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, anticonvulsants, 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 x200) 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>
<thead>
<tr>
<th>Patient</th>
<th>Suspected medication</th>
<th>Exposure duration</th>
<th>Clinical presentation</th>
<th>Immunology</th>
<th>Treatment</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-year-old woman</td>
<td>norfloxacin</td>
<td>2 days</td>
<td>RS/SCLE</td>
<td>ANA(+); Ro (+); La (+)</td>
<td>Culprit drug withdrawal, prednisolone, hydroxychloroquine</td>
<td>Baroni A et al. (10)</td>
</tr>
<tr>
<td>65-year-old woman</td>
<td>terbinafine</td>
<td>3 weeks</td>
<td>RS/SJS/TEN overlap</td>
<td>ANA(+); Ro (-); La (-)</td>
<td>Culprit drug withdrawal, prednisolone, hydroxychloroquine</td>
<td>Champagne C et al. (8)</td>
</tr>
<tr>
<td>81-year-old woman</td>
<td>terbinafine</td>
<td>5 weeks</td>
<td>RS/TEN</td>
<td>ANA(+); Ro (+); La (-)</td>
<td>Culprit drug withdrawal, local and systemic corticosteroids</td>
<td>Murad A et al. (9)</td>
</tr>
<tr>
<td>51-year-old woman</td>
<td>sodium valproate</td>
<td>5 months</td>
<td>SJS/TEN/ SLE</td>
<td>ANA(+); Ro (+); La (-)</td>
<td>Culprit drug withdrawal, prednisolone</td>
<td>Kacalak-Rzepk A et al. (11)</td>
</tr>
<tr>
<td>43-year-old woman</td>
<td>esomeprazole</td>
<td>6 months</td>
<td>RS/SCLE</td>
<td>ANA (+); Ro (+); La (-)</td>
<td>Culprit drug withdrawal, systemic corticosteroids, hydroxychloroquine</td>
<td>Schissler C et al. (12)</td>
</tr>
</tbody>
</table>
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 \( P. aeruginosa \), which led to a clinical improvement (Figure 1, B). The methylprednisolone dose remained unchanged due to already existing severe adverse effects.

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 chillblains 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 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.

**References:**


Joana Pozharashka, Lyubomir Dourmishev, Maria Balabanova, Snejina Vassileva, Ljubka Miteva

Department of Dermatology and Venereology, Medical University – Sofia, Sofia, Bulgaria

Corresponding author: Lyubomir Dourmishev MD, PhD
Department of Dermatology and Venereology
Medical University – Sofia, Bulgaria
1st Georgi Sofiiski Blvd.
1431 Sofia
Bulgaria

Received: March 18, 2018
Accepted: June 8, 2019