



# Toxic Epidermal Necrolysis-like Subacute Cutaneous Lupus Erythematosus: A Case Report

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## Case Report

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## Abstract

Toxic epidermal necrolysis (TEN)-like lesions have been described in the setting of lupus erythematosus, and have been considered as a specific hyperacute variant of cutaneous lupus erythematosus, with features different from classical drug-related toxic epidermal necrolysis.

This is a report of a case of subacute cutaneous lupus erythematosus in a 62-year old Caucasian woman, which evolved into a TEN-like presentation over the course of 4 weeks. The patient responded rapidly to treatment with high doses of prednisone.

**Keywords:** Toxic Epidermal Necrolysis; Subacute Cutaneous Lupus Erythematosus; Chloroquine; Prednisone

**Abbreviations:** TEN: Toxic Epidermal Necrolysis; LE: Lupus Erythematosus; UV: Ultraviolet; ANA: Antinuclear Antibodies; ASAP: Acute Syndrome of Apoptotic Pan-Epidermolysis; SCLE: Subacute Cutaneous Lupus Erythematosus; DIF: Direct Immunofluorescence; SSA/SSB: Sjögren's-Syndrome-Related Autoantibodies.

## Introduction

Cutaneous lupus erythematosus (LE) includes a wide spectrum of dermatologic manifestations [1]. A bullous eruption in the setting of lupus erythematosus can be a diagnostic challenge. The toxic epidermal necrolysis (TEN)-like presentations of acute or subacute cutaneous lupus erythematosus (TEN-like ACLE/SCLE) may closely mimic TEN [2,3]. Although the clinical and histological features of these rare conditions are very similar, several subtle differences can help in differentiation between them. In contrast to classic TEN, whose occurrence is usually associated with drug ingestion, TEN-like ACLE/SCLE are often triggered by extensive ultraviolet (UV) exposure and

the blistering eruption typically starts on UV-exposed areas [4]. A previous history of LE and lupus-specific response in histopathological finding could be additional clues for diagnosis of TEN-like LE. Also, the course of TEN-like LE is usually subacute, systemic symptoms (seen in TEN) are absent and mucous membranes are spared or mildly affected [5]. However, in some cases it can be difficult to distinguish these unusual, vesiculobullous forms of LE from classical TEN both clinically and histopathologically.

## Case Report

This is a report of a case of SCLE in a 62-year old Caucasian female, which gradually evolved into a TEN-like expression over the course of 4 weeks after prolonged sun exposure and irregular medication intake (chloroquine and prednisone). There was no history of recent infection or drug intake. The patient had a 3 months history of SCLE characterized by photo distributed annular and polycyclic erythematous plaques. The diagnosis was confirmed by histopathological examination and direct immunofluorescence of skin

lesions that were consistent with LE. Lupus band test on sun-protected non-lesional skin was negative. Antinuclear antibodies (ANA) and anti-Ro (SS-A) antibodies were elevated (1: 160 and 73.4 RU/ml, respectively). No other laboratory abnormalities were detected. She was treated with chloroquine and low/ mid dose systemic steroids (prednisone, 0.3-0.4 mg/kg/daily).

On physical examination the patient had symmetrically distributed, mostly dusky erythematous plaques and areas on the face, neck, trunk and extremities, with erosions and skin shedding (Figures 1a-c) and targetoid lesions, mostly on lower extremities (Figure 1d). All visible mucous membranes were unaffected. Nikolsky's sign was mildly positive, mostly on her upper trunk and proximal aspect of extremities. The patient was in good general health.



**Figure 1\*:** a, b and c) symmetrically distributed, mostly dusky erythematous plaques and areas on the face, neck, trunk and extremities, with erosions and skin shedding; d) targetoid lesions on lower extremities.

\*Photos taken 5 days upon admission.

Direct immunofluorescent test of the skin lesion was negative (probably due to prior treatment with systemic steroids). Laboratory investigations demonstrated normal complete blood cell count, serum chemistry, renal function

tests and urinalysis.

Histopathology showed numerous necrotic keratinocytes as well as extensive epidermal necrosis. Also, there was a superficial scarce perivascular and periadnexal infiltrate of lymphocytes (Figure 2a and b).

The diagnosis of TEN-like presentation of SCLE was made based on reported history, clinical presentation and histopathological findings.

The treatment with oral prednisone 1.0 mg/kg tapered quickly within next 3 weeks to 0.6 mg/kg then slowly over 2 months and chloroquine 250 mg daily, combined with potent topical steroid therapy, led to rapid improvement over the following week, with complete resolution of skin lesions within 3 weeks (Figures 2c & d).

In the follow-up period of 4 years, she experienced several minor flares of SCLE. Lesions presented as few annular erythematous plaques, localized on shoulders and chest area mainly, resolving on potent steroid ointments and topical calcineurin inhibitors. At present, she is treated with chloroquine, 250 mg daily, with 3 month-breaks per year.



**Figure 2:** a) hyperkeratosis, numerous necrotic keratinocytes as well as focally extensive epidermal necrosis, perivascular infiltrate of lymphocytes, haematoxylin-eosin (HE) x200; b) almost full thickness epidermal necrosis, HEx400; c and d) resolution of skin lesions.

## Discussion

Vesiculobullous skin lesions in the setting of SCLE as well as ACLE, either during the course of the disease or as a part of an initial clinical presentation, are considered as lupus-specific skin eruption as they exhibit typical histopathological features of LE [1,6]. Sontheimer, et al. pointed that lesions are the result of aggressive inflammatory epidermal basal layer damage, occurring as a dramatic extension of the interface dermatitis [1]. Differentiating a bullous eruption in the context of preexisting lupus remains difficult. There are distinguishing features although the differences can be subtle [5].

TEN-like lesions occurring in the context of ACLE/SCLE can create considerable diagnostic difficulties, particularly in the patients without preceding diagnosis of either ACLE or SCLE [3,6,7]. Ting, et al. proposed the term. Acute Syndrome of Apoptotic Pan-Epidermolysis“(ASAP) as a unifying designation for clinical entities characterized with acute and massive cleavage resulting from hyperacute apoptotic injury

of the epidermis [4]. All those entities may simulate TEN, definitive diagnosis may sometimes be impossible since histopathological findings, serology may be identical [7], but they differ widely in term of etiopathogenesis [8]. Although mucosal membrane involvement has been noticed, in TEN-like LE, oral mucosa being most commonly involved, other membranes are not affected [4,9]. The standard treatment of TEN-like ACLE/ SCLE remains controversial; corticosteroids have been shown to have beneficial effects [10].

Histopathological findings of TEN- like ACLE/SCLE demonstrate a full-thickness epidermal necrosis in up to 88% of cases [2]. Features used to differentiate full-thickness epidermal necrosis in the setting of SCLE according to Rayan, et al. are listed in Table 1 [5]. As patients with TEN-like ACLE/SCLE demonstrate full-thickness epidermal necrosis, Nikolsky’s sign is expected to be positive. However, Nikolsky’s sign may be absent, probably depending on the extent of skin lesions [3,5].

	TEN	TEN-like SCLE	SCLE with blisters
Clinical	Flu-like prodrome Dusky macules that coalesce Rapid progression Bullae and sloughing of epidermis	May have preceding diagnosis of lupus Subacute onset and slow progression Bullae and sloughing of epidermis	Annular plaques with vesicles/bullae at border Crusting
Nikolsky sign	positive	Positive or negative	negative
Mucosa membrane involvement	severe	Less severe and predominantly oral mucosa	absent
Serology	Negative	ANA positive	ANA positive Anti SSA/SSB positive in most cases
Histopathology	Full thickness epidermal necrosis with sparse superficial lymphocytic inflammatory infiltrate	Full thickness epidermal necrosis with sparse superficial lymphocytic inflammatory infiltrate Features of interface dermatitis	Basal vacuolar change, epidermal atrophy, dermal oedema and superficial mucin Intense vacuolar degeneration resulting in separation of dermis from epidermis
DIF	negative	May show lupus band	Most cases are positive
Drug etiology	Most cases	No	Reported
Course	Evolves over 3–5 days and heals over 3–4 weeks Scarring may occur Mortality up to 30–40%.	Subacute course with rapid improvement following treatment	May be chronic or with intermittent exacerbations

**Table 1:** Features used to differentiate full-thickness epidermal necrosis in the setting of subacute cutaneous lupus erythematosus (according to Rayan, et al.).

TEN, Toxic epidermal necrolysis; SCLE, Subacute cutaneous lupus erythematosus; DIF, direct immunofluorescence; ANA, Antinuclear antibodies; SSA/SSB, Sjögren’s-syndrome-related autoantibodies.

Our patient demonstrated a classical clinical pattern of SCLE that evolved to TEN over the course of 4 weeks. Although she had extensive skin lesions and positive Nikolsky's sign, she remained systemically well. The course was prolonged and her response to higher dose of prednisone was remarkably fast, which is atypical of classic TEN. Sun-exposed areas were the initial areas of involvement in our patient, suggesting UV exposure to be an important trigger or aggravating factor. Cases of TEN-like ACLE following UV exposure with or without sparing of covered lesions have been reported in up to 85% of patients [2,4]. Romero, et al. described initial TEN-like on preexisting LE lesions [2]. The diagnosis of TEN-like expression of SCLE in our patient and differentiation from classic TEN was made taking in consideration the preexisting SCLE, the subacute progression, photodistribution, positive autoimmune serology, absence of mucosal involvement and systemic symptoms as well as prompt response to systemic steroids. Lack of evidence of high risk drug intake also favor a diagnosis of TEN-like ACLE/SCLE. Our patient met the features highlighted by Rayan, et al. (Table 1) [5].

## Conclusion

TEN-like bullous eruptions in patients with SCLE can mimic TEN, which is usually associated with medication use. This case represents a rare and unusual expression of SCLE and also highlights the difficulties in differentiating between classic drug-induced TEN and TEN-like SCLE. Clinicians rely on corroborative history, positive serology and clinical course with supportive histopathology to make a diagnosis.

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