Rowell's Syndrome: A Case Report and Literature Overview

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Sir,

A 24-year-old female presented to us with multiple reddish lesions on body since two months. Initially, multiple itchy reddish lesions developed over hands, legs, and chest two months ago associated with fever, joint pain, and photosensitivity. Fever was of continuous and low grade in nature. The joints involved were bilateral knees, elbows, and ankle joints. A few days later she developed fluid-filled blisters on the hard palate of mouth which ruptured to form painless erosions. On examination, the patient was febrile with a temperature of 102^0F, multiple plaques with central dark red crust surrounded by two peripheral erythematous rings were found on both thighs [Figure 1a], legs [Figure 1b], and chest. Lesions were non-tender and associated with mild itching. Mucosal examination revealed multiple erosions over hard palate and genital area, hemorrhagic crust over lips and nasal mucosa [Figure 2], and ocular mucosa was not involved. There was no history of any drug intake before the onset of the lesion and no history suggestive of herpes infection was found. Systemic examination revealed no significant abnormalities. Based on the clinical features a diagnosis of Erythema Multiforme major was considered. Investigation reports revealed haemoglobin-10.5 mg/dl, TLC-12,870 cells/µL, Platelet-1,50,000/µL, ESR-95 mm/hr, routine urine analysis showed urine protein 3+ (150 mg/dl) and presence of cellular casts 1-3/LPF, ANA +++ speckled pattern, Anti-ds-DNA, and rheumatoid factor (17 IU/ml) were positive. Anti-Scl 70, anti-histone, anti-La, and anti-Ro antibodies were negative. Serology for retrovirus, herpes simplex virus, and syphilis were negative. A biopsy was done and histopathology revealed a necrotic epidermis with a subepidermal blister. Necrotic keratinocytes were present in the epidermis and at the dermo-epidermal junction. Apoptotic keratinocytes were found. The upper dermis was edematous and extravasated erythrocytes were present suggesting a picture of erythema multiforme [Figures 3 and 4].

The presence of target lesions and histopathology picture suggested a diagnosis of Erythema multiforme; however, presence of photosensitivity, oral erosion, proteinuria, ANA, and anti-ds-DNA positivity suggested underlying Systemic lupus erythematosus. Based on clinical, immunological, and histopathological findings, a diagnosis of Rowell's syndrome was considered. She was started oral prednisolone 1 mg/kg/day, hydroxychloroquine 6 mg/kg/day, azathioprine 1 mg/kg/day, topical mometasone furoate (0.1%) ointment and broad spectrum sunscreen.

Lupus erythematosus (LE) is an inflammatory connective tissue disorder classified into chronic cutaneous LE (CCLE), subacute cutaneous LE (SCLE), and acute cutaneous LE (ACLE). Erythema multiforme (EM) is an acute, immune-mediated mucocutaneous condition characterized by the presence of multiple symmetric, typical or atypical target lesions with concentric color variation mainly on extremities (hands, feet, and the extensor aspects of limbs) with or without itching and prodromal symptoms. Crusting may occur in the center of the lesion. Typical target lesions are defined as well-defined round, erythematous, edematous lesions with central dusky or dark red surrounded by an immediate zone of paler edematous ring and the outermost ring is bright red in color. Atypical target lesions resemble typical targets but with only two zones.[1] EM is usually triggered by infectious agents like herpes simplex virus, mycoplasma pneumoniae, drugs-like anticonvulsants,

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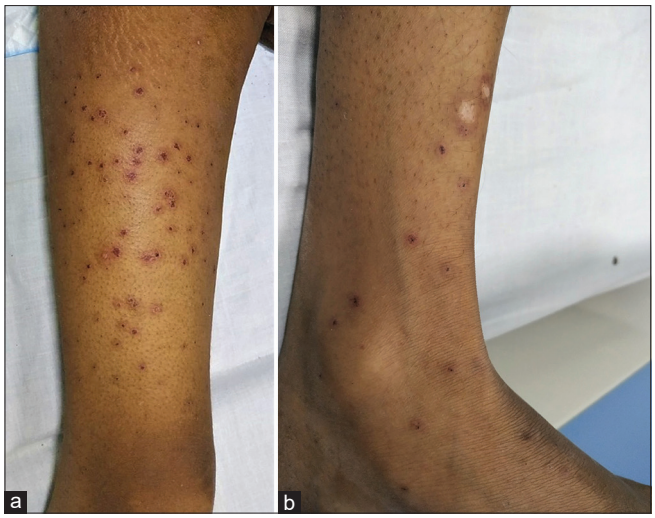

Figure 1: Erythema multiforme like skin lesions (Target lesions) on right thigh (a) and left leg (b)

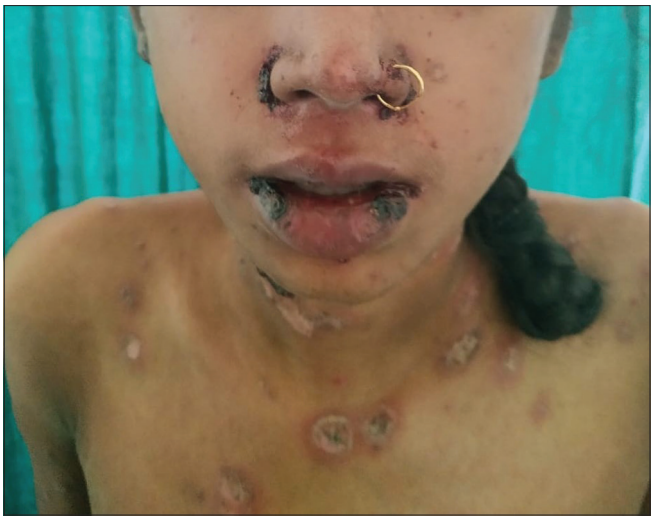

Figure 2: Hemorrhagic crusted lesions on lips and nasal mucosa

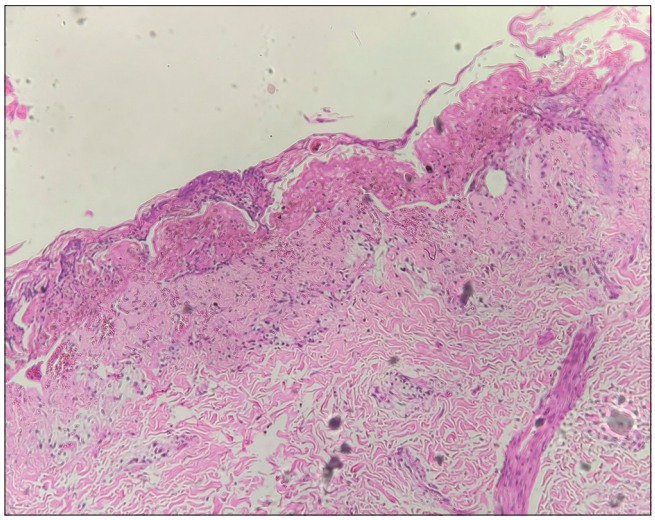

Figure 3: Low power view of histopathologic picture showing necrotic epidermis with subepidermal cleft. [H&E × 10]

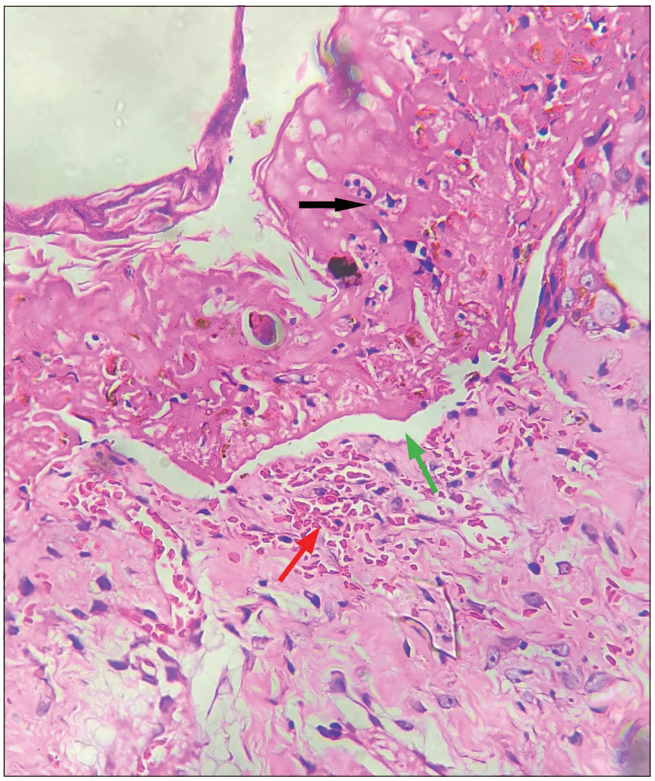

Figure 4: Histopathology showing necrotic epidermis with a subepidermal blister (green arrow), apoptotic keratinocytes (black arrow), and extravasated erythrocytes in the upper dermis (red arrow). [H&E × 40]

antibiotics, and non-steroid anti-inflammatory drugs and underlying malignancy.[1,2] EM is not associated with any specific autoimmune serological abnormality.[3]

Rowell's syndrome (RS) is an uncommon presentation of lupus erythematosus with erythema multiforme like lesions associated with specific serological changes. The association between LE and EM was first observed by Shlotz in 1922.[4] However, in 1963, Neville Rowell *et al*. described this as a distinct entity. While studying 120 patients of CCLE, he found four female patients having DLE with EM-like skin lesions, speckled pattern ANA, positive rheumatoid factor, and a precipitating antibody to saline extract of human tissues (anti-Sj-T) which is now regarded similar to Ro (SSA).[3] Though, originally the syndrome was described in DLE patients by Rowell, subsequently cases with different variants of cutaneous LE such as sub-acute cutaneous LE and systemic LE in association with EM were reported.[4,5]

In 1995, Chilblain was included by Lee *et al*. as a diagnostic criterion in RS.[6] Revised diagnostic criteria was formulated by Zeitouni *et al*. in 2000. Major criteria include (i) Lupus Erythematosus: DLE or SCLE or SLE, (ii) Erythema multiforme-like skin lesions with or without involvement of the mucous membranes, (iii) Speckled pattern ANA. Minor criteria include (i) chilblains, (ii) positive anti-Ro antibody or anti-La antibody, (iii) positive rheumatoid factor (RF). All three

major criteria and at least one minor criteria are required for the diagnosis of RS.[7]

Before considering a diagnosis of RS, it is important to rule out common triggering agents and other differentials of EM. In the present case, no precipitating factor for EM was identified. In our patient, as all the major criteria along with one minor criterion i.e., positive RF were present, we consider our case as a classic RS.

All subtypes of LE (discoid, sub-acute, acute) and all forms of EM (EM minor, EM major) can be associated with Rowell's syndrome.[3,5,7,8] Even RS associated with toxic epidermal necrolysis (TEN) has also been reported.[9] Approximately in 88% cases of RS, Speckled ANA pattern is present. Rheumatoid Factor is found positive in only 41% cases making it the least preserved feature of the syndrome.[7,10]

Histologic findings of RS are controversial. According to Torchia *et al*. there is no significant histological differences between CLE and EM lesions and the presence of necrotic keratinocytes is not specific for EM as it may also be found inSCLE lesions.[11]

RS should be managed similarly to that of SLE. Various therapeutic options include oral or injectable steroid, antimalarials like hydroxychloroquine or chloroquine, azathioprine, dapsone, cyclosporine, and cyclophosphamide. However, response to treatment is unpredictable and the patient may experience frequent episodes of clinical exacerbation.[8,11-13]

The existence of RS is still debated as a separate distinct clinical entity.[14] LE with EM-like lesion represents a subset of SCLE with targetoid lesions rather than a distinct entity according to E Antiga *et al*.[15] and Aygodan *et al*.[8] According to a few it may be an overlap syndrome between LE and EM or coincidence of DLE and EM.[13,15] In 2011, Torchia *et al*. proposed RS as an independent chronic cutaneous lupus erythematosus subtype.[11]

Our case is unique as the patient presented to us with features of EM and on investigation, we found underlying systemic lupus erythematosus, thus SLE presenting for the first time as EM. Very rarely, SLE may present first with recurrent episodes of EM-like lesions. A high index of suspicion is needed for diagnosing RS and it should be considered in all patients of LE with EM-like lesions where there is no evidence of a precipitating factor. Early diagnosis and prompt treatment of RS is required to prevent irreversible complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Sokumbi O, Wetter DA. Clinical features, diagnosis, and treatment of erythema multiforme: A review for the practicing dermatologist. Int J Dermatol 2012;51:889-902.
2. Ghosh I, Pahwa P, Dinda A, Raina V, Khanna N. Erythema multiforme associated with metastatic breast cancer. Indian J Dermatol 2013;58:485-6.
3. Rowell NR, Beck JS, Anderson JR. Lupus erythematosus and erythema multiforme-like lesions: A syndrome with characteristic immunological abnormalities. Arch Dermatol 1963;88:176-80.
4. Millard LG, Rowell NR. Chilblain lupus erythematosus (Hutchinson) A clinical and laboratory study of 17 patients. Br J Dermatol 1978;98:497-506.
5. Pandhi D, Singal A, Agarwal P. Rowell's syndrome and associated antiphospholipid syndrome. Clin Exp Dermatol 2004;29:22-4.
6. Lee S, Schloss E, Kowichi J. Rowell's syndrome: A case report with subacute cutaneous lupus erythematosus and erythema multiforme. Can J Dermatol 1995;7:807-10.
7. Zeitouni NC, Funaro D, Cloutier RA, Gagné E, Claveau J. Redefining Rowell's syndrome. Br J Dermatol 2000;142:343-6.
8. Aydogan K, Karadogan SK, Balaban Adim S, Tunali S. Lupus erythematosus associated with erythema multiforme: Report of two cases and review of the literature. J Eur Acad Dermatol Venereol 2005;19:621-7.
9. Mandelcorn R, Shear NH. Lupus-associated toxic epidermal necrolysis: A novel manifestation of lupus? J Am Acad Dermatol 2003;48:525-9.
10. Duarte AF, Mota A, Pereira M, Baudrier T, Azevedo F. Rowell syndrome-Case report and review of the literature. Dermatol Online J 2008;14:15.
11. 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.
12. Khandpur S, Das S, Singh MK. Rowell's syndrome revisited: Report of two cases from India. Int J Dermatol 2005;44:545-9.
13. Müller CSL, Hinterberger LR, Vogt T. Successful treatment of Rowell syndrome using oral cyclosporine A. Int J Dermatol 2011;50:1020-2.
14. Shteyngarts AR, Warner MR, Camisa C. Lupus erythematosus associated with erythema multiforme: Does Rowell's syndrome exist? J Am Acad Dermatol 1999;40:773-7.
15. Antiga E, Caproni M, Bonciani D, Bonciolini V, Fabbri P. The last word on the so-called "Rowell's syndrome"? Lupus 2012;21:577-85.