Case Report

Toxic epidermal necrolysis like acute cutaneous lupus erythematosus or drug induced toxic epidermal necrolysis: case report of a diagnostic dilemma

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disorder causing microvascular inflammation with generation of antinuclear auto-antibodies. It can have varied presentations and its coexistence with other disorders makes diagnosis and management all the more challenging. We describe a young male, known case of SLE and pulmonary tuberculosis on anti-tubercular treatment presenting with sudden onset diffuse maculopapular dusky rash, oral lesions, fever, joint pain and photosensitivity. Positive Nikolsky’s sign on clinical examination, epidermal necrosis on histopathology, negative direct immunofluorescence and Naranjo’s causality assessment clinched the diagnosis of streptomycin-induced toxic epidermal necrolysis (TEN) in SLE. Rash responded rapidly to systemic steroids and discontinuation of anti-tubercular drugs. Rifampicin, ethambutol and isoniazid have been previously incriminated in TEN but streptomycin-induced toxic epidermal necrolysis remains an extremely rare event. TEN like rash of lupus is a rare entity clinically indistinguishable from drug induced TEN. Moreover, TEN is known to occur with increased frequency in connective tissue disorders.

Keywords: Lupus erythematosus, Toxic epidermal necrolysis, Streptomycin

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by autoantibodies causing tissue damage in multiple organs. Skin is the second most commonly affected organ.1 Toxic epidermal necrolysis (TEN) is a life-threatening condition resulting in an acute erythematous blistering eruption.2 TEN-like presentation of LE is believed to occur in patients with subacute or acute cutaneous LE that typically develop features of TEN with unusual progression and apparent absence of high-risk drug ingestion.2 The term acute syndrome of apoptotic pan-epidermolysis (ASAP) has been proposed to include distinct settings of massive apoptotic epidermal injury resulting in extensive shedding (drug induced, LE, graft versus host disease, pseudo porphyria).3 Toxic epidermal necrolysis (TEN) is one of the most dreaded dermatological emergencies. TEN-like rash of lupus, which is clinically indistinguishable from drug-induced TEN, is a rare entity, with less than 50 cases reported worldwide.4,5 However, in some cases, it has also been reported in association with acute graft versus host disease (GVHD).5 Infection, and vaccinations.5,6 TEN is thought to be more prevalent in SLE.9

CASE REPORT

A 23 years old male presented with itchy rash and intolerance to spicy food since, 7-8 days associated with
fever, joint pain and photosensitivity. Detailed past history and scrutiny of old medical records revealed that he had been diagnosed with systemic lupus erythematosus (ANA and dsDNA positive) with lupus nephritis (significant proteinuria, renal biopsy-proven) and pulmonary tuberculosis three years ago. He had been given AKT cat 1 along with IV methylprednisolone 1gm over 3 days and IV cyclophosphamide 500 mg (6 fortnightly pulses).

Dermatological examination showed diffuse erythematous maculo papular rash with dusky hue over face, neck, chest, trunk, upper and lower limbs (Figure 1a) with erosions and crusts over malar area, nose and lip. Upper eyelid and post-auricular areas were spared (Figure 1b). Generalized skin tenderness with positive Nikolsky’s sign on back were elicited. Palmoplantar involvement and buccal mucosal congestion were noted Figure 1 (f and g) other mucosae, nails were normal.

Routine investigations were unremarkable except for anemia. Skin histopathology showed extensive epidermal necrosis, vacuolar degeneration of basal layer, necrotic keratinocytes and lymphocytic tagging at dermo epidermal junction Figure 2 (a and b). Direct immune-fluorescence (IgG, IgA, IgM, C3) was negative. An objective causality assessment using Naranjo rating scale pointed to streptomycin as the culprit drug (highly probable), leading to the diagnosis of toxic epidermal necrolysis (SCORTEN 1) with SLE. AKT was immediately withheld. He was administered injection dexamethasone 6 mg/day tapered to T. Prednisolone 30 mg/d over 2 weeks with complete resolution of lesions. Subsequently he was transferred to pulmonary medicine for management of tuberculosis.

**DISCUSSION**

Vesiculobullous lesions occurring in the setting of LE are classified as.¹⁰ TEN-like acute cutaneous LE (ACLE). TEN-like subacute cutaneous LE (SCLE). TEN occurring in systemic lupus erythematosus (SLE) patients not having conventional LE-specific skin lesions
vesiculobullous changes occurring at the active border of advancing annular subacute cutaneous LE.\textsuperscript{3} Vesiculobullous chronic cutaneous LE.

Coexistence of two unrelated dermatoses (drug induced TEN and SLE) that may potentially mimic each other (as in our case) is seldom seen. TEN is known to occur with increased frequency in connective tissue disease. Krabbe et al described a patient with SLE developing TEN-like lesions with hemophagocytic syndrome triggered by sulfasalazine.\textsuperscript{11} Although their patient lacked mucosal involvement, TEN was diagnosed due to absence of photosensitivity and histopathological finding of epidermal necrosis without evidence of LE. Despite some points of differentiation (Table 1), a patient of lupus erythematosus presenting with a TEN - like rash is a baffling scenario. In our case, concurrent photo distributed rash, arthritis and fever rendered it all the more difficult. Though anti TB drugs (rifampin, ethambutol, isoniazid) have been incriminated in TEN, he had tolerated these drugs well previously. Streptomycin (the only new addition to his recent AKT regimen) has been associated with minor allergic skin reactions (urticaria) but streptomycin-induced TEN (as indicated in our case by Naranjo adverse drug reaction probability scale) remains extremely rare.

Both ACLE and TEN are inflammatory and interface dermatoses sharing clinical and histopathological features with very subtle differences. Eventually, lack of immuno reactions on direct immunofluorescence helped clinch the diagnosis in favors of TEN.

**Table 1: Differences between TEN like LE and drug induced TEN.**

| Variables     | TEN like LE                                  | Drug induced TEN                                      |
|---------------|---------------------------------------------|-------------------------------------------------------|
| History       | No h/o drug intake                          | Drug induced phenomenon                                |
| Clinical features | Photo distributed eruptions, mild mucosal involvement | Rapidly progressive painful mucocutaneous erosions, flaccid bullae, systemic symptoms |
| Laboratory    | ANA+, ds DNA+, C3 and C4                    | Negative                                              |
| Histopathology| Vacular interface dermatitis along the basement membrane and scattered necrotic keratinocytes | Extensive epidermal necrosis, vacuolar degeneration of basal keratinocytes |
| DIF           | Dense granular continuous deposits of IgG, IgM, IgA, C3 along DEJ | Negative                                              |
| Management    | Steroid (long duration), immuno suppressants | Stop culprit drug, steroids (short duration), cyclosporine, IVIG, plamapharesis |

**CONCLUSION**

Drug-induced TEN and TEN-like LE pose a diagnostic challenge with practical implications for management, prognosis and counselling. A high index of suspicion combined with meticulous drug history, clinical clues, histopathology and immuno fluorescence studies can distinguish between these two confounding disorders.

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