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Lupus erythematosus-specific bullous lesions

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Abstract

Lupus erythematosus (LE)-specific bullous lesions are often difficult to distinguish from other bullous diseases presenting in patients with systemic lupus erythematosus. Herein, we describe a 49-year-old woman with systemic lupus erythematosus with recurrent tense bullae on the forearms. Clinical, histopathologic, and serologic findings led to the diagnosis of LE-specific bullous lesions. We also summarize the diagnostic clues for distinguishing LE-specific bullous lesions, bullous systemic lupus erythematosus, and erythema multiforme-like lesions in LE (Rowell syndrome).

Keywords: bullous lupus, blistering disease, lupus erythematosus, Rowell syndrome

Introduction

Lupus erythematosus (LE)-specific bullous lesions represent a distinct but underrecognized specific cutaneous manifestation of LE. However, bullous systemic lupus erythematosus (BSLE) and LE-specific bullous lesions can be difficult to distinguish, given that both manifest as tense vesicles and blisters. Notably, erythema multiforme-like (EM) lesions in LE (also known as Rowell syndrome) are also characterized by interface dermatitis. In this report, we describe an example of LE-specific bullous lesions in a patient with SLE.

Case Synopsis

A 49-year-old woman with a history of SLE on mycophenolate mofetil presented with recurrent episodes of bullae on the forearms. She denied any additional prescription or over-the-counter medications. On examination there were several tense bullae with surrounding erythema involving the right forearm (**Figure 1**). There was no mucosal involvement. Laboratory evaluation was significant for a speckled pattern of antinuclear antibody (ANA, titer 1:1280), anti-ribonucleoprotein (RNP)titer 232 (normal <20), and anti-Sjögren-syndrome-related antigen A (SSA) titer 90 (normal <20). Rheumatoid factor (RF) and double stranded DNA (dsDNA) were negative. Indirect immunofluorescence was negative for circulating antibodies directed against basement membrane zone antigens and enzyme-linked immunosorbent assay (ELISA) was negative for anti-collagen VII antibodies. Histopathology demonstrated epidermal necrosis, interface tissue reaction, and a perivascular and periadnexal lymphocytic infiltrate (**Figures 2-4**). Direct immunofluorescence (DIF) of perilesional, involved skin demonstrated granular IgG deposition along the basement membrane zone. Immunohistochemistry for collagen IV, a lamina

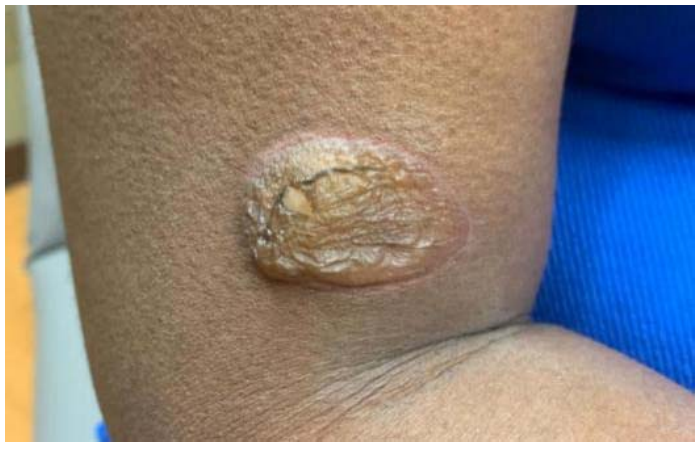

Figure 1. *Tense bulla on the arm.*

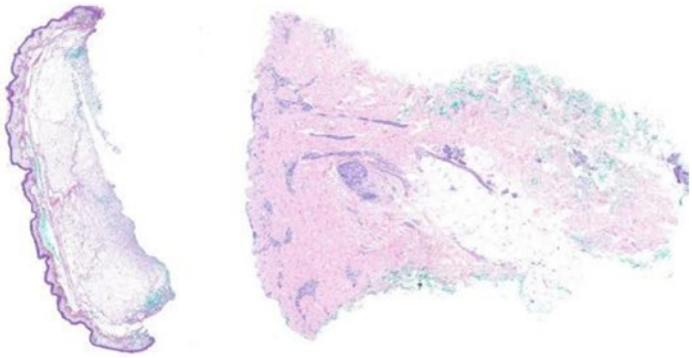

Figure 2. *Subepidermal separation and a superficial and deep perivascular and periadnexal lymphocytic infiltrate. H&E, 20×.*

densa protein, performed on lesional skin demonstrated staining along the dermal side of the blister, consistent with a cleavage plane above the lamina densa. Given the clinical, histopathologic, and serologic findings, a diagnosis of LE-specific bullous lesions was made. Prednisone 0.5mg/kg/day tapered over two weeks produced resolution.

Case Discussion

The differential diagnosis of bullous eruptions in patients with SLE can be challenging. Our patient presented with an acute onset of tense bullae in a photoexposed distribution. When observing blistering eruptions in the setting of SLE, one should consider the differential diagnosis of EM-like lesions in LE (Rowell syndrome), bullous systemic lupus erythematosus (BSLE), and LE-specific bullae. **Table 1** summarizes and compares the clinical, histopathologic, and serologic features of these disorders.

Rowell syndrome (RS) is defined as episodes of recurring EM-like lesions without an identifiable cause in patients with LE [1]. Rowell syndrome is also characterized by an interface dermatitis, positive RF, positive anti-SSA, and speckled pattern of ANA [2]. Importantly, targetoid dusky lesions which simulate EM are a major criterion for the diagnosis of Rowell syndrome and were lacking in the patient described here [1].

Bullous systemic lupus erythematosus is a rare autoimmune blistering disease caused by circulating autoantibodies directed against collagen VII and occurs in less than 5% of patients with SLE. Bullous systemic lupus erythematosus can be the initial presenting symptom of SLE and often represents uncontrolled systemic disease and correlates with autoimmunity against dsDNA [3]. Bullous systemic lupus erythematosus presents with tense bullae on sun exposed and sun protected including flexural skin. Histopathology consistently demonstrates a subepidermal blister with neutrophils; interface tissue reaction and mucin are variable. The cleavage plane is beneath the lamina densa. Direct immunofluorescence demonstrates linear or granular deposition of IgG at the dermoepidermal junction; in vivo ANA and granular deposition of IgM, IgA, or C3 are variable [4-5]. In the case presented here, a cleavage plane above the lamina densa and

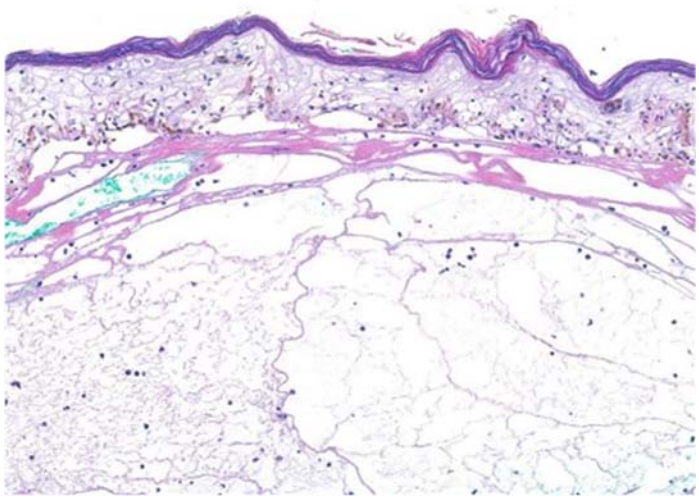

Figure 3. *Full thickness epidermal necrosis overlying a subepidermal blister with edema, fibrin, and mixed inflammation. H&E, 200×.*

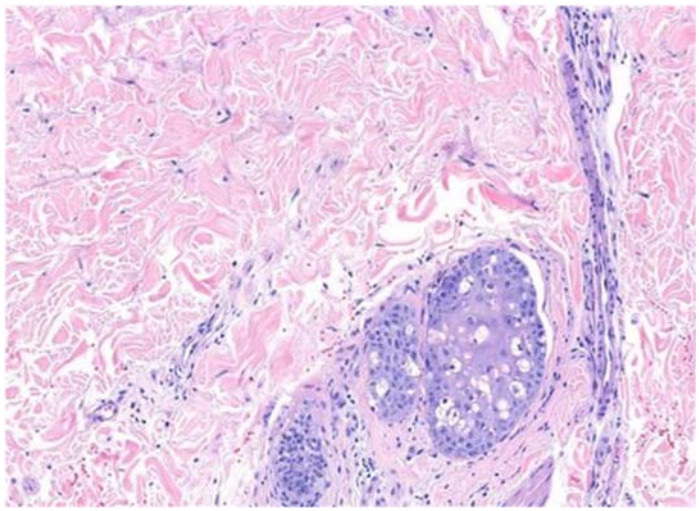

Figure 4. *Vacuolar interface dermatitis affecting the follicular epithelium and dermal mucin. H&E, 200×.*

Table 1. *Summary of distinguishing factors between Lupus erythematosus-specific bullous lesions, bullous lupus erythematosus, and Rowell syndrome.*

	Lupus erythematosus-specific bullous lesions	Bullous lupus erythematosus	Rowell syndrome
Histopathology	Interface dermatitis, extensive basal cell vacuolization, and apoptotic keratinocytes; lymphocytic infiltrate [2]	Subepidermal blister with neutrophils; can psimulate dermatitis herpetiformis due to prominent involvement of dermal papillae [2]	Apoptotic keratinocytes or full thickness epidermal necrosis, interface dermatitis, and a perivascular lymphocytic infiltrate [1,3]
Serology	Negative IIF and ELISA for anti-collagen VII; also less likely to be have positive ANA or anti-dsDNA antibodies [2]		Serology
Clinical manifestations	Tense bullae with an erythematous base	Tense bullae with a predilection for trunk, upper extremities, flexures, neck, face, and vermillion border	EM-like (targetoid, dusky) patches or plaques; chilblains [1]

IIF, Indirect immunofluorescence; ELISA, enzyme-linked immunosorbent assay; ANA, antinuclear antibody; dsDNA, anti-double stranded DNA; SSA, Sjögren's-syndrome-related antigen A; RF, rheumatoid factor; SSS, NaCl-split skin substrate; EM, erythema multiforme.

the absence of anti-collagen VII autoantibodies exclude BSLE.

Lupus erythematosus-specific bullous lesions are a specific manifestation of LE characterized by interface dermatitis and a lymphocytic infiltrate [3]. Robust interface tissue reaction leads to degeneration of the basilar epidermis, resulting in dermoepidermal separation and subsequent bulla formation. Lupus erythematosus-specific bullous lesions can be divided into three subtypes which include subacute cutaneous LE-associated bullous lesions, acute cutaneous LE-associated bullous lesions, and chronic LE-associated bullous lesions, all of which share the presence of exuberant interface dermatitis [2]. Direct immunofluorescence of LE-specific bullous lesions is nonspecific and demonstrates granular deposition of IgG, IgM, IgA, or C3 at the dermoepidermal junction (lupus band), [3,5]. Direct immunofluorescence does not distinguish BSLE from LE-specific bullous lesions [3].

Conclusion

Lupus erythematosus-specific bullous lesions require differentiation from BSLE and EM-like lesions in LE (Rowell syndrome).

Potential conflicts of interest

The authors declare no conflicts of interest.

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