Targetoid lesions in a patient with systemic lupus erythematosus

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Abstract

Rowell Syndrome is a rare presentation of lupus erythematosus manifesting as an eruption of erythema multiforme-like papules and plaques with immunological findings of positive rheumatoid factor, speckled antinuclear antibodies, and/or anti-Ro/La antibodies. This case highlights the unusual and highly debated presentation of Rowell Syndrome in a 66-year-old woman with newly-appearing erythematous, targetoid plaques in the setting of previously diagnosed systemic lupus erythematosus. Skin biopsy revealed histological features of full-thickness epidermal necrosis with focal sub-epidermal separation and a superficial perivascular lymphocytic infiltrate interpreted to favor Rowell Syndrome given her clinical history and presentation. Although no standard treatment exists, a prednisone taper and topical corticosteroids proved effective initially, with complete resolution at six months on mycophenolate mofetil and belimumab.

Keywords: Rowell syndrome, lupus erythematosus, targetoid lesions, erythema multiforme

Introduction

Rowell syndrome (RS) is an entity in which patients with lupus erythematosus (LE) develop characteristic lesions similar to those of erythema multiforme (EM), in the presence of specific serologic criteria. A diagnosis of RS is based on the presence of major and minor criteria seen in **Table 1** [1]. Major criteria include: 1) a diagnosis of systemic LE, discoid LE, or subacute cutaneous lupus erythematosus (SCLE), 2) EM-like skin lesions, and 3) speckled anti-nuclear antibody (ANA). Minor criteria include chilblains, anti-Ro/La antibody, and/or a positive rheumatoid factor [1]. Herein, we present a 66-year-old woman with a pre-existing diagnosis of systemic LE who developed RS.

Case Synopsis

A 66-year-old woman with a one-year history of systemic LE presented with one week of pruritic papules and plaques on the face, chest, and arms (**Figure 1**). She denied any new constitutional symptoms including fevers, exposure to new drugs, or other changes in general health. Her medical

Table 1: *Criteria for Rowell syndrome diagnosis by Zeitouni et al. [1].*

Major Criteria: Must meet all	Lupus erythematosus (LE): systemic LE, discoid LE or subacute cutaneous LE Erythema multiforme-like lesions with or without mucosal involvement Speckled pattern of anti-nuclear antibody
Minor Criteria: Need at least 1	Positive rheumatoid factor Anti-Ro antibody or Anti-La antibody Chilblains

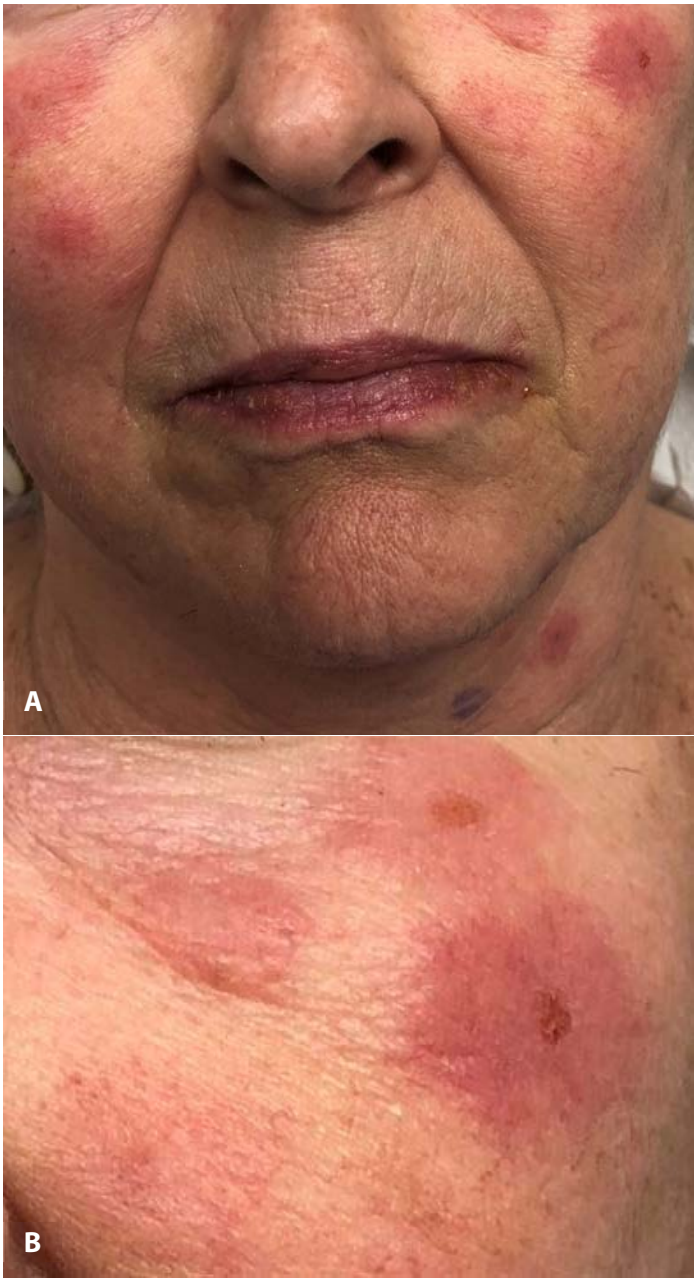

Figure 1. ***A)*** *Targetoid, erythematous papules and plaques on the face.* ***B)*** *Close-up of the skin lesions demonstrating central crusting.*

history included a several year history of non-specific inflammatory arthritis and alopecia secondary to LE, which was being treated with hydroxychloroquine 200mg twice daily. She also had a history of granuloma annulare (now resolved) and major depression which was well-controlled on medical therapy. On physical examination, she had targetoid, erythematous, indurated papules and plaques on sun-exposed areas including the face, neck, upper chest, and bilateral dorsal forearms. Some lesions were noted to have darker centers with crusting and others had central vesicles with serous fluid. She had no mucosal lesions. Two punch biopsy specimens of representative lesions on the neck and left forearm w ere obtained for routine histopathology (**Figure 2**). Additionally, two punch biopsy specimens were obtained for direct immunofluorescence from lesional skin on the left forearm and non-lesional, sun-protected skin on the right buttock.

Biopsy specimens revealed areas of full-thickness epidermal necrosis with focal sub-epidermal separation. The superficial dermis contained a perivascular lymphocytic infiltrate. These findings were consistent with a diagnosis of RS in the setting of the patient's known systemic LE. Direct immunofluorescence of both the left forearm and the right buttock lesions were negative for a lupus band. Her ANA titer a few years before presentation was 1:40 in speckled pattern and was now noted to be 1:360 in nuclear homogenous pattern. At the time of this evaluation, she tested positive for double-stranded deoxyribonucleic acid antibody and negative for anti-Ro and anti-La antibodies.

In addition to hydroxychloroquine, she was treated with 0.05% halobetasol propionate cream and oral prednisone starting at 60mg daily and tapered every three days to 40mg, 20mg, and 10mg, respectively, with significant resolution of her skin eruption. She

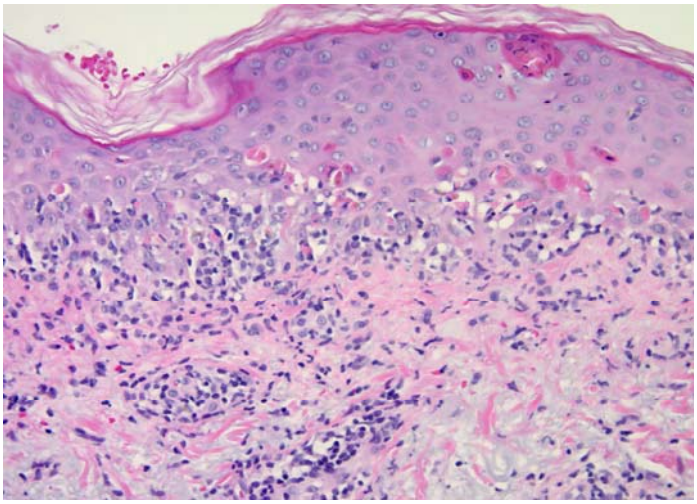

Figure 2. *Skin biopsy showed perivascular and interface lymphocytic infiltrate with keratinocyte necrosis. There is lymphocyte satellitosis to degenerating keratinocytes at all layers of the epidermis, which is characteristic of subacute cutaneous lupus erythematosus. H&E, 40×.*

subsequently had recurrence of skin lesions four to six weeks later and was transitioned to mycophenolate mofetil and belimumab with complete resolution of cutaneous LE at six months.

Case Discussion

Rowell syndrome was originally described in 1963 by Rowell et al. who identified four females with discoid LE, EM-like lesions, and presence of one of the following serology: speckled ANA, anti-Ro/La antibody, or rheumatoid factor (RF), [2]. In 2000, a revised set of criteria for RS were proposed with the patient needing to meet three major criteria plus one minor criteria for diagnosis (**Table 1**), [1]. Major criteria included 1) a diagnosis of systemic LE, discoid LE, or SCLE; 2) EM-like skin lesions; and 3) speckled ANA. Minor criteria included chilblains, anti-Ro/La antibody, or a positive RF [1]. Despite the original description and the later proposed criteria, the term RS has been loosely used in literature to describe any case of systemic or cutaneous LE with EM-like lesions [3]. In fact, several reviews have indicated that numerous case reports of RS do not meet the criteria originally established by Rowell [4]. Serology seen in RS is similar to that of SCLE. Many dermatologists now consider RS to be a morphologic variant of cutaneous LE rather than a distinct entity [5].

Clinically, targetoid lesions with central vesiculation or necrosis are seen. Some cases have reported annular plaques similar to those seen in SCLE but it is possible that these patients actually had SCLE misdiagnosed as RS [5]. Mucosal involvement is seen in 47-50% of cases [1,7]. A review of 95 RS cases found the median age of diagnosis to be 32 years and a female to male ratio of 8:1. Most patients have LE for years before developing EM-like lesions. In contrast to EM, skin lesions in RS do not have known infectious or drug triggers [7].

Histologically, this condition is characterized by apoptotic keratinocytes or significant epidermal necrosis such as in EM, interface dermatitis, and a superficial and deep perivascular lymphocytic infiltrate with variable interstitial mucinosis as in LE [8,9].

Although our patient's lesional skin direct immunofluorescence was negative for the lupus band, we favored a diagnosis of RS over EM when the histology was interpreted in light of her systemic LE, serology, and absence of any EM triggers. Of note, a negative direct immunofluorescence on non-lesional, sun-protected skin in systemic LE may have favorable prognostic implications with regards to severity of extra-cutaneous lupus, including lupus nephritis [10].

No standard treatment exists for Rowell syndrome. Drugs including but not limited to systemic and topical steroids, anti-malarials such as hydroxychloroquine and chloroquine, and immunosuppressive agents such as methotrexate, azathioprine, cyclosporine, and dapsone have been used with variable success [3,8].

Belimumab, a human monoclonal antibody directed against B lymphocyte stimulator, is often considered in recalcitrant cases of SLE. Although studies have shown that using belimumab for recalcitrant systemic SLE is efficacious, data regarding belimumab use in cutaneous SLE is limited [11]. In this particular case, our patient showed complete resolution when transitioning to combination treatment with mycophenolate mofetil and belimumab. More data is needed for developing treatment guidelines but the addition of belimumab to standard therapy should be considered in patients with recalcitrant cutaneous SLE or unique presentations of SLE, such as Rowell syndrome.

Conclusion

This case highlights a rare and unusual presentation of cutaneous lupus erythematosus. Rowell syndrome should be suspected in lupus erythematosus patients who present with erythema multiforme-like papules and plaques in the absence of triggers such as infections or medications.

Potential conflicts of interest

The authors declare no conflicts of interest.

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