DRUG INDUCED ROWELL'S SYNDROME: A RARE PRESENTATION

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ABSTRACT

Rowell's syndrome (RS) is a rare disorder characterized by erythema multiforme (EM)-like lesions in a patient with lupus erythematosus, either systemic lupus erythematosus (SLE) or cutaneous lupus erythematosus (CLE). A 35 years old female presented in our dermatology outpatient department (OPD) with complaint of hemorrhagic crusting of lips and multiple discrete targetoid lesions over the chest, upper limb, and gluteal region. Investigations revealed a speckled pattern of antinuclear antibody (ANA), anti-Smith antibody, anti-ds DNA antibody, and strongly positive anti-Ro antibody. According to the clinical evaluation and investigations, the diagnosis of drug induced RS was made. The likely role of proton pump inhibitors, namely esomeprazole as a triggering factor is discussed. After stopping esomeprazole and starting medications with oral steroids and hydroxychloroquine, her good response to treatment was noted.

KEYWORDS

Erythema multiforme, systemic lupus erythematosus, rowell syndrome

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INTRODUCTION

Erythema multiforme-like lesions as the initial presentation in a patient with systemic lupus erythematosus (SLE / DLE) is a rare finding.[1,2] Rowell's syndrome (RS) was originally proposed in 1963 by Rowell *et al.*[3] This criterion was revised by Zeitouni *et al*[4] in the year 2000. Major criteria included the coexistence of lupus erythematosus or subacute cutaneous lupus erythematosus with EM-like lesions with or without mucosal involvement and speckled pattern of ANA. Minor criteria were chilblains, anti-Ro/SSA or anti-La/SSB, and positive RF. For the diagnosis, all three major criteria with at least 1 minor criteria must be fulfilled.[4] Proton pump inhibitors were described in the literature for drug-induced RS.[5-7] We describe a rare overlap syndrome of SLE and EM-like skin lesions.

CASE REPORT

A 35 year old female presented in our dermatology OPD with chief complaints of hemorrhagic crusting of lips, multiple target shaped reddish lesions over the chest, trunk, upper limb and gluteal region for the past 1 week. These cutaneous lesions were followed by painful ulceration in oral cavity. History of photosensitivity was present. She also gave history of joint pain since past 1 year. There was also history of scalp hair loss since past few months which was diffuse in type.

On further inquiry, she revealed intake of esomeprazole and methylprednisolone a month ago for 2 weeks prior to the eruption of

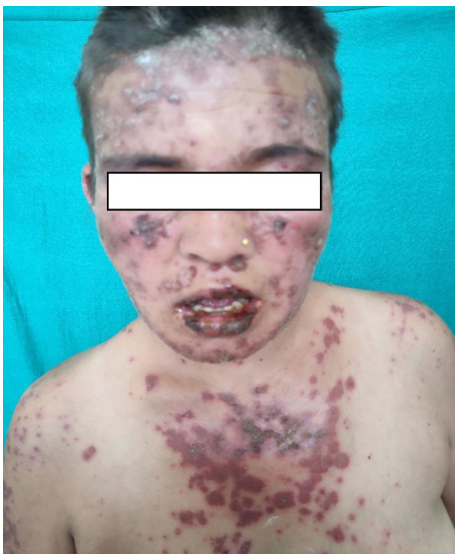

Fig. 1: Hemorrhagic crusting of lips and targetoid lesions on the face and upper anterior chest along with multiple discoid erythematous and scaly plaques on face and scalp.

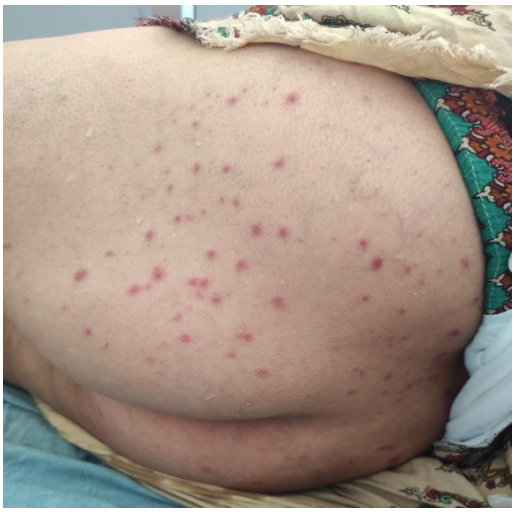

Fig. 2: Symmetrically distributed targetoid lesions on the gluteal region.

EM like lesions. There was no history of fever, sore throat, chest pain, shortness of breath, abdominal pain, redness of eye, hematuria, dry mouth, myalgia and dryness of eyes.

On cutaneous examination, there were multiple discrete to confluent bilaterally symmetrical erythematous targetoid lesions with crust formation over the face, scalp, upper chest, upper limb and gluteal region (Fig. 1 and 2).

There were multiple discoid erythematous and scaly plaques that coalesced on the upper part of the face and scalp. There was non-blanchable purpura on her palms and soles. Examination of other systems was normal.

Her chest x-ray showed mild pleural effusion bilaterally. Spot urine for protein creatine ratio was 25.2. ANA was positive with a speckled pattern and the intensity of 3+. There was strongly positive Anti SSA/Ro antibody (149.3 units), and Anti SSB/La (42.7 units). Anti-Sm (smith) antibody (60.0 units) and anti-ds DNA antibody (150.5 IU/ml) both were positive. The patient had increased transaminases on her liver function test, ALT (217 u/l), AST (757 u/l), and ALP (759 u/l). Other causes of hepatitis were excluded by performing viral serology. We considered her findings as a case of lupus hepatitis. Her ultrasonography abdomen and pelvis showed bilateral nephrolithiasis.

Histopathological examination of erythematous targetoid lesions of the chest showed vacuolar alteration, pigment incontinence. Dermis show perivascular lymphocytic and peri-adnexal lymphohistiocytic inflammation suggestive of basal vacuolar dermatitis. Direct immunofluorescence of skin sample was negative.

According to her clinical evaluation and laboratory findings, a diagnosis of SLE was made. The patient met the diagnostic criteria for SLE (2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria) by the presence of + ANA, +Dsdna, + Anti-Sm antibody, mucocutaneous manifestations, renal and joint involvement.[8]

According to criterion set by Zeitouni *et al*, our patient fulfilled three major criteria which included the coexistence of Lupus erythematosus, EM- like lesions and speckled pattern of ANA. One of the minor criteria which included anti-Ro and anti La antibody were also positive in our case. Hence all three major criteria with at least 1 minor criterion being positive, fulfilled the diagnostic criteria of RS.[4]

She was admitted to the medical ward and started on injection of hydrocortisone which

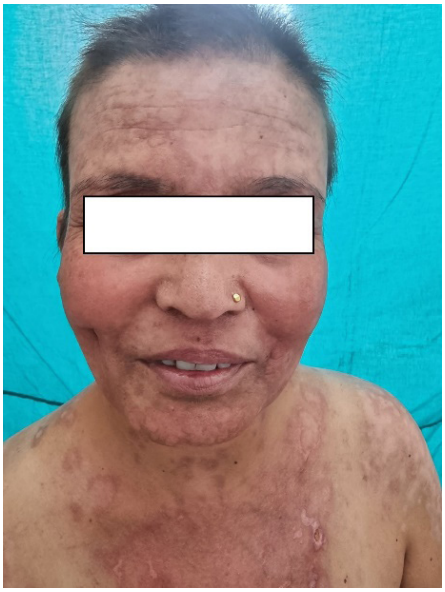

Fig. 3: Significant improvement during the course of treatment with residual skin hyper and hypopigmentation

was tapered and changed to prednisolone later as she remained free of lesions. Hydroxychloroquine was added subsequently. The patient showed gradual improvement. Her skin lesions disappeared gradually. As the patient gave history of intake of esomeprazole before the eruption of her EM like lesion, suspicion of drug induced RS was made. Hence, esomeprazole was stopped and the patient was started on medications- oral steroids and hydroxychloroquine, which showed a good response to treatment. Thus, the diagnosis of esomeprazole induced RS in our case should be documented.

Currently, she is in regular follow-up in our OPD, fortnightly. She is on a low dose of prednisolone (10 mg every alternate day) and hydroxychloroquine (200 mg/day). To date no further relapse of the lesion has been observed.

DISCUSSION

RS is a rare disease characterized by a combination of both LE and EM-like lesions with a peculiar immunologic pattern.[1,2] In 1963, Rowell *et al*[3] mentioned diagnostic criteria for RS: the presence of DLE and EM-like lesions, positive RF, speckled ANA, and saline extract of human tissue (anti-SJT) which is now known as similar to anti-RO/SSA positivity. To date, around 95 cases of EM-like lesions associated with LE have been described in the literature.[9] Most of them were lacking features of this original criteria.[1,10] This criterion was revised by Zeitouni *et al*[4] in the year 2000. Khandpur *et al*[11] mentioned that all major and at least one minor criteria, as proposed by Zeitouni *et al*[4] in the absence of histologic and immunopathologic features of LE in EM-like lesions, would be sufficiently helpful in establishing the diagnosis of RS. Chandra *et al*[2] reported a 18 year old girl with multiple ill-defined target lesions with crust formation over the forehead, cheek, scalp, upper chest and back with ulceration over hard palate. Her investigations revealed positive ANA with a speckled pattern, anti-SM antibody and strongly positive anti-Ro. She was also diagnosed with RS as per the criteria.

According to the criteria of Zeitouni *et al*,[4] our patient met all three major criteria which were the coexistence of lupus erythematosus (SLE) with EM-like lesions and speckled pattern of ANA. Minor criteria included positive anti-Ro/SSA and anti-La/SSB antibodies. A similar case report of a 43-year-old woman who developed RS during treatment with esomeprazole has been mentioned.[6] The woman was on treatment with esomeprazole. Subsequently, the woman developed skin eruption and was initially diagnosed with lupus erythematosus. She was eventually diagnosed with RS (time to reaction onset not stated) and was treated with corticosteroids and hydroxychloroquine and a positive outcome was achieved.[6]

Amatya *et al*[12] described a case of RS secondary to anti-tubercular therapy. There were erythematous targetoid lesions and non-blanchable purpura on her back and extremities including palms and soles. Murad *et al*[13] described a case of drug induced RS in an 81 year old woman with a 3-week history of crusted plaques and targetoid lesions

over her head, neck, and back. These lesions started after oral terbinafine intake for her onychomycosis 5 weeks prior. Almansouri *et al*[7] reported a 30-year-old woman who developed erosive oesophagitis during treatment with methotrexate for suspected rheumatoid arthritis, and RS during treatment with esomeprazole and azathioprine for erosive oesophagitis.

The abrupt onset and short duration of the targetoid lesions suggested the influence of the drug esomeprazole in our case. Thus, a detailed drug history should be inquired before treatment of such EM-like lesions. Associated symptoms and signs should be evaluated properly to find overlap syndrome like EM like lesions with lupus erythematosus. The management and prognosis in RS are similar to SLE or DLE occurring alone. A majority of the previously described cases followed an uneventful course and showed a good response to steroids and antimalarials.[2,15] In our patient, the lesions completely resolved following prednisolone and hydroxychloroquine. The demonstration of all major and at least one minor criteria, as proposed by Zeitouni *et al*[4] would be helpful to establish the diagnosis of this distinct clinical entity. Good coordination between specialists in Dermatology, Internal Medicine and Pathology is necessary to establish proper diagnosis, and management. Thus, this case highlights the overlapping clinical presentations in a single case: sudden onset of EM-like lesions with long duration history of scaly discoid lesions distributed in photo-exposed areas and fulfilling the criteria of SLE.

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REFERENCES

1. Arevalo AB, Nassar R, Krishan S *et al*. Lupus never fails to deceive us: a case of Rowell's Syndrome. *Case Rep Rheumatol* 2020; 22: 2020: 8884230.
2. Chandra A, Saha SK, Ray AK, Karmakar P. Rowell's syndrome: a rare but distinct entity in rheumatology. *Brit Med J Case Rep* 2020; 23: 13: e235173.
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. Zeitouni NC, Funaro D, Cloutier RA, Gagné E, Claveau J. Redefining Rowell's syndrome. *Br J Dermatol* 2000; 142: 343-6.
5. Pozharashka J, Dourmishev L, Balabanova M, Vassileva S, Miteva L. Rowell's Syndrome Triggered by Omeprazole. *Acta Dermatovenerol Croat* 2019; 27: 124-6.
6. Schissler C, Banea S, Tortel MC, Mahe A. A new case of Rowell's syndrome. *Annales de Dermatologie et de Venereologie* 2017; 144: 263-7.
7. Almansouri AY, Alzahrani ZA. A case of rhupus with Rowell syndrome. *Open Access Rheumatol* 2020; 12: 91-6.
8. Aringer M, Costenbader K, Daikh D *et al*. European league against rheumatism/American college of rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheumatol* 2019; 71: 1400-12.
9. 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.
10. Modi GM, Shen A, Mazloom A *et al*. Lupus erythematosus masquerading as erythema multiforme: does Rowell syndrome really exist? *Dermatol Online J* 2009; 15: 5.
11. Khandpur S, Das S, Singh MK. Rowell's syndrome revisited: report of two cases from India. *Int J Dermatol* 2005; 44: 545-9.
12. Amatya B, Maharjan L. Rowell syndrome secondary to anti-tubercular therapy: a case report and literature review. *Our Dermatol Online* 2017; 8: 200-3.
13. Murad A, Shudell E, Mulligan N. Rowell's syndrome induced by terbinafine. *BMJ Case Report* 2015; 28: 2015: bcr2015210360.
14. Kacalak-Rzepka A, Kiedrowicz M, Bielecka-Grzela S *et al*. 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: 702-4.
15. Fitzgerald EA, Purcell SM, Kantor GR, Goldman HM. Rowell's syndrome: report of a case. *J Am Acad Dermatol* 1996; 35: 801-3.