CASE REPORT

A case of Rowell syndrome with excellent improvement following anifrolumab

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INTRODUCTION

Rowell syndrome (RS), a rare and severe variant of cutaneous lupus erythematosus (CLE), is described as a cutaneous eruption resembling erythema multiforme (EM) with features of systemic lupus erythematosus (SLE) and characteristic serology. Therapeutic options for RS include those used to treat SLE, such as corticosteroids, hydroxychloroquine (HCQ), immunosuppression, and biologic therapies. In 2021, anifrolumab, a monoclonal antibody that selectively binds and inhibits the type 1 interferon-α receptor 1 (IFNAR1), received Food and Drug Administration-approval for the treatment of SLE.

CASE

A 43-year-old female presented to dermatology with a diffuse, blistering rash on the dorsal arms, chest, abdomen, and upper back that persisted for 3 months following one episode of sun exposure. She had a complex medical history, including SLE with secondary Sjogren’s syndrome (+ANA, +SSA, +SSB, +RF), anti-phospholipid antibody syndrome, uveitis (herpes zoster-related), HIV well controlled on highly active antiretroviral therapy, and breast cancer on tamoxifen. Her SLE was previously well controlled using HCQ and azathioprine, but as her SLE was in remission, these medications were discontinued. Upon discontinuation of HCQ and azathioprine and starting pregabalin for chronic pain, she developed the diffuse blistering rash on her dorsal arms, chest, abdomen, and upper back, as above. She described the eruption as painful and tender. She was evaluated by an outside dermatologist who prescribed 40 mg of prednisone with some improvement of the blistering. Topical clobetasol and triamcinolone were also trialed with no improvement. She denied any other symptoms, including fevers, chills, night sweats, mucosal ulcerations, or joint pain.

On physical exam there were dusky, targetoid plaques with associated blisters and crusting on the bilateral arms, chest, and back. Additionally, erythematous discrete plaques with central clearing, consistent with lupus erythematosus (LE), and...
hyperpigmented patches with serpiginous borders, consistent with postinflammatory pigment alteration, were present (Fig 1). No oral or mucosal lesions were present. Punch biopsy of a left chest lesion with direct immunofluorescence (DIF) was performed with a differential diagnosis of SLE, EM, drug reaction to pregabalin, and syphilis. Histopathology demonstrated interface dermatitis with superficial and deep perivascular and perianexal inflammation. A colloidal iron highlighted increased dermal mucin and staining for treponemal pallidum was negative. DIF was also negative. The microscopic differential diagnosis included connective tissue disease, such as LE or RS, and drug eruption secondary to pregabalin. Repeat biopsy 5 months later revealed interface dermatitis with scattered necrotic keratinocytes with serous crust, bacterial colonization, and mild spongiosis. Given her physical exam findings and serologic history, a clinical diagnosis of RS was favored.

She was started on a new course of prednisone 40 mg and her rash markedly improved over a few weeks. She also resumed HCQ 200 mg twice daily. However, whenever prednisone was tapered below 40 mg, the rash flared again in the absence of sun exposure. Flares required 2 hospitalizations for pulse dose steroids and pain control (Fig 2). While hospitalized, she was treated with a course of rituximab, and mycophenolate mofetil (MMF) 1 g twice daily was started in place of azathioprine. Despite these changes to her regimen, her CLE continued to flare, and she was unable to taper prednisone below 20 mg daily. Given the difficulty of tapering steroids and active skin lesions, she was started on monthly intravenous immunoglobulin (IVIg), which initially appeared to be effective, but she began to experience flares of her skin lesions several weeks prior to IVIg redosing, again requiring increased prednisone therapy. Subsequently, she was transitioned to anifrolumab 300 mg every 4 weeks, which she has now received monthly for 6 months. She tolerates it well and has had no skin flares while receiving monthly anifrolumab infusions, despite tapering her steroid to discontinuation within 2 weeks of beginning anifrolumab (Fig 3).

**DISCUSSION**

RS is characterized by lesions of both EM and LE, along with a unique immunologic pattern. It is most commonly observed in middle-aged women (median age, 32 years), though cases in pediatric, elderly, and male patients have been reported. In most cases, a history of LE precedes lesions of EM.

Cases of RS are described as early as 1922, though the first set of diagnostic criteria was not described by Rowell until 1963. Since then, several iterations of the diagnostic criteria have been proposed. There is currently no consensus on which set of diagnostic criteria should be used. However, all versions include the presence of LE lesions (SLE, subacute CLE, or discoid LE [DLE]), the presence of EM-like lesions, and positive ANA with a speckled pattern, anti-Ro/SSA or anti-La/SSB, and RF in either the major or minor diagnostic criteria. The most recent version also suggests inclusion of negative DIF on
EM-like lesions. Biopsy of EM lesions demonstrates necrotic keratinocytes, although this is not specific.1

The treatment of RS is similar to that of SLE or DLE occurring independently of RS.1 SLE treatments include the use of antimalarials, systemic corticosteroids, steroid-sparing immunosuppressive agents such as azathioprine, MMF, or cyclosporine, or biologic agents, including anti-B cell-activating factor, anti-IL 12/23, and JAK (Janus kinase) inhibitors.6,7 DLE lesion treatments include topical corticosteroids or calcineurin inhibitors, intralesional corticosteroids, and antimalarials.8

In 2021, IV anifrolumab was approved for the treatment of moderate-to-severe SLE in patients receiving standard therapy.3 It has also been demonstrated to reduce flares of SLE and reduce need for steroid exposure.9 Anifrolumab is a human monoclonal antibody targeting subunit 1 of the IFNAR1, which results in the binding and internalization of IFNAR1 to decrease levels of type 1 interferon.7 Type 1 interferon is found in high levels in a major subset of patients with SLE and lupus nephritis.3 In the studies which gained anifrolumab’s Food and Drug Administration-approval, levels of type 1 interferon decreased by 88%-90% after 12 weeks of treatment, which was sustained through 52 weeks. Notably, levels of type 1 interferon increased 8-12 weeks after discontinuation.3,10 Anifrolumab is administered as an infusion, once every 4 weeks at a recommended dosage of 300 mg. In phase III studies, most patients experienced adverse events, though these were mild to moderate in severity. The most common adverse events included upper respiratory tract infections (34%), infusion-related reactions (9.4%), herpes zoster (6.1%), cough (5.0%), respiratory tract infection (3.3%), and hypersensitivity reaction (2.8%).3

A case series of 3 patients with CLE highlighted the value of anifrolumab in managing patients with refractory disease. Patients were considered to have refractory CLE if they were not able to achieve adequate disease control when receiving standard of care treatments. Standard treatments included antimalarials, disease modifying agents, and biologics. All 3 patients were started on anifrolumab 300 mg infusions every 4 weeks, in addition to their standard CLE regimens. Patients 1 and 3 began taking anifrolumab along with MMF 1500 mg twice daily, a prednisone taper, and HCQ 300 mg daily, while patient 2 began anifrolumab with HCQ 200 mg twice daily and a prednisone and azathioprine taper. The patients began to see marked improvement in both symptoms and erythema between 8 and 30 weeks of treatment with anifrolumab, though repigmentation remains ongoing. All 3 patients remain on HCQ, and patient 1 also remains on MMF despite anifrolumab treatment.11

We present this case as literature reporting treatment for RS is limited, and typically recommends following current SLE therapy. This patient had severe RS resistant to several therapies, including rituximab and IVIg, with a complex past medical history. Given the patient’s excellent response to an emerging therapy used as monotherapy, we recommend that anifrolumab be considered in cases of refractory RS. Its use in other variants of LE may also warrant consideration.

Conflicts of interest
None disclosed.

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