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Case Report Open Access

Rowell syndrome and SLE flare: A case report

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Rowell syndrome (RS) is a disorder characterized by the occurrence of erythema multiforme-like lesions (EM) coexisting with systemic lupus erythematosus (SLE). It may be considered a rare subtype of lupus-specific skin lesions. Herein, we report a clinical presentation of RS in a 34-year-old woman with diagnosed SLE and no previous cutaneous lesion who presented with skin lesions and fever. Clinical, laboratory, and histopathology assessments confirmed the diagnosis of RS in the context of SLE flare-up. She was treated with methylprednisolone 1g intravenous daily for 3 days, then continued with oral prednisolone, hydroxychloroquine, and mycophenolate mofetil. With treatment, the patient's skin lesions and oral ulcers gradually subsided, and all skin lesions disappeared without scarring after one month.

Keywords: Rowell Syndrome; Systemic Lupus Erythematosus; Erythema Multiforme; Skin lesions

Introduction

Rowell's syndrome (RS), first described in 1963 by Dr. Neville Rowell, is an uncommon presentation of systemic lupus erythematosus (SLE) with erythema multiforme like lesions associated with specific serological changes [1]. Later, an analysis of 132 new cases proposed the latest diagnostic standards for RS [2]. Controversy surrounds the viability of RS as a distinct diagnosis, questioning whether RS is a real association, an overlap, a mere coincidence, or a variant of cutaneous LE. We report a unique case of RS in a 34-year-old woman with SLE who presented with annular and erythematous maculo-papular plaques with some atypical targetoid skin lesions, fever, and a high SLE activity index.

Case presentation

A 34-year-old married Iranian woman with a 15-year history of SLE referred to the emergency department with a burning sensation associated with a skin rash and 10 days of intermittent fever. She reported no sun exposure, upper respiratory infection, or new drug intake. Moreover, the patient had no history of photosensitivity, malar rash, or any cutaneous lesion. The first manifestation of SLE was polyarthritis, and the patient was initially treated with prednisolone, hydroxychloroquine (HCQ), and methotrexate. Because of her refractory arthritis and pregnancy plan, and considering her history of intolerance to azathioprine and severe pneumonia caused by severe hypogammaglobulinemia, after treatment

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with rituximab, her treatment had been switched to adalimumab 8 months prior to this presentation. The patient reported that she had experienced a flare-up of arthritis 3 months before, and since that time, she had been receiving 500 mg IV methylprednisolone per month. The patient was positive for antinuclear antibody (ANA), anti-double-stranded DNA (anti-dsDNA), anti-RO, and anti-cardiolipin antibodies (ACLA) IgG. On physical examination, she was conscious but ill with a blood pressure of 110/60 mmHg, heart rate of 96 beats per minute with a regular rhythm, respiration rate of 15 breaths per minute, and a temperature of 39ºC. Physical examination also revealed generalized annular and erythematous maculopapular plaques with some atypical targetoid lesions, especially in the proximal limbs, and hard palates (Figure1). Initial laboratory test results are shown in Table 1.

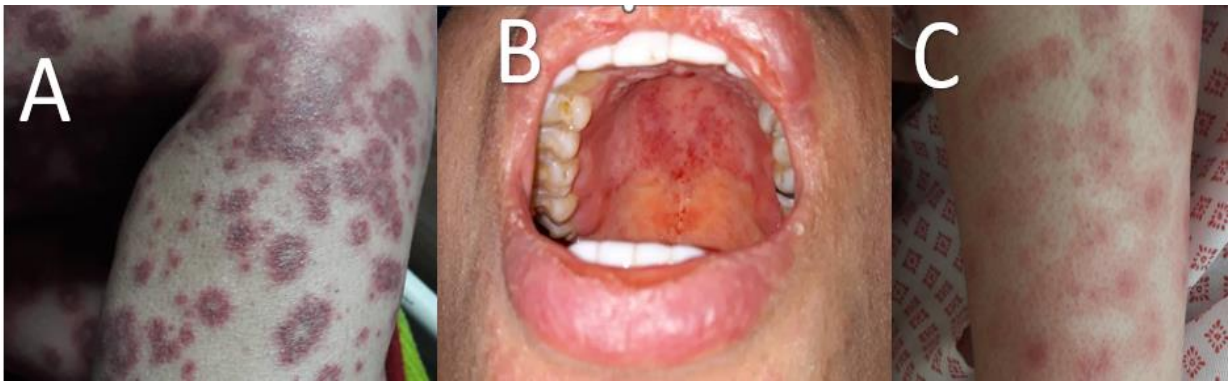

Figure 1: A: Annular lesion, B: Hard palate ulcer, C: Atypical targetoid lesion.

Table.1. Laboratory test on admission

Test	Result	Normal range	Test	Result	Normal range
WBC	6× 10^9/L	4.5-11	Cr	1.5 mg/dL	0.6-1.1
Hb	10.4 g/dl	11.5-14.5	ESR	38 mm/hour	Up to 20
MCV	78.4 Fl	80-100	CRP	73 mg/L	Normal<6
PLT	200× 10^9/L	239	LDH	667 U/L	Normal< 480
AST	16 IU/L	Up to 38	C3	40 mg/dL	90-180
ALT	12 IU/L	Up to 35	C4	10 mg/dL	10-40
Bilirubin	0. 5 mg/dL	Up to 1	CH50	110 mg/dL	70-150
Retic	0.5%	0.5-1.5	Coombs Direct	negative	
PBS	Schistocytes were seen		UA:	Protein: 2+ WBC:18-20 RBC: 4-6 Granular cast: 4-5 5/HPF	

ALT, Alanine Transaminase; AST, Aspartate Aminotransferase; Cr, Creatinine; CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate; Hb, Hemoglobin; HPF, High Power Field; LDH, Lactate Dehydrogenase; MCV, Mean Corpuscular Volume; PLT, Platelets; PBS, Peripheral Blood Smear; RBC, Red Blood Cell; Retic, Reticulocyte; UA, Urinalysis; WBC, White Blood Cell.

Chest computed tomography scan depicted basilar subpleural atelectasis. Echocardiography revealed ejection fraction: 55%, pulmonary arterial pressure: 26 mmHg, and no evidence of

vegetation. Subsequently, the patient was visited by a rheumatologist and a dermatologist. Based on clinical manifestations, urticaria vasculitis, EM secondary to a drug reaction or connective tissue disorder, subacute cutaneous lupus, and RS were considered as differential diagnoses. Two punch biopsies were taken from the patient's upper limb. Initially, she was managed conservatively with 12 mg dexamethasone IV daily, IV antibiotics, and oral acyclovir. She showed a dramatic response to treatment. The majority of skin lesions and oral ulcers subsided gradually after treatment with steroids, and she became afebrile 72 hours after receiving her medication. The requested laboratory test was completed at this time and showed Covid PCR: negative, blood culture: no growth, and urine culture: no growth. Antibodies of HBV, HCV, and HIV were negative, immunoglobulin levels were normal, and the 24-hoururinary proteine xcretion was 775 mg. As a result, all antibiotic and antiviral drugs were stopped. The systemic lupus erythematosus disease activity index 2000 (SLEDAI-2K) (3) was also measured, and based on the score of 25, flare-up of SLE was considered. Therefore, the patient was prescribed methylprednisolone 1 g IV daily for 3 days, followed by continued treatment with oral prednisolone.

Histopathology revealed vacuolar degeneration of the basal layer, Civatte body formation in the dermis and upper level of the epidermis, and pigment incontinence. The dermis showed superficial perivascular lymphoplasmacytic infiltration associated with RBC extravasation and vasculopathy effects (Figure 2). EM-like lichenoid reaction patterns in the background of changes related to SLE were compatible with RS. The patient was admitted for a 7-day duration. Serum creatinine, ESR, and CRP levels decreased, while proteinuria remained unchanged (Table 2).

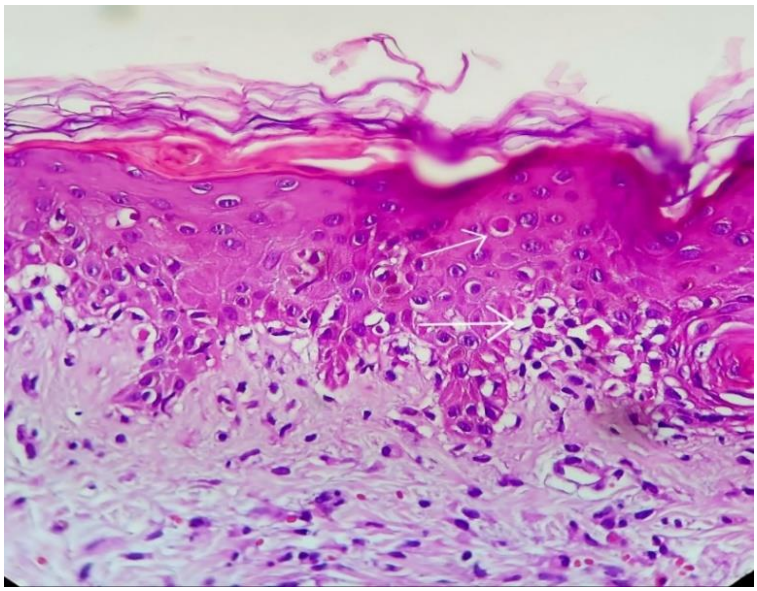

Figure 2. Civatte body formation in the dermis and upper level of the epidermis (arrows)

Table2. Laboratory test on admission and discharge

	On Admission	On Discharge
Cr (mg/dL)	1.5	1
ESR (mm/hour)	38	7
CRP (mg/L)	73	0.2
LDH (U/L)	667	589

Cr, Creatinine; CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate; LDH, Lactate Dehydrogenase.

Discussion

Erythema multiforme-like lesions are a classically self-limited reaction to a drug or infective agent without any specific serological antibodies. It is characterized by acral and/or mucosal targetoid lesions with a central dusky necrotic zone, a middle-skin-colored zone, and a peripheral erythematous zone[2, 4]. While our patient had no trigger factors, she was positive for ANA, dsDNA, and RO, which differentiated RS from erythema multiforme [5].

The diagnostic criteria for RS were redefined in 2000, whence three major criteria and one minor criterion were to be satisfied for diagnosis. The major criteria were LE in any form, EM-like lesions (mucosa may or may not be involved), and ANA positivity (speckled pattern). The minor criteria consisted of the presence of chilblains, RF, and anti-Ro, or anti-La antibody positivity [1]. Later, it was suggested that RS may be considered a rare subtype in the spectrum of lupus-specific skin lesions, and the latest diagnostic standards for RS were proposed. This diagnosis of RS required all four major and at least one minor criterion [2]. The major criteria were chronic cutaneous LE, EM-like lesions (typical target or targetoid lesions), at least one ANA positivity speckled pattern, anti-Ro/SSA and anti-La/ SS-B antibodies positivity, and negative direct immunofluorescence (DIF) on EM-like lesions. The minor criteria were the absence of triggering factors (infections or medications) and typical location (acral and mucosal) of EM, the presence of at least one of the criteria for an SLE diagnosis provided by the American College of Rheumatology (ACR) except for discoid or malar rash, photosensitivity, chilblains, oral ulcers, and ANA positivity. Our patient met the former diagnostic criteria for RS, although she had no history of chronic cutaneous lesion, and DIF was not performed to fully match later criteria. Furthermore, based on her high SLEDAI-2K score, a flare-up of SLE was considered to have possibly been caused by adalimumab. A review of other case reports of RS for lupus disease activity in other organs revealed interesting results that confirmed our presumption that RS occurred in the context of SLE activity. This syndrome has been reported in a patient with SLE in the context of stopping immunosuppressive drugs; the patient, who had withdrawn his treatment one month earlier, referred with skin rash all over his body, laboratory evidence of hemolysis, low serum levels of C3 and C4, raised ESR and CRP, red cell casts in U/A, positive ANA with a speckled pattern, a positive anti-La, and anti-Ro. The patient did not experience a recurrence of skin lesions after restarting treatment with oral prednisolone, HCQ, and azathioprine [6]. RS has also been reported as the first manifestation of SLE in an 18-year-old girl who presented with skin rashes, fever, polyarthralgia, alopecia, lymphadenopathy, pancytopenia, raised ESR, low serum levels of complement C3, C4, microalbuminuria, as well as positive ANA and anti-RO antibodies. She was treated with prednisolone and HCQ and responded well, which led to the disappearance of her skin lesions and oral ulceration over the next days [7]. RS has even been reported in a patient with end stage renal disease caused by lupus nephritis who had skin rash, pancytopenia, and low C3 and C4 simultaneously; treatment with pulses of methylprednisolone and rituximab maintained the remission of skin disease and cytopenia [8]. Gallo et al. reported a unique case of RS. Their patient presented with lymphadenopathy and hepatomegaly, rash, fever, arthralgia, leukopenia, and elevated ESR levels; prednisone and HCQ administration led to gradual improvement of the patient's skin manifestations and elimination of related symptoms after two months of follow-up [9]. Another case of RS was reported in a patient with multiple reddish lesions, fever, joint pain, photosensitivity, anemia, raised ESR, the presence of cellular casts in U/A, a positive test for ANA speckled pattern, and anti-ds-DNA [10]. A review of the mentioned cases established that skin symptoms lead to earlier referral of patients, which may be considered a leading indicator for the diagnosis of SLE flare-up. According to the mentioned case reports, RS has similar prognoses and treatments to SLE or DLE which occur alone (7-10). Likewise, our patient responded well to corticosteroids, HCQ, and MMF, and 6 months of follow-up indicated no further recurrence of skin lesions.

Conclusion

Because RS may be a symptom of SLE activity

and organ involvement, it is concluded that this is more of a subtype of SLE than a separate clinical entity.

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Conflict of interest

None

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