International Journal of Research in Dermatology
Chavan RB et al. Int J Res Dermatol. 2020 Jul;6(4):563-566
http://www.ijord.com

DOI: http://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20202667

Case Report

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

R. B. Chavan, V. A. Belgaumkar*, N. S. Deshmukh, A. M. Pawar

Department of Dermatology, Venereology and Leprosy, Sassoon General Hospitals, Pune, Maharashtra, India

Received: 09 February 2020
Revised: 09 May 2020
Accepted: 13 May 2020

***Correspondence:**
Dr. V. A. Belgaumkar,
E-mail: doc_vasudha@yahoo.co.in

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.[4,8] However, in some cases, it has also been reported in association with acute graft versus host disease (GVHD).[5] Infection, and vaccinations.[6,7] 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).

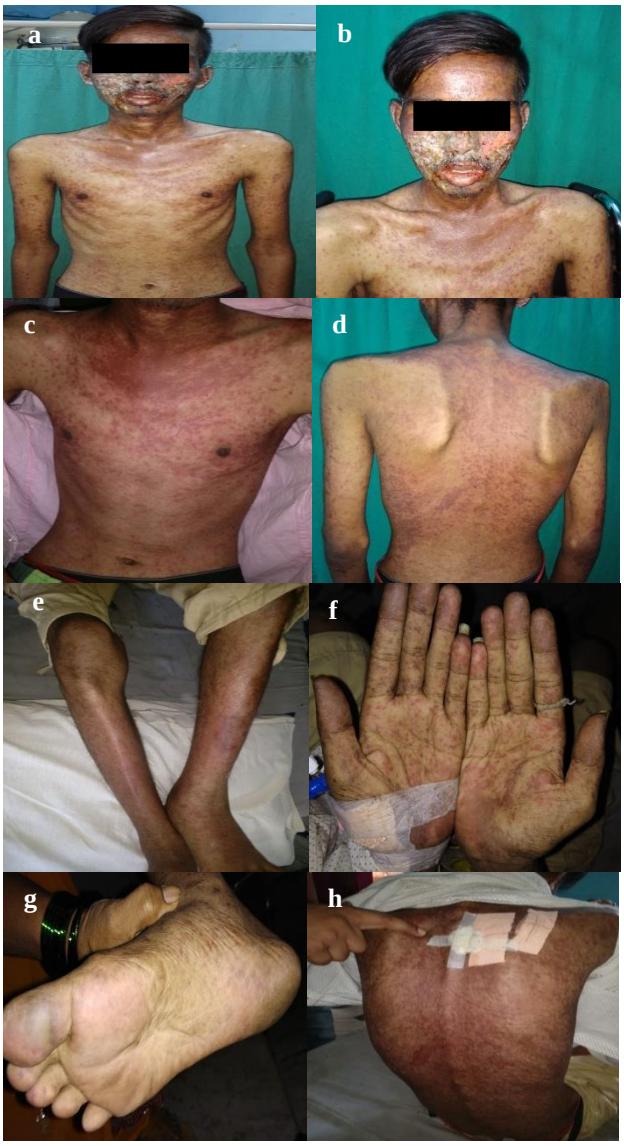

Figure 1: (a) Diffuse maculo-papular rash with dusky hue over face, neck, chest, abdomen, upper limb, (b) erosions and crusts over malar area, nose and lip, upper eyelid and post-auricular areas spared, (c and d) diffuse maculo-papular rash with dusky hue over chest and back, (e) diffuse maculo-papular rash with dusky hue over lower limbs, (f and g) palmoplantar involvement, and (h) clinical examination: Nikolsky sign - positive.

T azathioprine 50 mg/d and T hydroxychloroquine were added later. The treatment course was completed uneventfully and he was apparently asymptomatic in the intervening period. A month before onset of current rash, he complained of chest pain and breathlessness. A diagnosis of reactivated sputum positive pulmonary and abdominal tuberculosis was made based on lung consolidation and mediastinal and upper abdominal lymphadenopathy on HRCT. AKT Cat II (streptomycin) was initiated followed by appearance of rash 15 days later.

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.

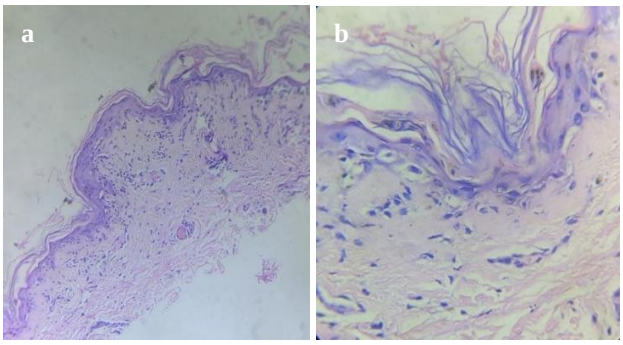

Figure 2 (a and b): Skin biopsy (H and E) shows vacuolar degeneration of basal layer, perivascular mononuclear tagging of lymphocytes at DEJ, necrotic keratinocytes.

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.[5] 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.[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 histopathogical 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	Vacuolar 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	Steroids (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.

ACKNOWLEDGEMENTS

Dr Vasudha Belgaumkar is supported by the BJGMC-JHU HIV-TB training program funded by Fogarty international center of the US national institutes of health (grant #D43TW00957). The content of this publication is solely the responsibility of the authors and does not represent the official views of the national institutes of health.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Obermoser G, Sontheimer RD, Zelger B. Overview of common, rare and atypical manifestations of cutaneous lupus erythematosus and histopathological correlates. Lupus. 2010;19:1050-70.
2. Lyell A. Toxic epidermal necrolysis: an eruption resembling scalding of the skin. Br J Dermatol. 1956;68:355-61.
3. Ting W, Stone MS, Racila D, Scofield RH, Sontheimer RD. Toxic epidermal necrolysis-like acute cutaneous lupus erythematosus and the spectrum of the acute syndrome of apoptotic pan-epidermolysis (ASAP): a case report, concept review and proposal for new classification of lupus erythematosus vesiculobullous skin lesions. Lupus. 2004;13:941-50.
4. Torchia D, Romanelli P, Kerdel FA. Erythema multiforme and Stevens-Johnson syndrome/toxic epidermal necrolysis associated with lupus erythematosus. J Am Acad Dermatol. 2012;67:417-21.
5. Takeda H, Mitsuhashi Y, Kondo S, Kato Y, Tajima K. Toxic epidermal necrolysis possibly linked to hyperacute graft-versus-host disease after allogeneic bone marrow transplantation. J Dermatol. 1997;24:635-41.
6. Fournier S, Garin BS, Mentec H, Revuz J, Roujeau JC. Toxic epidermal necrolysis associated with Mycoplasma pneumoniae infection. Eur J Clin Microbiol Infect Dis. 1995;14:558-9.

7. Ball R, Ball LK, Wise RP, Braun MM, Beeler JA, Salive ME. Stevens-Johnson syndrome and toxic epidermal necrolysis after vaccination: reports to the vaccine adverse event reporting system. Pediatr Infect Dis J. 2001;20:219-23.
8. Mandelcorn R, Shear NH. Lupus-associated toxic epidermal necrolysis: a novel manifestation of lupus. J Am Acad Dermatol. 2003;48:525-9.
9. Kelly JP, Auquier A, Rzany B, Naldi L, Garin BS, Correia O, et al. An international collaborative case-control study of severe cutaneous adverse reactions (SCAR). Design and methods. J Clin Epidemiol. 1995;48:1099-108.
10. Cisneros CG, Romiti R, Santi CG, Aoki V, Valente NY, Nico MM. Toxic epidermal necrolysis-like cutaneous lupus erythematosus: a series of three patients. Acta Derm Venereol. 2010;90:175-8.
11. Krabbe S, Gul C, Andersen B, Tvede N. Toxic Epidermal Necrolysis-Like Lesions and Systemic Lupus Erythematosus Possibly Triggered by Sulfasalazine. Case Reports Rheumatol. 2016;2016:3.

Cite this article as: Chavan RB, Belgaumkar VA, Deshmukh NS, Pawar AM. Toxic epidermal necrolysis like acute cutaneous lupus erythematous or drug induced toxic epidermal necrolysis: case report of a diagnostic dilemma. Int J Res Dermatol 2020;6:563-6.