Systemic lupus erythematosus–associated neutrophilic dermatosis with palmoplantar involvement

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INTRODUCTION

Neutrophilic infiltrates in the setting of systemic lupus erythematosus (SLE) are commonly associated with bullous or vasculitic disease. Recently, an increasing number of reports describe a nonbullous, nonvasculitic SLE-associated neutrophilic dermatosis. Prior cases of SLE-associated neutrophilic dermatosis describe an urticarial eruption involving the trunk and extremities. Here we report the case of a 27-year-old woman with SLE-associated neutrophilic dermatosis with palmoplantar involvement, thus, expanding the clinical spectrum of this disease. Neutrophilic dermatosis may represent the initial cutaneous manifestation of systemic disease in one-third of patients. Thus, prompt recognition of this distinct cutaneous entity should promote screening for SLE.

CASE REPORT

A 27-year-old woman with a 9-month history of SLE was admitted to the hospital with 4 days of worsening pleuritic chest pain, dyspnea, and arthralgias. She also had a 1-day history of a burning, annular eruption on her trunk, palms, and soles. Upon admission, the patient was found to have recurrent pericardial and bilateral pleural effusions in the setting of an acute SLE flare. Although complete blood count and basic metabolic panel were unremarkable, the patient's anti–double-stranded DNA antibody was 266 IU/mL, C3 was 41.4 mg/dL (laboratory-specific reference range, 90–180 mg/dL), and C4 was 6.62 mg/dL (laboratory-specific reference range, 10–40 mg/dL).

Abbreviations used:

BMZ:	basement membrane
DEJ:	dermoepidermal junction
DIF:	direct immunofluorescence
LE:	lupus erythematosus
SLE:	systemic lupus erythematosus

From prior workup of SLE, antinuclear antibody was 1:640 with speckled pattern and was anti-Smith antibody positive and antiribonucleoprotein antibody positive. Anti–SS-A antibody was 7.3 (normal <0.9 antibody index) and anti–SS-B antibody was 0.6 (normal <0.9 antibody index). Erythrocyte sedimentation rate was 45 mm/h.

On physical examination, the patient had blanchable, erythematous macules and annular, urticarial papules and plaques bilaterally distributed on the palmoplantar surfaces (Fig 1). Additionally, there were faint, blanchable, erythematous macules on the chest and back. Shave biopsy findings of the left plantar surface showed neutrophils aligned along the dermoepidermal junction (DEJ) associated with vacuolar alteration and rare dyskeratosis (Fig 2). There was also a superficial, perivascular, and interstitial predominantly neutrophilic infiltrate with lymphocytes and leukocytoclasia, without vasculitis or a significant increase in dermal mucin (Fig 3).

At the time of presentation, the patient was taking hydroxychloroquine (200 mg twice daily), prednisone (50 mg/d), omeprazole, atovaquone, and cholecalciferol. She was treated with intravenous methylprednisolone and underwent a thoracentesis

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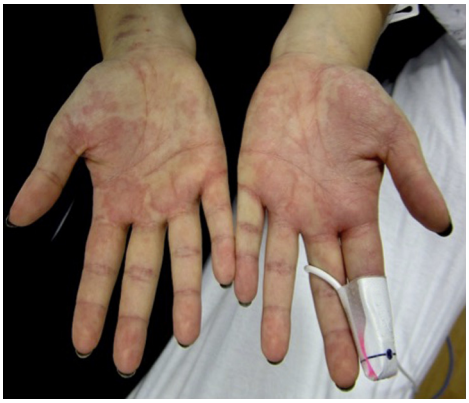

Fig 1. SLE-associated neutrophilic dermatosis. Erythematous macules and annular, urticarial papules and plaques bilaterally distributed on the palmar surfaces.

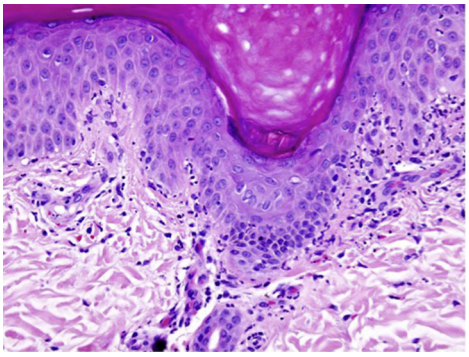

Fig 2. Acral skin with neutrophils aligned along the DEJ associated with vacuolar alteration and rare dyskeratosis. (Hematoxylin-eosin stain.)

with improvement in respiratory status and resolution of chest pain. Palmoplantar surfaces were treated with clobetasol ointment twice daily with only modest improvement; however, shortly after an increase in systemic glucocorticoids and the initiation of mycophenolate mofetil, the eruption subsided. At 5-month follow-up, the patient remained free of the cutaneous eruption while maintained on hydroxychloroquine (200 mg twice daily) and mycophenolate mofetil (1500 mg twice daily). Methylprednisolone had been tapered down to 10 mg daily.

DISCUSSION

Ackerman was among the first to consider SLE in the histologic differential diagnosis of nonbullous, nonvasculitic neutrophilic inflammatory dermatosis.[1,2] He described the presence of neutrophils and neutrophilic dust immediately beneath the epidermis of an interface dermatitis and postulated that these histopathologic features may represent a "muted" expression of bullous SLE.[2] The first clinical

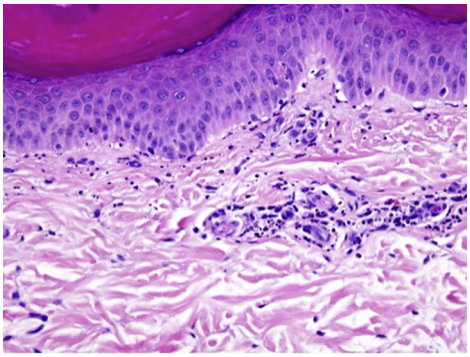

Fig 3. Neutrophil-medicated vacuolar alteration along the DEJ with a necrotic keratinocyte. There is also a perivascular and interstitial neutrophilic infiltrate with leukocytoclasia in the absence of vasculitis. (Hematoxylin-eosin stain.)

case of SLE associated with a Sweet's syndrome–like dermatosis was reported in 1985.[3] Since then, close to 50 cases of SLE-associated neutrophilic dermatosis distinct from Sweet's syndrome, pyoderma gangrenosum, and bullous lupus erythematosus (LE) have been reported.[3-8]

The literature on neutrophil-dominant manifestations of SLE is fraught with confusion, in part because of the overlap in terminology. A variety of terms have been used to describe nonbullous, nonvasculitic, neutrophilic dermatosis and include nonbullous neutrophilic dermatosis, nonbullous neutrophilic LE, Sweet's syndrome–like neutrophilic dermatosis, and SLE-associated neutrophilic dermatosis. However, reproducible clinical and histopathologic reports confirm that SLE-associated neutrophilic dermatosis represents a distinct entity that is closely associated with and may herald the development of systemic disease.[4-8] Clinical and histopathologic differential diagnoses of SLE-associated neutrophilic dermatosis are vast (Table 1).[8-10] Although there are no known prognostic or therapeutic differences for SLE-associated neutrophilic dermatosis, recognition of this distinct cutaneous entity should prompt screening for SLE.

The cutaneous findings of SLE-associated neutrophilic dermatosis include erythematous papules and plaques, many of which are described as urticarial and some of which have an annular morphology, most commonly involving the trunk and extremities, and without bulla formation or mucosal involvement.

Histopathologic features include an interstitial and perivascular predominantly neutrophilic infiltrate with leukocytoclasia and variable vacuolar alteration along the DEJ, without the presence of vasculitis or bullae.[5] The degree of neutrophilic infiltrate varies from paucicellular to cell rich Sweet's syndrome like, which suggests a spectrum

Table I. Clinical and histopathologic differential diagnoses of SLE-associated neutrophilic dermatosis with separate discussion for generalized and palmoplantar cutaneous eruptions

Diagnosis	Clinical features	Histopathologic features
SLE-associated neutrophilic dermatosis	• Erythematous papules and plaques • Urticarial or annular morphology • Trunk or extremities	• Interstitial neutrophilic infiltrate, leukocytoclasia • ±Vacuolar interface alteration, increased dermal mucin, BMZ thickening, positive DIF (C3, IgG, IgM along DEJ) • No vasculitis or bulla formation
Generalized eruption		
Neutrophilic urticarial dermatosis*[9]	• Erythematous macules or thin plaques • Resolve within 48 hours • Trunk or extremities	• Interstitial neutrophilic dermal infiltrate, leukocytoclasia • No vasculitis
Neonatal lupus erythematosus*	• Erythematous macules, papules, plaques • Head and neck, ±trunk, extremities • Maternal history of anti-Ro/SS-A lupus	• Interstitial neutrophilic infiltrate • ±Vacuolar interface alteration, increased dermal mucin
Bullous SLE*	• Widespread, symmetric, vesiculobullous eruption • History of SLE or SLE-related manifestations • Mucosal involvement often observed	• Subepidermal neutrophil-mediated separation • Interstitial neutrophilic infiltrate
Dermatitis herpetiformis	• Erythematous excoriated papules, plaques • Symmetric distribution over extensor surfaces	• Neutrophilic microabscesses in papillary dermis • Leukocytoclasia • ±Eosinophils • Granular IgA deposits in dermal papillae
Linear IgA bullous dermatosis*	• Vesicles or bulla on erythematous or urticarial skin, often annular or polycyclic • Trunk and limbs, ±mucosal involvement	• Neutrophils aligned along DEJ • Interstitial neutrophilic infiltrate with admixed eosinophils • ±Subepidermal blistering • IgA deposits in linear pattern along DEJ
Still's disease	• Evanescent, salmon-pink erythema that waxes and wanes with fever • Favor the extremities • Intermittent high fevers ± arthralgia	• Paucicellular to moderately cellular neutrophilic infiltrate in papillary dermis • ±Vacuolar interface alteration
Behcet's disease	• Aphthous or herpetiform ulcers in oral cavity and genitalia • ±Pseudofolliculitis, acneiform lesions • Erythema nodosum	• Cell-rich or Sweet's-like neutrophilic infiltrate • ± Suppurative folliculitis or vasculitis
Pyoderma gangrenosum*	• Deep ulceration with violaceous, undermined border • Pathergy	• Cell-rich pan-dermal neutrophilic infiltrate • No vasculitis
Sweet's syndrome*	• Erythematous to violaceous edematous papules, plaques, nodules • Fever • Leukocytosis	• Cell-rich neutrophilic infiltrate with leukocytoclasia • Papillary dermal edema • No vasculitis

Continued

Table I. Cont'd

Diagnosis	Clinical features	Histopathologic features
Palisaded neutrophilic and granulomatous dermatitis*	• Symmetrically distributed umbilicated papules • Favor extensor surfaces of the extremities	• Palisaded granulomas with neutrophils • Variable small vessel leukocytoclastic vasculitis
Leukocytoclastic vasculitis*	• Palpable purpura • ±Urticarial lesions	• Perivascular small vessel neutrophilic infiltrate with extension into vessel walls • Leukocytoclasia • Fibrinoid necrosis of vessel walls • Extravasation of erythrocytes
Hypocomplementemic urticarial vasculitis*[10]	• Painful, pruritic urticarial papules • Persist for >24 hours • Hyperpigmentation after resolution • Hypocomplementemia with low C1q, C3, C4 • Positive C1q antibody	• Small vessel leukocytoclastic vasculitis • Variable, perivascular neutrophilic infiltrate
Palmoplantar eruption		
Palmoplantar eccrine hidradenitis	• Abrupt onset of erythematous, tender papules, nodules • Most commonly in children	• Neutrophilic peri-eccrine infiltrate • ±Mixed perivascular infiltrate
Palmoplantar pustulosis	• Persistent, painful sterile pustules that coalesce • Resolve to brown macules and hyperkeratosis	• Intraepidermal pustules • Spongiform alterations • ±Mixed perivascular infiltrate
Erythema multiforme	• Erythematous targetoid papules and plaques • ±Mucosal ulceration	• Vacuolar interface dermatitis with conspicuous keratinocyte necrosis • Sparse superficial perivascular lymphocytic infiltrate

BMZ, basement membrane; *DIF*, direct immunofluorescence.
*Neutrophil-dominant dermatoses that may occur in association with SLE.

of neutrophilic dermatoses within SLE patients. Perivascular lymphocytes are also typically present in small numbers. Histopathologic changes that are consistent with SLE, such as interface changes, dermal mucin, and basement membrane thickening, are variably present. When performed, direct immunofluorescence is positive for immunoreactants at the DEJ in 50% of cases, with deposition of C3, IgG, and IgM along the DEJ.[8] Currently, treatment is targeted at the underlying disease, and the eruption usually responds to immunomodulatory or immunosuppressive therapy.[6]

The pathogenesis of these nonbullous lesions remains unclear. Many patients develop the eruption while on immunosuppressive therapy, which may inhibit the formation of bullae and supports the idea of a forme fruste variant of bullous LE, as suggested by Ackerman.[2] Other patients have the eruption as the presenting symptom of SLE without concurrent systemic therapy, suggesting that this could be a distinct cutaneous manifestation of SLE. Although absent in some cases, histopathologic findings characteristic of SLE, such as vacuolar alteration and immunoreactants along the DEJ, raise the possibility of an antibody-mediated pathogenesis. The occurrence of this entity in patients with other autoimmune connective-tissue disorders, such as rheumatoid arthritis, Still's disease, and Sjögren's syndrome, has been reported, suggesting that the disorder represents a clinicopathologic response in individuals predisposed by diverse autoimmune connective-tissue disorders and not exclusively SLE.[6]

This case shows unique palmoplantar involvement of SLE-associated neutrophilic dermatosis. Increased awareness and recognition of the clinical spectrum of neutrophilic dermatoses in the setting of SLE is imperative, particularly in the one-third of cases in which cutaneous manifestations are the presenting symptoms of systemic disease.

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