

ANA-negative systemic lupus erythematosus with targetoid lesions: Rowell syndrome or just a rare presentation of lupus erythematosus

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Abstract Rowell syndrome is usually diagnosed by the presence of erythema multiforme (EM)-like targetoid lesions in the patients of cutaneous or systemic lupus erythematosus (CLE/SLE) and characterized by specific serological or immunological profile like speckled antinuclear antibody (ANA) pattern, antibody against saline extract of human tissues (anti-SjT) and positive serum rheumatoid factor (RF). The absence of universally accepted criteria and their poor specificity usually make the diagnosis very difficult. Moreover in the light of histopathological revelation of dermal mucin deposition along with interface changes and necrotic basal keratinocytes in the absence of serum positivity for ANA antibody and RF, true existence of this syndrome is still doubtful. Here we report a case of ANA-negative SLE having targetoid lesions on distal extremities and histopathological evidence of both the disease i.e LE and EM.

Key words

Lupus erythematosus, erythema multiforme, Rowell syndrome.

Introduction

Patients with CLE or DLE may develop EM-like lesions and characteristic serological abnormalities like speckled ANA pattern, anti-SjT and positive serum RF. It was first described by Rowell in 1963 so termed as Rowell syndrome.¹ Over the time, major and minor criteria were proposed to refine its diagnosis but due to lack of specificity and consistency of these criteria, true existence of this syndrome has always been questioned.²⁻¹³ Histopathological features further suggests to consider it merely a rare presentation of lupus erythematosus.

A 19-year-old female was admitted in our department of dermatology presenting with erythematous and hyperpigmented papules, plaques and few vesicular lesions on the face, trunk, upper and lower extremities and oral mucosa associated with pruritus, fever and arthralgia for 10 days. She had past history of similar episodes 1 month back. She did not have any history of extensive sunlight exposure, herpes virus infection, upper respiratory tract infection, chest pain, dyspnea, cough or spontaneous bleeding tendencies. She had no history suggestive of Raynaud's phenomenon. She denied any history of drug intake prior to developing similar lesions in the previous episode. There was no such family history.

On cutaneous examination, there were widespread erythematous and hyperpigmented confluent papules and plaques all over the

Case Report

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Figure 1 Erythematous and hyperpigmented papular and plaque type lesions.



Figure 2 ulceration on hard palate. **Figure 3** EM like targetoid lesions on palm and soles.



Figure 4 Sparse and brittle 'lupus hairs'.

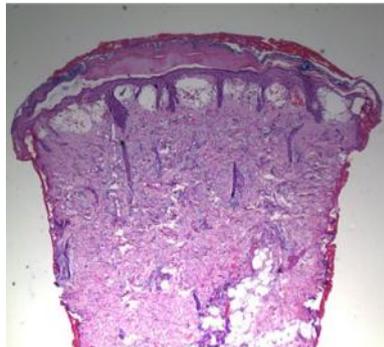


Figure 5 moderately dense superficial perivascular lymphocytic infiltrate with extensive interface change.

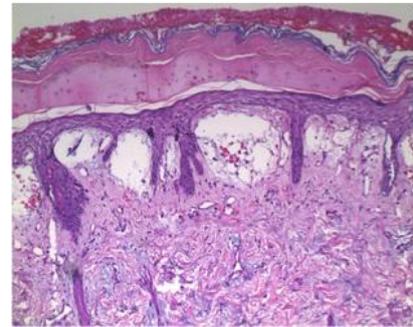


Figure 6 Abundant dermal mucin and necrotic keratinocytes at dermoepidermal junction and epidermis.

body and a few vesicular lesions on distal parts of both upper and lower limbs (**Figure 1**). Among mucosal sites, only oral mucosa was involved having erosions and ulcerations with crusting on lips (**Figure 2**). Targetoid lesions were prominent on both palms and soles (**Figure 3**). Hair on scalp was sparse and brittle (lupus hair) with diffuse alopecia over

vertex (**Figure 4**). On general examination, patient was febrile and anemic. Systemic examination was not significant.

Histopathological examination of biopsy samples taken from both targetoid and plaque type lesion revealed moderately dense superficial perivascular lymphocytic infiltrate



Figure 7 Healed lesions with scarring and atrophy

Box 1 Diagnostic criteria for Rowell syndrome [3]

Major criteria

- i. Cutaneous LE (ACLE, SCLE, DLE) OR SLE
- ii. EM-like lesions
- iii. Speckled pattern of ANA.

Minor criteria

- i. Chilblains
- ii. Anti-Ro antibody or anti-La antibody
- iii. Positive RF

with extensive interface change (**Figure 5**). There was subepidermal blister, the roof of which was formed by completely necrotic epidermis. To the side of the blister the epidermis showed scattered necrotic keratinocytes in mid-epidermis and at dermoepidermal junction. Interstitial dermis shows abundant mucin (**Figure 6**). Among laboratory parameters, hemogram revealed hemoglobin-7.5gm%, TLC 3750/mm³, platelet count 152000/mm³, PCV-25.4%, RBC count 3.49 million/mm³, MCH 21.5pg and ESR-121 mm at 1st hr. Peripheral blood smear suggested microcytic hypochromic anemia with anisopoikilocytosis. Urine examination and microscopy showed hematuria and proteinuria. Apart from these parameters patient was ANA, RF and anti-Ds DNA negative.

This patient met the ARA criteria for SLE as having oral ulceration, skin rash, arthralgia, hematological and renal abnormalities i.e. 5 out of 11 positive. So diagnosis of ANA-negative SLE was made and along with topical potent steroids and emollients, 40 mg oral

prednisolone was also started. Within 15 days, patient became asymptomatic, targetoid lesions started subsiding and papulosquamous lesions healed with scarring and atrophy (**Figure 7**).

Discussion

RS is a rare syndromic entity with EM-like lesions in patients of LE. This association was first noted by Scholtz in 1922. Later in 1963 during a study on 120 patients of DLE, Rowell found distinct clinical and serological findings in 4 female patients having EM-like lesions, positive RF, positive anti-SjT (analogous to anti-Ro/La antibody) and speckled pattern of ANA.¹ Most consistent serological finding is speckled ANA (90%) and least are serum RF and anti-SjT or anti-Ro/La antibody. Clinically chilblains-like lesions can also be present which was suggested by Lee *et al.*⁴ in 1995. Due to inconsistency of these findings and to make it more clear, originally described syndrome was redefined by Zeitouni *et al.*³ in 2000 and following major and minor criteria were proposed (**Box 1**).

In order to make a diagnosis of RS, all major and at least one minor criteria should be fulfilled but their specificity and consistency is always lacking. Apart from the least preserved immunological profile like serum RF and anti-Ro/La, even ANA can also be negative in SLE in 5-10% cases. In DLE, ANA is more likely to be negative. Hence in view of non-specific

serological profile with poor sensitivity also, existence of RS is frequently questioned. Furthermore, histopathological examination of targetoid lesions reveals orthohyperkeratosis, keratotic plugging, basal cell vacuolar degeneration with colloid bodies, necrotic basal keratinocytes, perivascular and periadnexal lymphocytic infiltrates, melanin incontinence and dermal mucin deposition, consistent with LE. Basal cell vacuolar degeneration and necrotic basal keratinocytes are seen in both LE and EM because of dysregulated apoptosis preceded by immunologic response initiated by unidentified HSV, EBV or other viral infections crossreacting with lupus autoantigens. Thus, with these clinical, histopathological and immunological scenario and being described with all forms of LE (DLE, SCLE, ACLE, SLE), it invites an open area of debate to accept or deny the existence of this syndromic entity on the basis of some valid ground.

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