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Case Report

A Diagnostic Conundrum: Unusual Presentation of Acute Cutaneous Lupus Erythematosus Mimicking Toxic Epidermal Necrolysis

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Abstract

Systemic lupus erythematosus (SLE) is an intricate autoimmune disorder with diverse clinical presentations, encompassing various cutaneous manifestations. This case report describes a diagnostically challenging occurrence of acute cutaneous lupus erythematosus (ACLE) exhibiting a toxic epidermal necrolysis (TEN)-like rash in a 28-year-old female already diagnosed with SLE. The patient's rapid progression from itching to maculopapular skin eruptions involving the face, extremities, and torso within days, coupled with facial puffiness and systemic symptoms, presented a clinical conundrum. Histopathological findings of epidermal hyperkeratosis, acanthosis, and a subcorneal neutrophilic abscess guided the exclusion of other conditions, emphasizing the distinctive features of TEN-like ACLE. The patient exhibited a favorable response to pulse methylprednisolone, mycophenolate mofetil, and hydroxychloroquine.

Keywords: Systemic lupus erythematosus, acute cutaneous lupus erythematosus, toxic epidermal necrolysis (TEN)-like rash, histopathology, pulse methylprednisolone, immunosuppressants

Introduction

Systemic lupus erythematosus (SLE) presents with a wide array of cutaneous manifestations. Acute cutaneous lupus erythematosus (ACLE) can be the initial presentation or can occur as a disease flare. Clinical manifestations include malar erythema, maculopapular rash on photo-exposed areas, bullous lesions, and toxic epidermal necrolysis (TEN)-like rash.

TEN-like ACLE is a very rare manifestation of SLE, and differentiating it from drug-induced TEN is very difficult.[1] Extracutaneous organ involvement is also seen in TEN-like SLE. Diagnosis can be supported by a skin biopsy.

Case Presentation

The patient, a 28-year-old housewife, initially complained of itching over the neck, which rapidly progressed to a maculopapular and painful skin eruption. Within 4 days, the rash extended to the face, upper extremities, torso, and, to a lesser extent, the lower limbs. Concurrently, the patient experienced facial puffiness, low-grade intermittent fever, and anorexia. A history of postpartum cardiomyopathy and recent hospitalization for pneumonia with hydropneumothorax added complexity to the medical background. She was diagnosed with SLE and hypothyroidism during a previous hospitalization and was started on steroids and hydroxychloroquine (HCQs) and mycophenolate mofetil (MMF) in a low dose. However, she stopped medications on her own. One month later, she presented with the above-mentioned skin involvement. She denied any history of over-the-counter medications or antibiotics. Notably, she denied any other rheumatological, respiratory, or neuropsychiatric symptoms of an SLE flare.

Upon physical examination, the patient exhibited erythematous and dusky macules and papules with mild desquamation, predominantly affecting the face, neck, abdomen, and chest. Superficial necrosis was observed on the flexor and extensor aspects of the extremities. Hemorrhagic crusts, petechiae, and purpura were evident on the palms and soles, accompanied by purulent discharge from the eyelids and hemorrhagic crust over the lips (Figure 1). Notably, there was no peeling of the skin or targetoid lesions. There

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were no corneal ulcers. Given the severity and clinical features, a probable diagnosis of TEN or TEN-like ACLE was considered.

Laboratory investigations at our facility revealed low hemoglobin (7.3 gm/dL), leucopenia (2.5 × 10^3/L), and thrombocytopenia (96 × 10^3/L). The erythrocyte sedimentation rate was elevated (38 mm/h). Hypoalbuminemia (1.69 g/dL) and hypokalemia (2.9 mmol/L) were noted, along with elevated 24-hour urine protein of 340.2 mg/kg/day. Specific autoantibodies testing revealed positive double-stranded DNA antibodies, positive Ro antibodies, positive U1 snRNP antibodies, positive SmD1 antibodies, positive La antibodies, and positive DFS-70 antibodies. Anti-Jo antibody was negative, excluding drug-induced SLE. Additionally, skin biopsy findings included epidermal hyperkeratosis, acanthosis, and a subcorneal neutrophilic abscess in the stratum corneum, supporting the diagnosis of TEN-like ACLE.

Histopathological examination of the skin biopsy played a pivotal role in distinguishing TEN-like ACLE from other conditions. Biopsy findings were suggestive of epidermal hyperkeratosis, acanthosis, and preserved granular layer. The stratum corneum showed collection of dense neutrophilic exudate and abscess. The superficial dermis showed mild perivascular and peri-adnexal neutrophilic infiltrate. The deeper dermis appeared unremarkable. No interface dermatitis or basal cell layer vacuolar degeneration was seen. There wasn't any destruction of superficial vessel walls. No bullae were seen at the dermo-epidermal junction (Figure 2).

Management involved a multidisciplinary approach. The patient was treated in the intensive care unit with higher antibiotics, fluid resuscitation, and local skin care. The patient responded positively to pulse methylprednisolone. This was followed by oral prednisolone, mycophenolate mofetil, and hydroxychloroquine. Rituximab therapy was deferred as she had systolic cardiac dysfunction revealed on echocardiography.

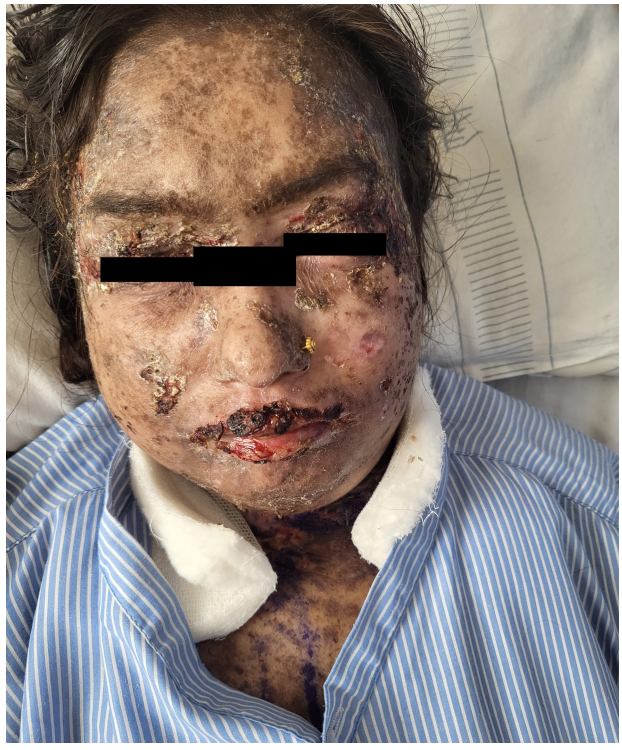

Figure 1. Erythematous scaly rash over the face and neck with ruptured vesicles and bullae with crusting and bleeding, causing facial, periorbital, and lip edema.

The skin lesions healed completely after 1 month (Figure 3A and B).

On follow-up, the patient was symptomatically better. Her oral steroids were tapered to Tab prednisolone 10 mg daily, and mycophenolate mofetil was de-escalated and continued at a dose of 500 mg twice daily. Hydroxychloroquine and local treatment by a dermatologist were continued.

Written informed consent has been obtained from the patient to publish the photographs and case details. This study was approved by the Ethics Committee of AIIMS Nagpur (Approval No: IEC/Pharmac/2023/1141, Date: 09/12/2023).

Discussion

Systemic lupus erythematosus (SLE) is renowned for its heterogeneity, presenting with diverse clinical manifestations that include predominantly cutaneous involvement. Between 59% and 85% of SLE patients have cutaneous manifestations, which occur as chronic lupus erythematosus, subacute lupus erythematosus, and acute lupus erythematosus. All 3 have subtypes that can occur independently or with SLE. Acute cutaneous lupus erythematosus (ACLE) is an uncommon

Main Points

- Rare presentation of ACLE with TEN-like vesiculobullous eruptions and mucocutaneous involvement
- Significance of histopathological findings in differentiating ACLE from TEN
- Favorable outcome of ACLE with pulse methylprednisolone and immunosuppressant mycophenolate mofetil

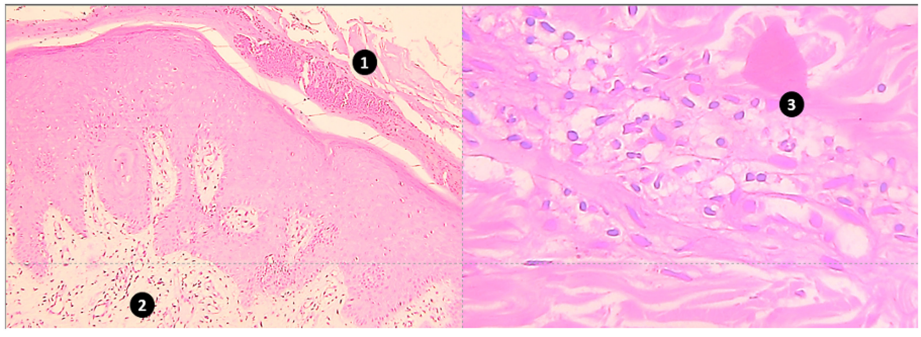

Figure 2. Hematoxylin and eosin-stained section of skin showing epidermis and dermis along with hyperkeratosis in the epidermis with the presence of neutrophils in the stratum corneum, moderate perivascular mixed inflammation around superficial dermal vessels, and perivascular inflammation composed of lymphocytes and neutrophils.

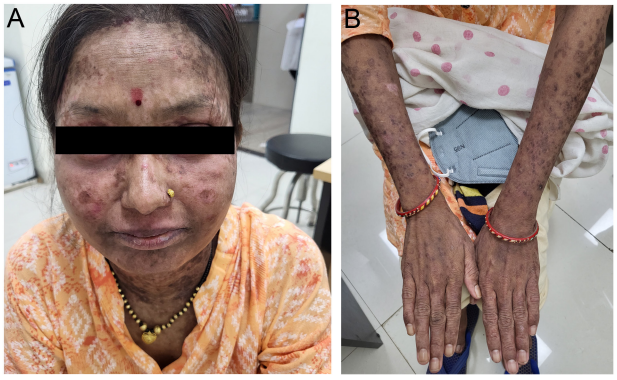

Figure 3. After 1 month: (A) complete healing of facial lesions; (B) healing of lesions over forearms with postinflammatory hyperpigmentation.

manifestation, and its presentation as toxic epidermal necrolysis (TEN)-like lesions is rarer. Less than 5% develop vesiculobullous lesions, which manifest in the form of vesicles, bullae, erosion, and crust. [1] It poses a diagnostic challenge. In this case, the patient exhibited a unique combination of ACLE and a rash resembling TEN, emphasizing the importance of a comprehensive diagnostic approach.

The patient was a known case of SLE, proven by the presence of autoantibodies and other clinical manifestations. She had multiorgan involvement and had received steroids for a short time. She was non-compliant with the prescribed treatment. When she presented with acute cutaneous lesions, it could have been an acute flare of lupus or TEN secondary to infection or drug induced. The diagnostic dilemma in this case was distinguishing between ACLE with TEN-like features and true TEN. The literature reveals that TEN-like ACLE is a rare occurrence, with only 43 reported cases, predominantly affecting women.[2]

Ting et al[3] proposed the term "acute syndrome of apoptotic pan-epidermolysis" (ASAP) to describe conditions with TEN-like presentation, emphasizing the hyper-acute apoptotic injury leading to massive cleavage of the epidermis. The proposed classification includes classic TEN, lupus erythematosus (LE), acute graft-versus-host disease, and pseudoporphyria as potential causes of ASAP.

There are other distinguishing factors concerning the pathogenesis of SLE and TEN; in SLE, the key element is the ultraviolet light that increases the levels of chemokine CCL27 and induces keratinocyte apoptosis. Moreover, TEN is associated with specific haplotypes affecting drug metabolism and high levels of granulysin, which is the most critical cytotoxic molecule in TEN induced apoptosis.[4]

Clinically, the patient's hemodynamically stable condition, lack of culprit drugs, and limited mucosal involvement favored the diagnosis of ACLE over TEN. These findings align with the observations by Merklen-Djafri et al, where patients with TEN-like ACLE had an acute or prior SLE diagnosis, sheet-like skin detachment, and a photo-distributed pattern of skin lesions.[5]

Histopathological findings played a pivotal role in the diagnosis. The main differential diagnoses of TEN-like ACLE on histopathology are TEN and drug-induced TEN. The histopathological features on skin lesion biopsy in TEN are full-thickness epidermal necrosis with sparse to absent lymphocytic infiltrate. In drug-induced TEN, there is extensive epidermal necrosis and vacuolar degeneration of basal keratinocytes. Direct immunofluorescence is negative in TEN and drug-induced TEN. In our case, the skin biopsy revealed epidermal hyperkeratosis, acanthosis, and a preserved granular layer. Perivascular inflammatory infiltrate with lymphocytes was seen. Notably, a subcorneal neutrophilic abscess was observed, aligning with the findings in other cases of TEN-like ACLE reported in the literature.[3,5] This unique histological feature, combined with the clinical presentation, led to the exclusion of other conditions like drug reactions or pseudo porphyria.

Romero et al[2] in their case series indicated that 60% of their patients had a confirmed diagnosis of SLE prior to developing TEN-like ACLE, highlighting the importance of recognizing and managing cutaneous manifestations in SLE patients. The absence of eosinophils and dermal edema on histopathology, along with a low score on the RegiSCAR criteria,[6] ruled out drug reaction with eosinophilia and systemic symptoms (DRESS) in our case.

Interestingly, the skin biopsy in our case revealed a subcorneal neutrophilic abscess, a finding shared with the skin lesion biopsy of SLE patients in studies by Freire et al[7] and Gheisari M et al[8] Additionally, the patient's non-compliance with medications may have triggered the TEN-like ACLE lesions.

Systemic corticosteroids remain the mainstay of therapy for SLE, with skin changes responding in tandem with the systemic response. Additional immunosuppressive agents, including MMF, are used as adjuvant therapy for their steroid-sparing effects. Hydroxychloroquine, as highlighted in a 2017 meta-analysis, plays a beneficial role in treating skin lesions of ACLE, being 2.5 times more effective compared to other lupus cutaneous skin lesion types.

In conclusion, the presented case underscores the diagnostic challenges in differentiating TEN-like ACLE from true TEN. Comprehensive clinical, histopathological, and laboratory evaluations are crucial for accurate diagnosis and appropriate management. The successful outcome with pulse methylprednisolone, MMF, and HCQ supports the effectiveness of this therapeutic approach in TEN-like ACLE. Awareness of such atypical presentations is essential for clinicians to enhance early recognition and prompt intervention in SLE patients with cutaneous manifestations.

Ethics Committee Approval: This study was approved by the Ethics Committee of AIIMS Nagpur (Approval No: IEC/Pharmac/2023/1141, Date: 09/12/2023).

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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