CASE STUDIES

Rowell syndrome: A case report and review of literature

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Abstract

Rowell syndrome is a rare disease consisting of lupus erythematosus associated with erythema multiforme-like lesions. The present case study discusses the occurrence of this syndrome in a 38-year-old female who presented with erythematous scaly lesions on face, neck and back, along with the targetoid lesions on upper arms and back of the neck, with oral erosions. Laboratory investigations revealed speckled pattern of anti-nuclear antibody (ANA) with a titer of 1:640, and anti-dsDNA and anti-La (SS-B) positivity. Histology of the targetoid lesion was consistent with erythema multiforme. Significant improvement within four weeks was noted with the use of oral steroids and anti-malarials.

Keywords: Rowell syndrome, Lupus erythematosus, Erythema multiformae, Speckled ANA.

Introduction

Rowell syndrome, described in 1960s, is a rare presentation of lupus erythematosus (LE) with erythema multiforme (EM)-like lesions associated with antinuclear antibody (ANA), anti-La (SS-B)/anti-Ro (SS-A) antibodies and rheumatoid factor (RF) positivity.[1, 2]

Case report

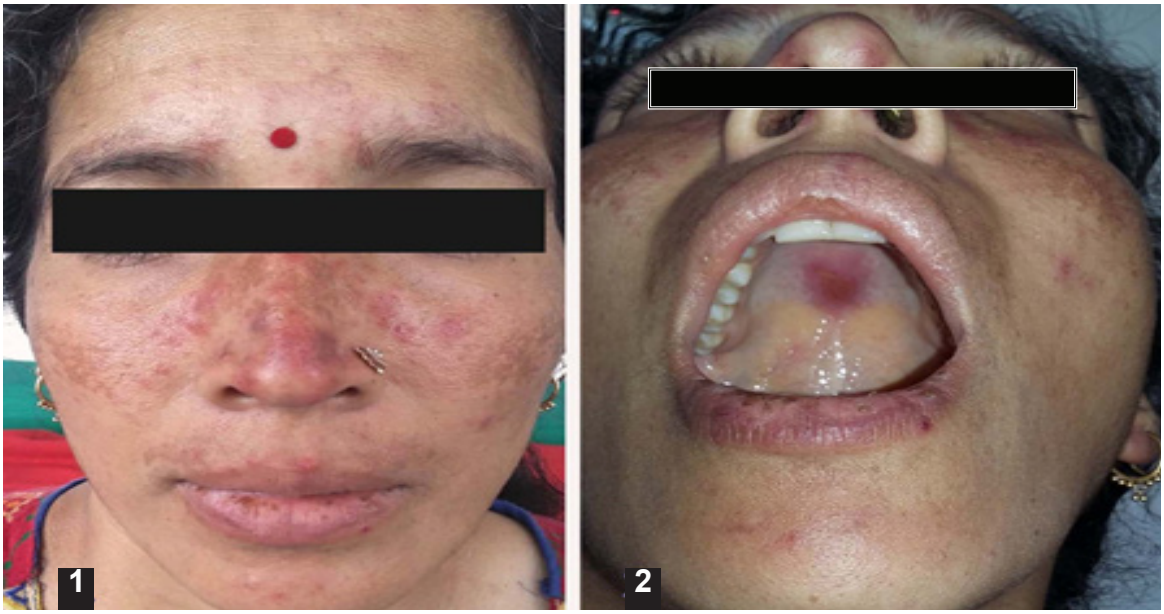
A 38-year-old married female presented with a one-month history of multiple reddish colored lesions on various body parts, low-grade fever, generalized body ache and lethargy. The patient had reddish, painful lesions over the back of neck and upper arms and painful oral lesions for past 1 week. The patient history also revealed photosensitivity, chilblains and pain in the limb joints. She did not have decreased urination, hematuria, chest pain, cough, dyspnea, palpitations or spontaneous bleeding tendencies. Detailed cutaneous examination revealed that the patient had multiple, well-defined, erythematous, scaly plaques approximately 2x1 cm in size over face (predominantly nasal area and forehead), neck, pre-sternal area, trunk and back (Fig. 1 and 3). There was hemorrhagic crusting on the lips, and well-defined painful erosions over the palatal surface (Fig. 2). A few well-defined erythematous papules with central duskiness giving targetoid morphology were present over upper arms and back of the neck (Fig. 4). Other systemic examinations were normal. Due to the concurrent presence of lupus eryththematosus and EM-like lesions, the possibility of Rowell syndrome was considered and the patient was subjected to baseline investigations. Complete hemogram was normal except anemia (Hb:8.6 g/dl) and raised TLC (12,680 /ul). Serum chemistry and urine analysis were also normal. ANA by immunofluorescent assay (IFA) was positive with a titer of 1:640 and speckled pattern. Anti-dsDNA done by IFA was also positive (+2). Anti SSB-LA performed by enzyme immuno-assay (EIA) was also raised with a value of 59.51U (normal<20.00U). RF (nephelometric method) was found to be negative. Histologic examination of lesional skin of the upper arm revealed hyperkeratosis, epidermal necrosis, vacuolar degeneration of the dermal-epidermal junction, and papillary dermal edema suggestive of EM.

Diagnosis of Rowell syndrome was concluded and the patient was started on oral prednisolone 60 mg/day, hydroxycholoroquine 200 mg twice daily and other supportive medications. Significant improvement was seen within 4 weeks, steroids were gradually tapered off and hydroxychloroquine was continued with other topical agents.

Discussion

The association of LE with EM was first reported by Shlotz in 1922.[3] In 1963, Rowell defined this association as a distinct entity upon discovering different clinical and immunologic findings in four patients with discoid lupus

Fig. 1, 2, 3 and 4: Skin and oral mucosal lesions



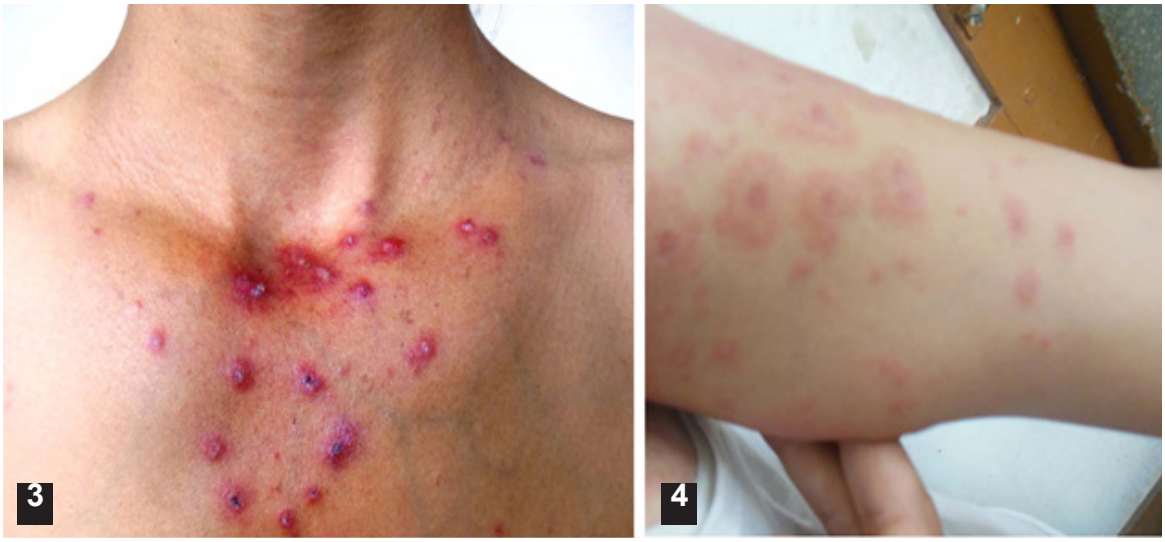


Table 1: Revised diagnostic criteria for Rowell's syndrome by Zeitouni *et al.*[4]

Major criteria	Minor criteria
Lupus erythematosus- SLE, DLE or subacute cutaneous LE	Chilblains
EM-like lesions with or without mucosal involvement	Positive anti-Ro or anti-La antibodies
Speckled pattern of ANA	A reactive rheumatoid factor

Abbreviations: SCLE: Subacute cutaneous LE, DLE: Discoid lupus erythematosus, ANA: Antinuclear antibody, SLE: Systemic lupus erythematosus

Table 2: Differential diagnosis of erythema multiforme[7]

Differential diagnosis of EM	Features that distinguish from EM		
	Clinical features	**Pathologic features**	**Laboratory studies**
Urticaria	Transient plaques with central zone of normal skin or erythema, may have assciated mucosal edema	Papillary edema with mild perivascular and interstitial infiltrate of eosinophils, lymphocytes and mast cells	None
Stevens-Johnson syndrome	Macular atypical targetoid lesions, widespread dusky erythema with blisters. Painful, tender skin with severe mucosal involvement.	Extensive epidermal necrosis with paucity of inflammatory cells	None
Fixed drug eruption (FDE)	Dusky plaques with/without central necrosis. Less frequent mucosal involvement. Typically with medication history.	Similar to EM, but may have deeper extension of infiltrate, few neutrophils, prominent melanin incontinence	None
Bullous pemphigoid	Pruritic urticarial plaques, tense bullae, may have mucosal involvement	Eosinophilic spongiosis or subepidermal bullae with numerous eosinophils. DIF findings of linear C3 and IgG basement membrane zone deposition.	BP180 and BP230 auto-antibodies. IIF showing anti-basement membrane IgG antibodies.
Paraneoplastic pemphigus	Polymorphous, progressive skin lesions, severe mucosal involvement. Presence of underlying malignancy.	Suprabasilar acantholysis, vacuolar or lichenoid interface dermatitis. Findings of cell-surface IgG or combined cell surface and basement membrane zone of IgG and C3 deposition.	Autoantibodies against Dg1 and Dg3; demonstration of antiplakin antibodies through IIF.
Sweet's syndrome	Edematous, erythematous plaques, pyrexia. No mucosal involvement.	Dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis	Peripheral leukocytosis, neutrophilia
Cutaneous small-vessel vasculitis (CSVV)	Typical palpable purpura, lesions that resolve with bruise-like discoloration	Leukocytoclastic vasculitis	Elucidating etiologic factors (infection, drugs, connective tissue disease, etc)

Abbreviations- HSV: Herpes simplex virus, BP: Bullous pemphigoid, DIF: Direct immunofluorescence, IIF: Indirect immuno-fluorescence, Dg: Desmoglein, IgG: Immunoglobulin G

erythematosus (DLE).[2] The original criteria of Rowell's syndrome consist of LE, EM-like lesions and immunological abnormalities such as speckled pattern of ANA, RF and saline extract of human tissue (anti-SJT) positivity, which is now regarded as similar to anti-Ro.[1, 2, 4] In 2000, Zeitouni *et al.* proposed the revised diagnostic criteria for Rowell syndrome (Table 1). Three major criteria and at least one minor criterion are required for diagnosing the syndrome.[4] Speckled ANA pattern is the most consistent feature of RS occurring in about 88% of the cases, whereas RF is the least preserved feature, present in only 41%.[2, 5] Khandpur *et al.* have reported two cases of RS in SLE who were negative for anti-Ro/SSA and anti-La/SSB. The present patient had characteristic lesions of sub-acute cutaneous

LE, lesions of EM, speckled pattern of ANA, positive anti-dsDNA and anti-La/SSB, and history of chill blains, but negative RF. The patient fulfilled the required criteria of Rowell's syndrome.

Recent evidence has indicated that viral infections may be triggering factors for both SLE and EM. Unidentified Herpes simplex virus, Epstein–Barr virus or other viral infections may cross-react with lupus autoantigens and may initiate the immunologic response, thereby triggering the EM-like lesions in SLE. Dysregulated apoptosis may be the cause for many of the major manifestations of LE and EM skin lesions. Similar immunopathogenetic mechanisms described in both diseases may be responsible for the concurrence of these two diseases.[6] Before making a diagnosis of RS, it is important to rule out other mimics of EM (Table 2) and common causes of EM such as herpes and drugs.[7]

The present case did not have any identifiable precipitating factor for EM. Rowell should be suspected in patients with EM of longer duration or those not responding to a course of oral acyclovir.[8] The treatment of the syndrome is similar to that of SLE. Oral steroids in tapering doses, azathioprine, antimalarials like hydroxychloroquine or chloroquine, dapsone, cyclosporine and cyclophosphamide have been used with good results.[1, 5, 9, 10]

Despite the refined diagnostic criteria, recent literature has debated on whether RS is an overlap syndrome or co-occurrence of DLE and EM. Some studies have proposed that the RS is a subentity of subacute LE with EM while others have variously suggested that RS is a different variant of cutaneous LE, a subtype of chronic LE or an independent LE subtype.[1, 9] The addition of new cases (like the present one) to the literature further strengthens the opinion that Rowell's syndrome is a distinct clinical entity with specific diagnostic features. Although it is not so common, a diagnostic suspicion should always be kept in mind while dealing with patients of LE with EM-like lesions.

Competing interests
The authors declare that they have no competing interests.

Citation
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