

Rowell's Syndrome Triggered by Omeprazole

Dear Editor,

Rowell's syndrome is a rare disease, characterized by the appearance of erythema multiforme (EM)-like lesions in patients with lupus erythematosus. It was initially reported by Rowell (1) in 1963 and its existence as a separate clinical entity is currently under debate (2,3). A few cases may have been induced by drugs such as systemic antimycotics, antibiotics, anti-convulsants, and more recently proton pump inhibitors (PPIs).

CASE REPORT

We present the case of a 67-year-old woman with subacute cutaneous lupus erythematosus (SCLE) and EM-like lesions who fulfilled all the criteria for Rowell's syndrome. The patient had lupus arthritis for two years and was treated with oral methylprednisolone 8 mg/day and hydroxychloroquine 200 mg/day. She

started receiving 20 mg of omeprazole daily for gastroprotection. The patient also had arterial hypertension with no current treatment, osteoporosis, and an L₁ vertebral fracture.

The dermatological examination revealed multiple erythematous infiltrated plaques involving mainly the sun-exposed areas (neck, chest, upper back, and shoulders). Cutaneous lesions had an annular or target pattern and a tendency to form hemorrhagic crusts and scales at the margins (Figure 1, A). The mucous membranes were unaffected.

Histological examination (hematoxylin and eosin ×200) found epidermal atrophy, vacuolar degeneration of the basal layer, and sparse perivascular lymphocytic infiltrate in the dermis – features corresponding to lupus erythematosus (Figure 2, A). Single eosinophilic necrotic keratinocytes characteristic for

Table 1. Case reports of drug-induced Rowell's syndrome

Patient	Suspected medication	Exposure duration	Clinical presentation	Immunology	Treatment	Reference
70-year-old woman	norfloxacin	2 days	RS/SCLE	ANA(+); Ro (+); La (+)	Culprit drug withdrawal, prednisolone, hydroxychloroquine	Baroni A <i>et al.</i> (10)
65-year-old woman	terbinafine	3 weeks	RS/SJS/TEN overlap	ANA(+); Ro (-); La (-)	Culprit drug withdrawal, prednisolone, hydroxychloroquine	Champagne C <i>et al.</i> (8)
81-year-old woman	terbinafine	5 weeks	RS/TEN	ANA(+); Ro (+);	Culprit drug withdrawal, local and systemic corticosteroids	Murad A <i>et al.</i> (9)
51-year-old woman	sodium valproate	5 months	SJS/TEN/ SLE	ANA(+); Ro (+); La (+)	Culprit drug withdrawal, prednisolone	Kacalak-Rzepk A <i>et al.</i> (11)
43-year-old woman	esomeprazole	6 months	RS/SCLE	ANA (+); Ro (+); La (-);	Culprit drug withdrawal, systemic corticosteroids, hydroxychloroquine	Schissler C <i>et al.</i> (12)



Fig. 1 (a) Multiple erythematous infiltrated plaques affecting the back with annular and target character and a tendency to form haemorrhagic crusts and scales at the margins; (b) The improvement of skin lesions after 4 weeks treatment

erythema multiforme were observed in the epidermis (Figure 2, B). Direct immunofluorescence (IF) from lesional skin showed granular deposits of C3 on the dermo-epidermal junction. Lupus band test from sun-protected, nonlesional skin was negative. On indirect IF a speckled pattern antinuclear antibodies (ANA) with >1:1280 titers were detected. Anti-Ro (>200 U/mL) and anti-La (>200 U/mL) antibodies were also positive. The blood cell count and differential analysis were within reference ranges. The 24-hour urine protein test showed a non-significant proteinuria – 0.36 g/24h. Photo-testing was impossible considering the extent of the skin lesions.

The therapeutic approach consisted of increasing the hydroxychloroquine dose to 400 mg/day, substituting PPI with famotidine 20 mg/day p.o. and ceftriaxone 2 g/day for the superinfection with *Ps. aeruginosa*, which led to a clinical improvement (Figure 1, B). The methylprednisolone dose remained unchanged due to already existing severe adverse effects.

DISCUSSION

The diagnosis was based on Zeitouni et al.'s classification (4). The three main criteria are as follows: lupus erythematosus, EM-like lesions, and speckled pattern of ANA. Our patient met all three major and one minor criteria, namely the presence of anti-Ro and anti-La antibodies. As for the other minor criteria, RF was negative and no chilblains were found.

Although there was a continuous time lapse (more than 1 year) between the initiation of omeprazole intake and the diagnosis of Rowell's syndrome, we suggest that the connection is probable. For instance, the latency differs depending on the incriminated medication in drug induced SCLE. Longer periods are reported for diuretics and calcium blockers, while the time interval is shorter for chemotherapeutic drugs and antimycotics (5). Our suspicions were further confirmed by the fact that the lesions improved promptly

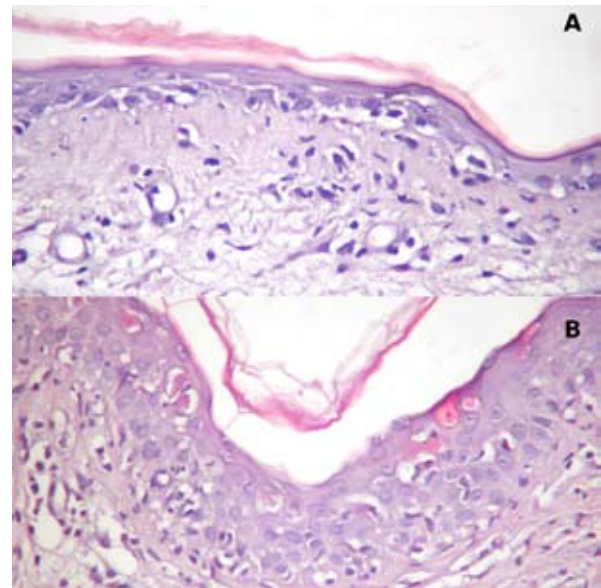


Fig. 2 (a) Skin biopsy revealing epidermal atrophy, vacuolar degeneration of the basal layer, sparse perivascular lymphohistiocytic infiltrate in the dermis - features corresponding to lupus erythematosus (hematoxylin and eosin x200); (b) Single eosinophilic necrotic keratinocytes in the epidermis, characteristic for erythema multiforme (hematoxylin and eosin x200).

within a month after discontinuation of omeprazole and doubling the dose of hydroxychloroquine.

PPIs are reported to be a major cause of drug-induced SCLE (6,7). According to Laurinaviciene et al., the most common drugs involved are PPIs, thiazide diuretics, antifungals, chemotherapeutics, statins, and antiepileptics (6). However, very few cases of Rowell's syndrome are found to be drug-related. The culprit drugs include: oral terbinafine (8,9), norfloxacin (10), sodium valproate (11) and esomeprazole (12) (Table 1).

CONCLUSION

Despite the common clinical and immunological features shared between SCLE, drug-induced SCLE and EM, Rowell's syndrome seems to be a separate entity rather than a coincidental association. Finally, according to our knowledge this case would be the second of Rowell's syndrome due to PPIs.

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