SHORT COMMUNICATION

Concurrent Drug-induced Rowell Syndrome and Acute Generalized Exanthematous Pustulosis

Yu-Han Alice HSU[1,2], Kuan-Yu CHU[1,2] and Cheng-Che Eric LAN[1,2*]

*[1]Department of Dermatology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, and [2]Department of Dermatology, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan. *Email: laneric@cc.kmu.edu.tw*

Submitted Feb 4, 2026. Accepted after revision Mar 19, 2026
Published Apr 16, 2026. DOI: 10.2340/actadv.v106.adv-2026-0400 Acta Derm Venereol 2026; 106: adv-2026-0400.

Acute generalized exanthematous pustulosis (AGEP) is a severe drug-related pustular eruption characterized by the abrupt onset of sterile nonfollicular pustules. Rowell syndrome (RS) is a rare variant of cutaneous lupus erythematosus presenting with erythema multiforme–like targetoid lesions. Although medications have been associated with both conditions, their concurrent presentation is rare. Here, we report a patient with systemic lupus erythematosus (SLE) who developed AGEP accompanied by the acute onset of typical cutaneous manifestations of RS.

CASE PRESENTATION

A 45-year-old woman presented with a 3-day history of generalized pruritic erythematous rash with a fever of up to 39.5 °C, fatigue and dyspnoea. She had been diagnosed with SLE 2 weeks earlier, manifesting with a malar rash. Serological testing revealed positive antinuclear antibodies (ANA, >1 : 160, speckled pattern), anti-Ro (>240 U/mL), anti-Smith antibodies (14 U/mL; reference range, <7 U/mL) and low complement 4 level (6.7 mg/dL; reference range, 10–40 mg/dL). The patient was initially treated with prednisolone (5 mg/day), hydroxychloroquine 200 mg/day and azathioprine 50 mg/day. Two weeks after treatment initiation, the malar rash persisted. Therefore, the azathioprine dose was increased to 100 mg/day, while hydroxychloroquine was maintained at 200 mg/day. Three days after the azathioprine dose escalation (17 days after initiation of hydroxychloroquine and azathioprine), the patient developed an acute exacerbation of widespread cutaneous eruptions. Physical examination revealed generalized maculopapular eruptions with nonfollicular sterile pustules and erosions on the face and trunk (**Fig. 1**a, d). Erythematous papules were noted on the dorsal hands, fingers and periungual areas, with sparing of the knuckles, consistent with chilblain lupus (Fig. 1b). In addition, multiple reddish to violaceous annular patches with a targetoid configuration and without scaling were observed on the upper limbs, dorsal hands and shoulders, resembling erythema multiforme (Fig. 1a, b and c). No oral or genital mucosal involvement was present. Laboratory test showed leukocytosis (12,000 /μL) with neutrophilia (80%), and immunoglobulin M antibodies for herpes simplex virus (HSV) and Mycoplasma pneumoniae were negative. Histopathological examination of the pustule of the trunk revealed subcorneal neutrophilic accumulation (**Fig. 2**a) and perivascular lymphohistiocytic infiltrates with numerous eosinophils (Fig. 2b), consistent with AGEP. A biopsy from a targetoid lesion of the upper limb demonstrated basal vacuolar degeneration with perivascular lymphocytic infiltration (Fig. 2c). Direct immunofluorescence was negative. With a clinical impression of azathioprine and hydroxychloroquine induced AGEP with acute exacerbation of RS,

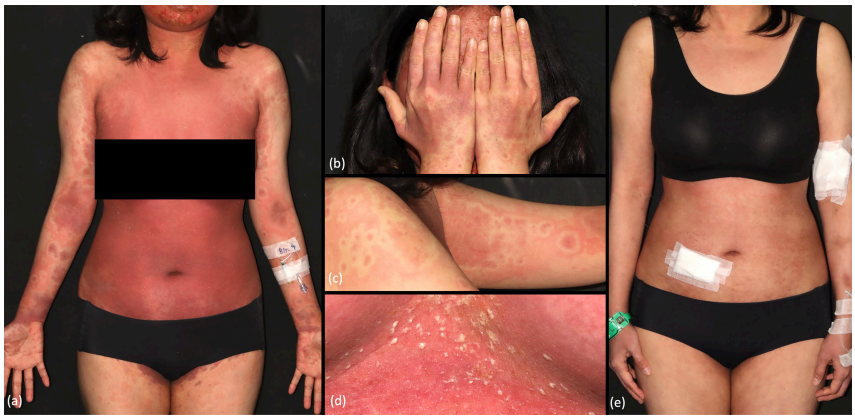

Fig. 1. Cutaneous manifestations at presentation and follow-up. (a) Erythematous annular patches with a targetoid configuration on the upper limbs. Maculopapular eruptions with pustules and erosions involving the face and trunk. (b) Chilblain lupus and targetoid patches on the dorsal hands. (c) Targetoid patches on shoulder and upper limbs. (d) Nonfollicular centric pustules with erythema on the chest. (e) Resolution of the lesion in 1 week.

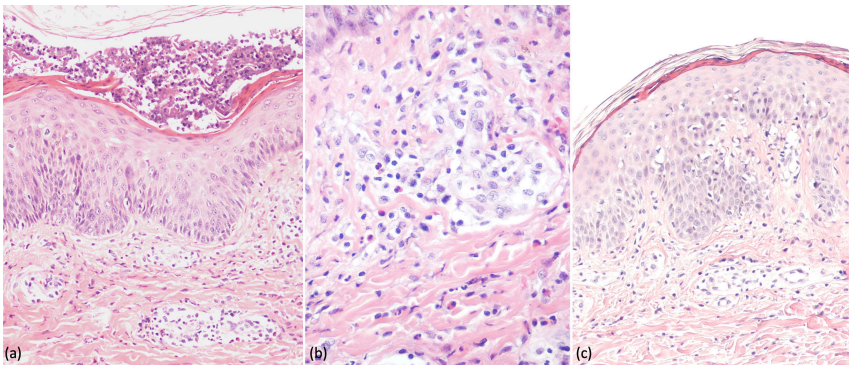

Fig. 2. Histopathologic features. (a,b) Haematoxylin and eosin staining from specimen on the trunk revealed subcorneal neutrophilic accumulation and perivascular infiltration of lymphocytes, histiocyte and numerous eosinophils. (a, magnification ×100) (b, magnification ×200). (c) Haematoxylin and eosin staining from the targetoid lesion on the limb revealed basal vacuolar degeneration with perivascular lymphocytic infiltration (magnification ×100).

the suspected culprit drugs were discontinued, and intravenous methylprednisolone (40 mg every 8 h) and topical desoximetasone 0.25 % ointment were initiated. Fever and malaise subsided, the pustules gradually dried, and the targetoid eruptions resolved with post-inflammatory hyperpigmentation within two weeks. (Fig. 1e). No recurrence of skin lesions was observed during 1 year of follow-up. The patient remains in remission on prednisolone 5 mg daily and mycophenolic acid 360 mg twice daily.

DISCUSSION

RS is a rare disorder that usually appears in middle-aged female characterized by the coexistence of lupus erythematosus (LE) and erythema multiforme (EM)-like lesions. Diagnostic criteria included the presence of LE lesions (especially discoid lupus erythematosus (DLE) and/or chilblain), EM-like lesions, positive speckled ANA, anti-Ro/SSA or anti-La/SSB antibodies and rheumatoid factor (1). The absence of trigger factors for EM including infection (e.g. mycoplasma pneumonia, HSV) was also needed for the diagnosis of RS (2). Herold M et al. proposed that RS should be considered a distinct variant within the spectrum of cutaneous LE, based on the enrichment of CD123+plasmacytoid dendritic cells, which aid in its distinction from EM. Furthermore, unlike subacute cutaneous LE (SCLE), annular lesions in RS show a targetoid configuration, with a central dusky erythematous zone surrounded by peripheral erythema (3).

Drug-induced lupus (DIL) is an autoimmune syndrome triggered by certain medications and may manifest as SLE, SCLE, or less commonly chronic cutaneous lupus erythematosus (CCLE), with cutaneous forms often presenting with generalized rash and photosensitivity (2). Procainamide and hydralazine are the most common causes of DIL (4). Drug-associated RS has been reported in association with some medications (**Table I**). The latency period between drug exposure and eruption varied considerably, ranging from a few hours after re-exposure to several months of treatment. Clinical outcomes were generally favorable, with most patients showing improvement following

Table I. Published cases of drug-induced Rowell syndrome

Author	Patient profile	Cutaneous findings	Culprit drug	Systemic symptoms	Latency	Laboratory data	Treatment	Time of remission after drug withdrawal
Kacalak-Rzepka et al. (5)	51F with SLE	Target-like lesions on the face and neck, erosion on buttocks and thighs, mucosal involvement	Sodium valproate	Arthralgia, general fatigue and subclinical fever	5 months; 2 weeks when rechallenging	ANA+anti-Ro+anti-La+RF +	Prednisolone	3 weeks
Murad et al. (6)	81F	Targetoid lesions on head, neck, back	Terbinafine	None	3 weeks	ANA+anti-Ro+	Systemic corticosteroids	10 days
Pozharashka et al. (7)	67F with SCLE	Target lesions with haemorrhagic crusts at the margins on neck, chest, upper back and shoulder	Omeprazole	None	>1 year	ANA+anti-Ro+anti-La+	Hydroxychloroquine, methylprednisolone	1 month
Baroni et al. (8)	´70F	Target lesions on back, chest, extremities and face	Norfloxacin	None	Hours after the third dose (re-exposure)	ANA+anti-Ro+anti-La+RF +	Hydroxychloroquine, prednisone	Not reported
Champagne et al. (9)	65F	Targetoid lesions with central blisters on head, trunk and limbs, mucosal erosions and epidermal detachment	Terbinafine	Fever and tachycardia	3 weeks	ANA+anti-Ro+ RF+	Prednisolone, hydroxychloroquine	Rapid improvement
Schissler et al. (10)	43F, SCLE	Target-like lesions with erosion and crust on chest and arms, oral mucosal involvement	Esomeprazole	None	6 months	ANA+anti-Ro+	Prednisolone, hydroxychloroquine	1 year
Present case	45F. SLE	Targetoid patches on trunk and upper limbs, pustules on trunk, erosions on face	Hydroxychloroquine, azathioprine	Fever, fatigue and dyspnoea	17 days	ANA+anti-Ro+anti-La+	Methylprednisolone	2 weeks

ANA+:Antinuclear antibodies positive; anti-La+:Anti-La/SSB antibodies positive; anti-Ro+:Anti-Ro/SSA antibodies positive; F:female; RF+:Rheumatoid factor positive; SCLE:subacute cutaneous lupus erythematosus; SLE:systemic lupus erythematosus.

withdrawal of the offending drug and treatment with systemic corticosteroids or antimalarial agents. Compared with previously reported cases, the present case is unique in that the eruption showed features of AGEP, which has not been previously reported in drug-induced RS.

AGEP is a drug eruption characterized by the abrupt onset of numerous, small, nonfollicular sterile pustules on an erythematous base, typically accompanied by fever >38 °C and leukocytosis, and resolving rapidly following drug discontinuation in 15 days. In the present case, the diagnosis was supported by a EuroSCAR score of 7, consistent with probable AGEP. AGEP is commonly associated with pristinamycin, aminopenicillins, quinolones, antimalarials, sulfonamides, terbinafine, and diltiazem. (11). Azathioprine-induced AGEP has been reported in a few articles (12–14). In this case, the eruption occurred 17 days after initiation of hydroxychloroquine and azathioprine and three days after azathioprine dose escalation, suggesting a drug-induced reaction. Although the short interval following azathioprine dose escalation may indicate a potential role for azathioprine, hydroxychloroquine is also a recognized trigger of AGEP, therefore, both drugs remain possible culprits.

Histopathologically, RS demonstrates interface dermatitis with basal vacuolar change, and AGEP demonstrates subcorneal or intraepidermal pustules, papillary dermal edema and a dense mixed perivascular infiltrate rich in neutrophils and eosinophils.

AGEP and DIL share drug-specific T-cell–mediated mechanisms. In AGEP, drug-specific T cells activate innate immune pathways, leading to the release of interleukin (IL)-1, IL-17 and tumour necrosis factor-α, which promote neutrophilic infiltration. In DIL, T-cell–mediated immune dysregulation results in autoantibody production and immune complex deposition (15). These observations suggest that drug-induced T-cell activation may trigger distinct immune pathways, giving rise to divergent clinical manifestations that can occur simultaneously in the same individual.

In conclusion, we report a rare case of AGEP with concurrent Rowell syndrome in lupus erythematosus, highlighting that early recognition and drug withdrawal result in favorable outcomes.

ACKNOWLEDGEMENTS

Ethics committee: Written informed consent for publication was obtained from the patient. IRB approval was not required for this case report.

The authors have no conflicts of interest to declare.

REFERENCES

1. 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: 417–421. https://doi.org/10.1016/j.jaad.2011.10.012
2. Marzano AV, Vezzoli P, Crosti C. Drug-induced lupus: an update on its dermatologic aspects. Lupus 2009; 18: 935–940. https://doi.org/10.1177/0961203309106176
3. Herold M, Nielson CB, Braswell D, Merkel K, Walker A, Auerbach J, et al. Clinicopathologic comparison of Rowell syndrome, erythema multiforme, and subacute cutaneous lupus erythematosus. J Am Acad Dermatol 2019; 81: 1435–1438. https://doi.org/10.1016/j.jaad.2019.06.008
4. Siegel CH, Sammaritano LR. Systemic lupus erythematosus: a review. JAMA 2024; 331: 1480–1491. https://doi.org/10.1001/jama.2024.2315
5. Kacalak-Rzepka A, Kiedrowicz M, Bielecka-Grzela S, Ratajczak-Stefanska V, Maleszka R, Mikulska D. Rowell's syndrome in the course of treatment with sodium valproate: a case report and review of the literature data. Clin Exp Dermatol 2009; 34: 702–704. https://doi.org/10.1111/j.1365-2230.2008.02972.x
6. Murad A, Shudell E, Mulligan N. Rowell's syndrome induced by terbinafine. BMJ Case Rep 2015; 2015: bcr2015210360. https://doi.org/10.1136/bcr-2015-210360
7. Pozharashka J, Dourmishev L, Balabanova M, Vassileva S, Miteva L. Rowell's syndrome triggered by omeprazole. Acta Dermatovenerol Croat 2019; 27: 124–126.
8. Baroni A, Piccolo V, Russo T, Cozzolino D, Mascolo M, Chessa MA. Norfloxacin-induced subacute cutaneous lupus with erythema multiforme-like lesions: the enigma of the Rowell syndrome. J Dtsch Dermatol Ges 2014; 12: 1039–1042. https://doi.org/10.1111/ddg.12392
9. Champagne C, Ratnavel R, Wong T. Severe Rowell syndrome associated with oral terbinafine. Clin Exp Dermatol 2012; 37: 822–823. https://doi.org/10.1111/j.1365-2230.2012.04363.x
10. Schissler C, Banea S, Tortel MC, Mahé A. Un nouveau cas de syndrome de Rowell. Ann Dermatol Venereol 2017; 144: 263–267. https://doi.org/10.1016/j.annder.2017.02.005
11. Sidoroff A, Dunant A, Viboud C, Halevy S, Bavinck JNB, Naldi L, et al. Risk factors for acute generalized exanthematous pustulosis (AGEP)-results of a multinational case-control study (EuroSCAR). Br J Dermatol 2007; 157: 989–996. https://doi.org/10.1111/j.1365-2133.2007.08156.x
12. Elston GE, Johnston GA, Mortimer NJ, Harman KE. Acute generalized exanthematous pustulosis associated with azathioprine hypersensitivity. Clin Exp Dermatol 2007; 32: 52–53. https://doi.org/10.1111/j.1365-2230.2006.02257.x
13. Parisi R, Shah H, Navarini AA, Muehleisen B, Ziv M, Shear NH, et al. Acute generalized exanthematous pustulosis: clinical features, differential diagnosis, and management. Am J Clin Dermatol 2023; 24: 557–575. https://doi.org/10.1007/s40257-023-00779-3
14. Avgerinos A, Giannikaki E, Krüger-Krasagakis S, Koutroubakis IE. Acute generalized exanthematous pustulosis induced by azathioprine in a patient with ulcerative colitis. Am J Gastroenterol 2011; 106: 1005–1007. https://doi.org/10.1038/ajg.2010.500
15. Chang C, Gershwin ME. Drugs and autoimmunity--a contemporary review and mechanistic approach. J Autoimmun 2010; 34: J266–75. https://doi.org/10.1016/j.jaut.2009.11.012