

**Exploring the Clinical Complexity of Bullous Systemic Lupus Erythematosus: A Case Report and Comprehensive Insights into Pathogenesis Histology and Therapeutic Strategies in Bullous Erythema Gyratumrepens – like Lupus Erythematosus**

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**Abstract**

A rare case of a 26-year-old male with a bullous eruption resembling erythema gyratumrepens within the context of systemic lupus erythematosus (SLE) is presented. The patient showed a unique combination of clinical and histological features, prompting insights into the complexity of cutaneous lupus manifestations. The discussion delves into the pathogenesis of Bullous Systemic Lupus Erythematosus (BSLE), emphasizing the role of autoantibodies to type VII collagen and the impact of B cell-activating factor (BAFF) and Type I Interferon Receptor 1 (IFNAR1) in SLE. The conclusion stresses the importance of personalized evaluations for treatment decisions in SLE.

**Keywords:** Cutaneous lupus manifestations; B Cell-Activating Factor (BAFF); Type I Interferon Receptor 1 (IFNAR1); Personalized treatment

## Introduction

First described in 1959, "Lupus erythematosus gyrateusrepens" is considered a distinct clinical and histological variant of annular subacute cutaneous lupus erythematosus, with potential links to internal malignancies [1]. Non-paraneoplastic erythema gyratumrepens in the context of cutaneous lupus erythematosus is rare [2]. Additionally, an annular bullous eruption with a gyrate periphery is seldom reported [3]. Bullous Systemic Lupus Erythematosus (BSLE) is a rare blistering eruption observed in patients with Systemic Lupus Erythematosus (SLE) [4]. While skin manifestations occur in up to 85% of SLE patients, less than 5% demonstrate vesicles and blisters [5]. The eruption is typically transient, subepidermal, and heals without scarring or milia. Bullae preferentially appear on the trunk, upper extremities, neck, face, and vermillion border, and may affect mucosal membranes [6]. Multiple case reports suggest that BSLE can be the initial presentation of SLE, with some cases associated with increased SLE activity, especially lupus nephritis. Therefore, timely diagnosis of BSLE is crucial to prevent complications associated with SLE [7]. Herein, we describe a very rare case of a Caucasian male with a bullous erythema gyratumrepens-like cutaneous eruption evolving in the setting of systemic lupus erythematosus.

## Case Presentation

The presented case involves a twenty-six-year-old man with a previously diagnosed, refractory systemic lupus erythematosus. He experienced an abrupt onset of erythematous polycyclic and annular plaques with vesicles and tense blisters distributed on palmar zone (Figure 1) and erythema gyratumrepens-like patches on the shins (Figure 2). General symptoms included asthenia, malaise, arthralgia, and subfebrile temperature (37.2 °C).



**Figure 1:** Erythematous patches, erosions and intact vesicles on the dorsal aspect of the right hand.

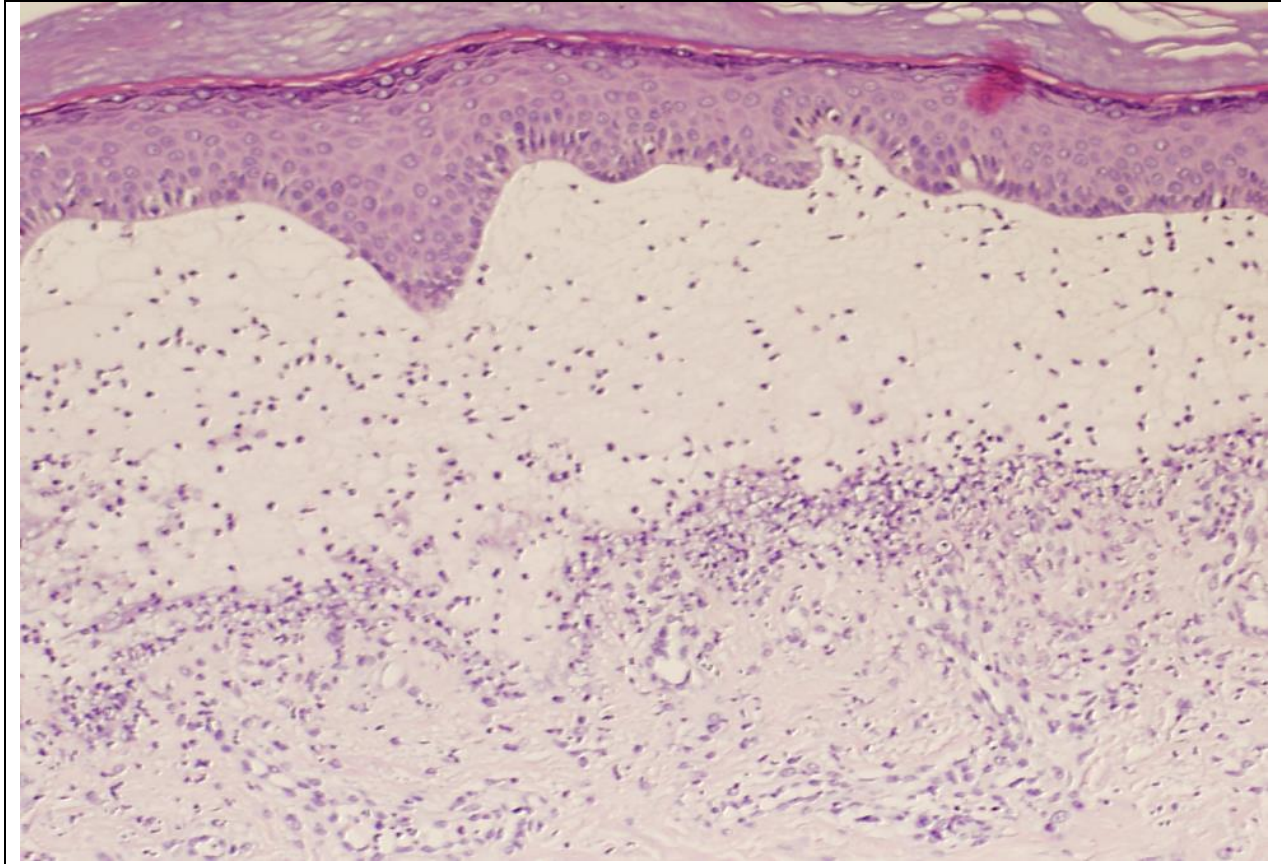


**Figure 2:** Erythema gyratumrepens-like eruption with central blister formation, localized to the left shin.

A skin biopsy revealed a subepidermal blister with an extensive inflammatory infiltrate of polymorphonuclear cells (**Figure 3**). Autoimmune serology indicated positive antinuclear antibody, anti-double-stranded DNA antibody, anti-Smith antibody, anti-ribonucleoprotein antibody, and anti-Ro antibody. Laboratory analysis revealed abnormalities such as lymphopenia, low serum C3 and C4, elevated erythrocyte sedimentation rate, and urinary abnormalities. Joint involvement and lupus nephritis were also established.

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**Figure 3:** Sub epidermal clefting with prominent mixed inflammatory infiltrate with plenty of neutrophils in the papillary dermis (H&E, x 100).

The patient was diagnosed with a relapse of a bullous erythema gyratum repens-like pattern of systemic lupus erythematosus. Due to previous therapeutic failures, anifrolumab was introduced, resulting in rapid lesion resolution. The skin lesions resolved with milia (**Figure 4**) and postlesional hypopigmented macules, disappearing within a few months. Clinical remission remained stable in the subsequent year.



Figure 4: Multiple milia on the postlesional erosive lesions on the dorsal hand.

### **Discussion**

BSLE primarily affects young women, often of African descent, typically within their second to fourth decades [8]. The presentation is commonly acute, featuring tense vesicles and bullae over inflamed or normal skin. Blisters tend to appear on sun-exposed areas but can also affect non-sun-exposed skin and mucosa. Unlike some other conditions,

BSLE usually spares extensor surfaces, especially acral sites [9]. Healing of blisters in BSLE typically occurs without scarring, but hypopigmented macules may persist.

Annular, concentric lesions with elevated blistering periphery in a wood-grain pattern are anecdotally described in BSLE patients, particularly on acral sites [10]. The histopathology of BSLE demonstrates a predominance of neutrophils in the upper dermis, micro abscesses concentrated within dermal papillae, subepidermal blistering, dermal edema, and perivascular inflammatory infiltrate. Large deposits of mucin in the reticular dermis are a distinguishing feature [11]. The pathogenesis of BSLE is likely related to autoantibodies to type VII collagen, particularly non-collagenous domain types 1 and 2. Type VII collagen is a major component of anchoring fibrils that attach the dermis to the epidermis [7,12]. Autoantibodies may also target laminin-5, laminin-6, and BP antigen 1. Complement is found almost exclusively in perilesional tissue, supporting the theory that antibody-mediated complement activation causes bulla formation. Erythema Gyrratum Repens shows nonspecific histology findings, mainly demonstrating mild parakeratosis and perivascular lymphocytic infiltrates in the superficial dermis [3]. The presented patient exhibited a unique combination of histological features with a predominance of neutrophils and blisters arranged in an EGR pattern. Despite recent scientific knowledge, SLE pathogenesis remains obscure. Loss of tolerance to chromatin is considered the cornerstone, with key triggers including hereditary overproduction of IFN-I, defects in apoptosis, opsonins, or chromatin clearance [13]. B cell-Activating Factor (BAFF) and Type I Interferon Receptor 1 (IFNAR1) play crucial roles [14]. IFNAR1 signaling is central in monogenic interferonopathy-related SLE, involved in innate sensing of self-chromatin and priming adaptive anti-chromatin immunity [15,16]. Toll-like receptor 7, a viral RNA recognition receptor, plays a key role in driving murine and human SLE and is resistant to glucocorticoids [17]. IFNAR1 mediates SLE activity when chromatin release into the extracellular space boosts anti-chromatin immunity, as seen in cell death related to sunburns or trauma. Viral infection-related flares of SLE likely involve IFNAR1. Recent studies proved that local IFNAR1 activation may occur in organs like the skin, synovium, central nervous system, kidneys, and blood vessels due to infection, UV light, or plasmacytoid dendritic cell migration [18]. BAFF-related B cell functions, including antigen presentation, production of autoantibodies, and circulating immune complexes, predominate as drivers of human SLE activity. Flares of SLE activity involve BAFF-dependent B cell functions, such as autoantigen presentation and expansion of autoreactive T and B cell clones [19].

## Conclusion

While both BAFF and IFNAR1 play crucial roles in SLE pathogenesis, BAFF is primarily associated with B cell functions driving SLE activity, and IFNAR1 is implicated in flares triggered by viral infections and chromatin release. The expression of IFNAR1 in peripheral tissues may vary in different SLE manifestations, providing insights into potential targeted therapies. Personalized evaluations of risks and benefits, along with collaborative decision-making, are crucial to determine the most suitable treatment for each patient.

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### **Citation of this Article**

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