostic and therapeutic challenges. This report describes a unique case of BSLE with dominant and extensive oral involvement, a presentation rarely documented in the literature. A 29-year-old female presented to the Oral Medicine Clinic with severe, diffuse oral ulcerations of one week's duration (VAS pain score 8/10), which impaired swallowing and were accompanied by fever, without any history of new medication or food exposure. A 29-year-old female presented to the Oral Medicine Clinic with severe diffuse oral ulcerations for one week (VAS pain score 8/10) that impaired swallowing and were accompanied by fever, without any history of new medications or food exposure. Clinical examination identified widespread erythematous bullae and erosions across the oral mucosa, as well as non-scrapable white plaques on the dorsum and lateral tongue. Histopathological analysis revealed subepidermal separation with predominant neutrophilic infiltration, confirming BSLE and distinguishing it from other vesiculobullous disorders in the absence of direct immunofluorescence (DIF) testing. Management consisted of a multimodal approach, including topical therapy (dexamethasone ointment, antiseptic rinses, saline compresses, and protective emollients) and systemic therapy with high-dose intravenous methylprednisolone and oral cyclosporine, supported by antibiotics and analgesics under dermatology supervision. Notably, all oral lesions resolved completely within four weeks without the need for more aggressive systemic treatment. This case highlights the diagnostic value of a multidisciplinary, clinicopathological approach in confirming BSLE with dominant oral involvement, even when advanced immunofluorescence testing is unavailable, and demonstrates the effectiveness of a tailored, minimally invasive therapeutic strategy that achieved complete healing without the need for aggressive systemic therapy.

Keywords: bullous systemic lupus erythematosus, oral ulcerations, autoimmune blistering disease, non-communicable diseases, case report

Background

Lupus erythematosus is a chronic autoimmune disease characterized by a broad spectrum of clinical manifestations, ranging from cutaneous lesions to multi-organ systemic involvement.[1] Bullous systemic lupus erythematosus (BSLE) is a rare subepidermal blistering disease caused by autoantibodies against type VII collagen,[2] affecting fewer than 5% of systemic lupus erythematosus (SLE).[3] The estimated prevalence of BSLE ranges from 0.19% to 0.41% in SLE patients, with a higher predilection in women, consistent with the epidemiology of SLE.[4,5] BSLE is particularly uncommon as an initial or isolated manifestation.[6]

Clinically, BSLE may present with vesicles, bullae, erosions, and ulcers on the skin and mucous membranes, including the oral cavity, which can cause severe discomfort and dysphagia.[7,8] Oral lesions are frequently observed in

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both adult- and juvenile-onset SLE patients, further complicating the clinical differentiation from other autoimmune bullous diseases.[9] BSLE must be carefully distinguished from other autoimmune blistering diseases such as pemphigus vulgaris, mucous membrane pemphigoid, epidermolysis bullosa acquisita, and linear IgA bullous dermatosis, as these conditions share overlapping clinical features. Therefore, histopathological and immunological assessments are essential for accurate diagnosis. However, in many clinical settings, direct immunofluorescence (DIF), the gold standard for confirming BSLE, may not be available, posing additional diagnostic challenges.

Bullous systemic lupus erythematosus with predominant oral manifestations represents a rare clinical entity that is often underrecognized. This report presents a case involving a young female patient with extensive oral and perioral involvement as the primary manifestation of BSLE. Diagnosis was confirmed by histopathological analysis, without direct immunofluorescence (DIF) testing. This case highlights the importance of a multidisciplinary clinicopathological approach. It demonstrates that effective disease control can be achieved through minimally invasive treatment, resulting in complete healing without the need for aggressive systemic therapy.

Case Report

A 29-year-old female presented with severe, diffuse oral ulcerations and erosions that had persisted for one week, accompanied by pain (VAS 8/10) and fever. She reported difficulty swallowing and speaking, but denied any history of new medications, food allergies, or systemic symptoms such as arthralgia, malar rash, or photosensitivity before onset. The chronological pattern of lesion onset indicated that the mucocutaneous eruptions developed without any preceding drug exposure. The patient denied the use of medications commonly associated with drug-induced lupus, such as hydralazine, isoniazid, or penicillamine. This clinical course, along with positive ANA and anti-double-stranded DNA antibodies, supported idiopathic BSLE rather than a drug-induced form.

Extraoral examination revealed erosive lesions with peeled epidermis on the back, representing ruptured bullae, bullous and erosive lesions involving the neck, erosive and crusted lesions on the upper and lower extremities (Figure 1). Additionally, hemorrhagic crusts and erosive lesions were observed on the lips, oral commissures, and perioral region (Figure 2A). Intraoral examination showed diffuse erythematous and erosive lesions affecting the labial and buccal mucosa as well as the palate (Figure 2B–F). Non-scrapable white plaques covered most of the dorsum and lateral surfaces of the tongue, accompanied by erosive lesions on the lateral tongue (Figure 2G and H). Dental examination revealed retained roots in the upper right and lower left molars, pulp necrosis in the lower right first molar, and an impacted lower third molar. The Oral Hygiene Index–Simplified (OHI-S) was categorized as moderate.

Laboratory investigations revealed normocytic normochromic anemia (Hb 8.7 g/dL; hematocrit 26.3%; erythrocyte count 4.47 × 10^6/μL) and a normal platelet count. Coagulation studies showed a prolonged prothrombin time of 16.4 seconds. Biochemical analysis demonstrated hypoalbuminemia (2.71 g/dL) and markedly elevated urea levels (68.9 mg/dL). Antinuclear antibody (ANA) and anti-double-stranded DNA (anti-dsDNA) antibodies were positive, whereas complement levels (C3 and C4) were not assessed due to healthcare system limitations. Urinalysis was normal, with no proteinuria or hematuria.

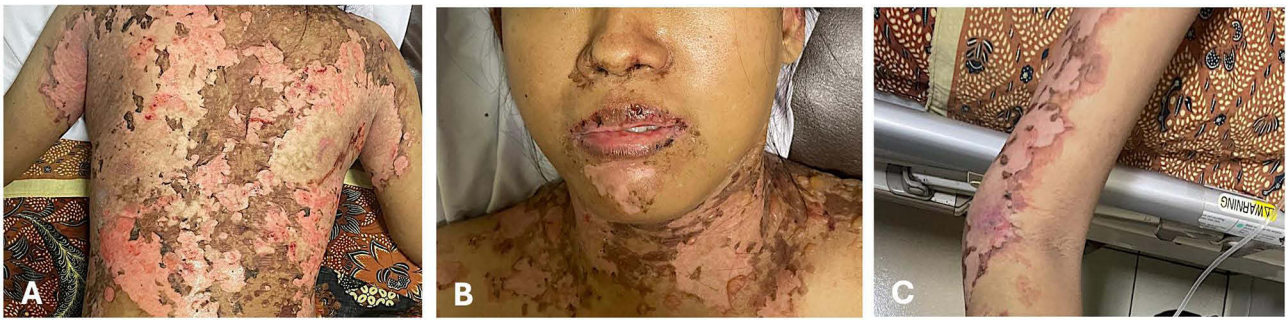

Figure 1 Cutaneous manifestations of BSLE at the first visit. (**A**) Erosive lesions with peeled epidermis on the back, representing ruptured bullae; (**B**) Bullous and erosive lesions involving the neck; (**C**) Erosive and crusted lesions on the upper and lower extremities.

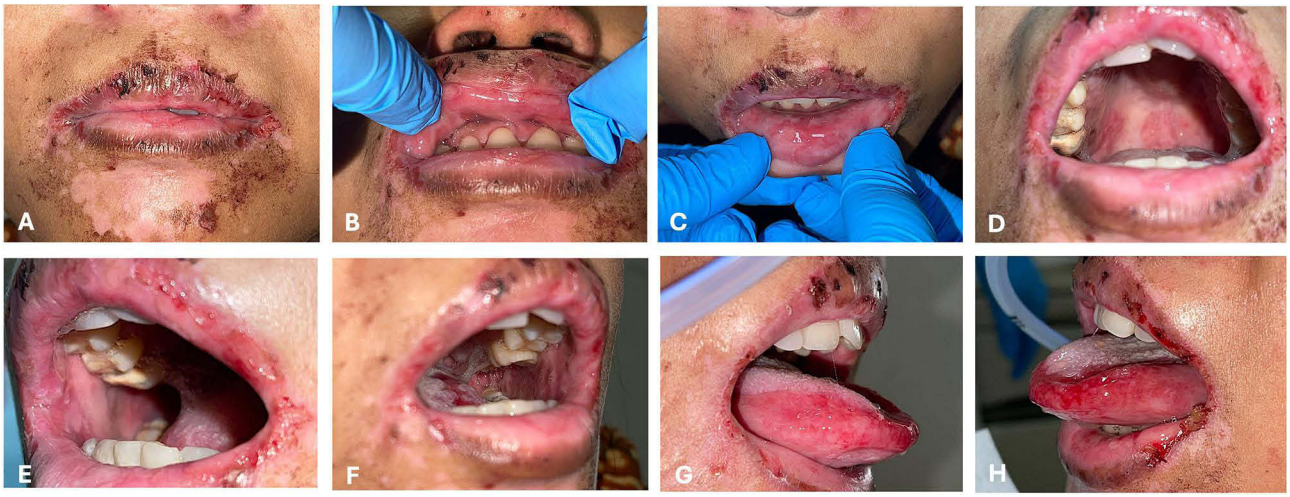

Figure 2 Extraoral and intraoral clinical features. (**A**) Hemorrhagic crusts and erosive lesions involving the lips, oral commissures, and perioral region; (**B**–**F**) Diffuse erythematous and erosive lesions affecting the labial and buccal mucosa as well as the palate; (**G** and **H**) Non-scrapable white plaques covering most of the dorsum and lateral tongue surfaces, accompanied by erosive lesions on the lateral tongue.

Based on these findings and the clinical presentation, the patient fulfilled the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE, with mucocutaneous involvement as the predominant manifestation. The SLE Disease Activity Index (SLEDAI-2K) score indicated mild disease activity, correlating with the onset of bullous and extensive oral lesions. No evidence of renal, musculoskeletal, or neurological involvement was observed during hospitalization.

A skin biopsy from the right abdominal area was performed. Histopathological examination revealed subepidermal separation with neutrophilic infiltrates in the upper dermis, confirming the diagnosis of BSLE (Figure 3). Direct immunofluorescence (DIF) could not be performed due to the unavailability of the test in the hospital laboratory. Indirect immunofluorescence (IIF) was also unavailable at the hospital, and referral to an external reference laboratory was not feasible due to healthcare system limitations and the patient's financial constraints. This reflects a diagnostic challenge in resource-limited clinical settings.

The patient was managed collaboratively by the Department of Dermatology and Venereology and the Department of Oral Medicine. Topical and systemic therapies for cutaneous lesions were administered under a dermatologist's supervision, whereas oral lesions were managed by the oral medicine team, including oral care and follow-up. Topical treatment for cutaneous lesions included hydrogel applied twice daily to crusted areas, open compresses with 0.1%

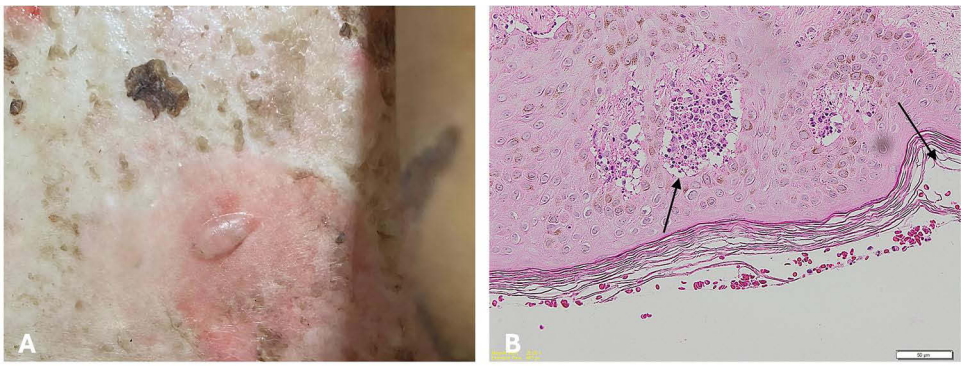

Figure 3 Histopathological confirmation of BSLE. (**A**) Biopsy site showing a bullous lesion on the right abdominal skin marked for histopathological analysis; (**B**) Subepidermal separation at the dermoepidermal junction (black downward arrow), accompanied by a neutrophil-predominant inflammatory infiltrate in the superficial dermis (black upward arrow), confirming the histological pattern characteristic of bullous systemic lupus erythematosus (hematoxylin and eosin stain, original magnification ×40).

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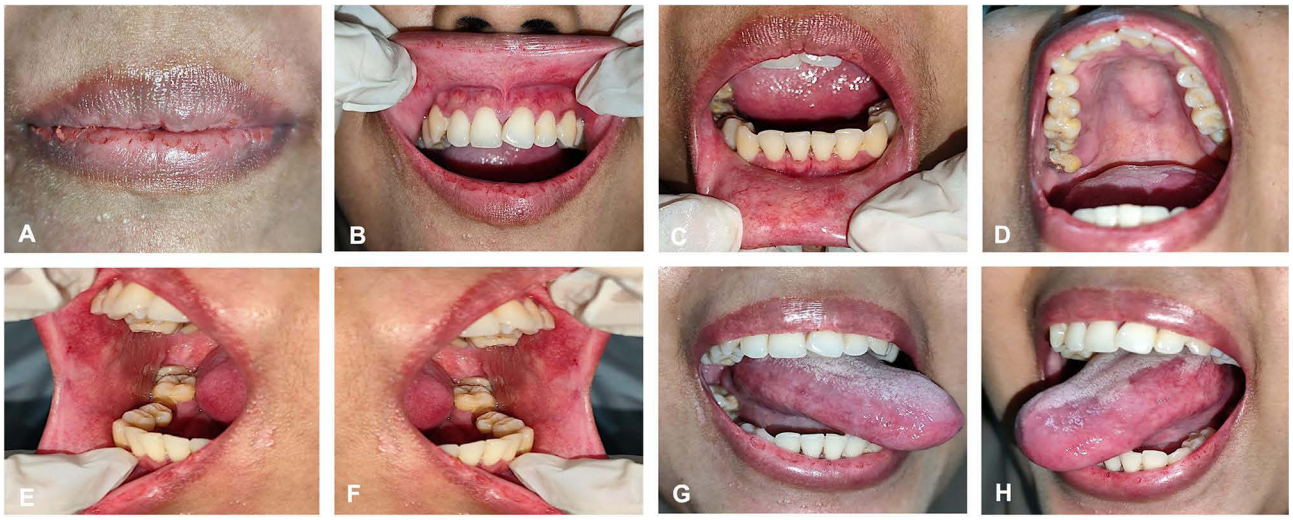

Figure 4 Clinical improvement following combined topical and systemic therapy over the three-week treatment period. (**A**) Progressive healing of erosive and crusted lesions on the lips and perioral region; (**B**–**F**) Resolution of erythematous and erosive lesions on the labial and buccal mucosa, and the palate; (**G** and **H**) Complete healing of erosive lesions on the lateral tongue.

salicylic acid solution for eroded surfaces, mupirocin 2% cream for abrasions, and wound dressings using Sorbact Cutimed for eroded regions and Hydrofiber Ag for the buttocks. Systemic therapy consisted of intravenous (IV) fluids (0.9% sodium chloride, 2000 mL per 24 hours), IV methylprednisolone administered at 125 mg in the morning and 62.5 mg in the evening (equivalent to 4.5 mg/kg/day on day 3), omeprazole 40 mg IV twice daily, oral cyclosporine 50 mg twice daily, paracetamol 500 mg orally three times daily or 1 g IV if the temperature exceeded 38°C, and ceftriaxone 1 g IV twice daily starting on day 2.

Oral care instructions included gentle tooth cleaning and compressing the lips with saline-moistened gauze three times daily. For pain management, the patient was advised to rinse with a mixture of diphenhydramine hydrochloride (12.5 mg/5 mL) and milk (5 mL), gargling for 30 seconds and then expectorating, three times daily. In addition, she was instructed to rinse with 10 mL of 0.1% povidone–iodine twice daily for one minute, avoiding meals for 30 minutes afterward. A thin layer of dexamethasone ointment was applied to the lips three times daily, followed by petroleum jelly to maintain moisture and protection. A multivitamin supplement was also prescribed. Significant improvement was observed within two weeks, and complete healing of all oral lesions occurred after four weeks of treatment (Figure 4). The patient was able to resume normal eating and maintain regular oral hygiene thereafter.

Informed written consent for publication of the clinical details and images in this report was obtained from the patient. The case adhered to the Declaration of Helsinki and received institutional approval for publication.

Discussion

This case highlights several important clinical and diagnostic aspects of BSLE. Although oral involvement in BSLE is uncommon, our patient presented with extensive erosive lesions of the lips and oral mucosa as the predominant manifestation, a presentation rarely documented in the literature. Such findings emphasize the importance of careful intraoral examination in patients with vesiculobullous lesions and suspected autoimmune disease.

As reported in previous literature, BSLE typically manifests as widespread vesicles and tense bullae filled with serous or hemorrhagic fluid, affecting both mucosal and non-mucosal surfaces. Unlike other cutaneous manifestations of SLE, BSLE lesions often occur on non-sun-exposed areas such as the trunk, proximal limbs, and perioral region.[10] BSLE more frequently affects the skin than the mucosa. However, when oral lesions occur, they present as painful erosions, hemorrhagic crusting, and bullous formations that significantly impair oral function and hygiene.[11] The predominance of oral lesions in this case highlights an unusual mucosal-dominant presentation of BSLE.

Histopathological analysis revealed subepidermal cleft formation with a neutrophil-predominant inflammatory infiltrate, consistent with an autoimmune blistering disorder. Although DIF, the gold standard for BSLE confirmation, could not be performed due to unavailability in the hospital, clinicopathological correlation supported the diagnosis. This limitation reflects healthcare system constraints frequently encountered in developing regions and underscores the need for practical diagnostic pathways when advanced testing is not accessible.

Direct immunofluorescence remains the gold standard for confirming BSLE, as it demonstrates immune complex deposition at the basement membrane zone. However, both DIF and indirect immunofluorescence (IIF) were unavailable at the hospital, and referral to an external reference laboratory was not possible due to healthcare system limitations and the patient's financial constraints. Although IIF can theoretically detect circulating autoantibodies, its diagnostic value in BSLE is limited. Previous studies have shown that many BSLE patients with positive DIF findings exhibit negative IIF results, reflecting the low sensitivity of serum-based testing for this condition. Moreover, IIF requires specific substrates, such as 1 M NaCl-split human skin or monkey esophagus, which are technically demanding and not routinely available in most local pathology laboratories. This limitation highlights the diagnostic challenges faced in resource-constrained settings.

Because of its clinical and histopathological overlap with other autoimmune blistering diseases, BSLE must be differentiated from bullous pemphigoid (BP), epidermolysis bullosa acquisita (EBA), and linear IgA bullous dermatosis (LABD). EBA, like BSLE, involves autoantibodies against type VII collagen; however, DIF in EBA typically reveals linear IgG deposits along the basement membrane zone (BMZ), whereas BSLE demonstrates a broader immunoglobulin profile.[12] Moreover, BP is distinguished by eosinophilic infiltration rather than the neutrophilic predominance seen in BSLE.[13]

The primary pathogenic mechanism of BSLE involves autoantibodies targeting type VII collagen, particularly its non-collagenous (NC1 and NC2) domains, disrupting dermoepidermal adhesion and leading to blister formation.[14] Additional autoantibodies against BP180, BP230, laminin 5, and laminin 6 may further contribute to disease progression.[15] The inflammatory cascade in BSLE is primarily neutrophil-mediated, leading to dermal-epidermal separation and subsequent subepidermal blistering.

Management of BSLE typically includes systemic corticosteroids and immunosuppressive agents. Dapsone is often considered first-line therapy because of its efficacy in controlling neutrophil-mediated blister formation. However, dapsone therapy carries the risk of hemolytic anemia and agranulocytosis, particularly in patients with pre-existing hematological abnormalities.[16] Second-line treatments for BSLE include immunosuppressive agents such as azathioprine, mycophenolate mofetil, hydroxychloroquine, and cyclophosphamide, particularly in refractory or severe cases.[17,18] Recent studies have also explored the role of biologic therapies, such as rituximab and intravenous immunoglobulin (IVIG), for managing BSLE with systemic involvement.[19,20]

In this case, dapsone was contraindicated due to pre-existing normocytic normochromic anemia (Hb 8.7 g/dL), which increased the risk of dapsone-induced hemolysis. In addition to this hematologic limitation, dapsone is not readily available for non-leprosy indications in Indonesia, as its clinical distribution is largely restricted to the national leprosy control program. Consequently, cyclosporine was chosen as a steroid-sparing immunomodulator. Cyclosporine is effective in reducing both cutaneous and systemic lupus activity by inhibiting T-cell activation and cytokine release. Its safety profile is favorable in patients with anemia, and several reports have demonstrated successful outcomes of BSLE treated with cyclosporine, either as monotherapy or in combination with corticosteroids.[21,22] Therefore, the choice of cyclosporine in this case was guided by patient-specific safety considerations, therapeutic efficacy, and local drug accessibility, reflecting a rational, individualized management strategy within a resource-limited healthcare setting.

In the present case, high-dose intravenous methylprednisolone combined with oral cyclosporine was selected to address both BSLE and underlying SLE activity. For patients with extensive mucosal involvement, including the oral cavity, a combination of topical and systemic therapy is often required. Intraoral management included dexamethasone ointment applied to the lips three times daily, followed by petroleum jelly to maintain hydration and barrier function. Antiseptic rinses and diphenhydramine-based mouthwashes were also used to manage pain and reduce the risk of secondary infection.

The patient demonstrated significant improvement, with complete resolution of oral and cutaneous lesions within approximately four weeks. This favorable outcome supports the effectiveness of a conservative, multidisciplinary management strategy combining systemic corticosteroids, cyclosporine, and topical/oral therapy, achieving complete remission without the need for cytotoxic or biologic immunosuppressants.

This case is noteworthy for several reasons. It represents a rare oral-dominant presentation of BSLE, a manifestation that has been seldom described in the literature. The diagnosis was established through clinicopathological correlation in the absence of direct immunofluorescence, reflecting real-world diagnostic challenges in resource-limited healthcare systems. Furthermore, the patient achieved complete healing within four weeks using a minimally invasive, multidisciplinary therapeutic approach that combined systemic corticosteroids, low-dose cyclosporine, and targeted topical and oral care. These features not only highlight the rarity of the presentation but also underscore the practical value of a tailored, resource-adapted management strategy that can yield favorable outcomes even without access to advanced immunopathological testing. Therefore, this case offers both practical and educational value, demonstrating that even in the absence of advanced diagnostic facilities, accurate diagnosis and effective management of BSLE can be achieved through close clinicopathological collaboration and a carefully tailored, conservative therapeutic approach.

Conclusion

This case illustrates a rare oral-dominant presentation of BSLE, emphasizing the importance of recognizing extensive mucosal involvement as a potential manifestation of the disease. The diagnosis, established through clinicopathological correlation in the absence of direct immunofluorescence, highlights the practical diagnostic approach applicable in resource-limited healthcare systems. The patient's complete recovery within four weeks using a minimally invasive, multidisciplinary therapeutic strategy demonstrates that effective disease control can be achieved without escalation to cytotoxic or biologic therapy. These findings provide meaningful clinical and educational insights into the diagnosis and management of BSLE with predominant oral involvement.

Informed Consent

The patient provided written informed consent for the disclosure of all photographs and clinical information presented in this case report. This case complies with the ethical principles outlined in the Declaration of Helsinki, and institutional approval for publication has been obtained.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, or interpretation. They took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

Disclosure

The authors declare no conflicts of interest in this work.

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