Background: Subacute cutaneous lupus erythematosus (SCLE) is characterized by annular, nonscarring, photodistributed, or papulosquamous lesions. The disease may be idiopathic, drug induced, or drug exacerbated.

Observations: A 66-year-old woman with a history of hypertension, parkinsonism, rheumatoid arthritis, anxiety and depression, and symptoms of Sjogren syndrome was seen with a 1-month history of an eruption on her upper extremities and upper trunk. The eruption had begun 2 to 3 weeks after subcutaneous injection of golimumab for rheumatoid arthritis. She had developed SCLE 2 years previously due to furosemide use and 10 years previously due to hydrochlorothiazide use. Physical examination revealed scaly, annular, erythematous plaques photodistributed on the arms, legs, and upper trunk. A punch biopsy specimen demonstrated vacuolar interface dermatitis and lymphohistiocytic perivascular inflammation. Serological abnormalities included a positive antinuclear antibody, an elevated anti-La/SS-B antibody level, and an elevated anti-Ro/SS-A antibody level. She was diagnosed as having SCLE and was initially treated with desonide lotion, photoprotection, prednisone (40 mg/d) tapered over 6 weeks, and hydroxychloroquine sulfate (200 mg twice daily). Because of persistent disease, methotrexate sodium (12.5 mg/wk) was subsequently added to the regimen, and her eruption cleared completely.

Conclusions: Golimumab should be added to the list of medications capable of inducing or exacerbating SCLE. Our patient demonstrated variable times to the resolution of SCLE, possibly attributable in part to the different half-lives of the agents administered.


Subacute cutaneous lupus erythematosus (SCLE) was first described by Sontheimer et al in 1979. This entity comprises approximately 10% to 15% of cutaneous lupus erythematosus cases and is seen with nonscarring, erythematous, papulosquamous lesions or with annular plaques having an overlying scale in a photodistribution. Most patients with SCLE have anti-Ro/SS-A antibodies, and approximately 50% fulfill at least 4 American College of Rheumatology criteria for the diagnosis of systemic lupus erythematosus. Despite this, the development of associated severe systemic involvement is uncommon.

Drug-induced SCLE (DI-SCLE) was first described in 1985 by Reed et al, who reported a series of 5 patients with the disease induced by hydrochlorothiazide use. The list of drugs associated with DI-SCLE has since grown to include 50 or more medications, the most common of which include terbinafine, hydrochlorothiazide, calcium channel blockers, various chemotherapeutic agents, and angiotensin-converting enzyme inhibitors. The clinical, serological, and histopathological features of SCLE do not differ significantly between individuals with idiopathic vs drug-induced or drug-exacerbated disease. Hillesheim et al recently showed that tissue eosinophilia is not a reliable differentiating histopathological feature of DI-SCLE; however, the results of a 2011 study suggest that patients with DI-SCLE more often are seen with bullous lesions, malar erythema, targetoid lesions, vasculitic lesions, and widespread disease.

Golimumab is a fully human monoclonal antibody against tumor necrosis factor (TNF) approved in 2009 for the treatment of psoriatic arthritis, rheumatoid arthritis, and ankylosing spondylitis. It is administered as a monthly subcutaneous injection and has a 2-week half-life. The most commonly reported adverse effects include nasopharyngitis, injection-site erythema, and upper respiratory tract infections. To date, no golimumab-associ-
ated cutaneous adverse effects have been reported in the literature. We describe a patient who developed an exacerbation of SCLE after subcutaneous injection of golimumab for the treatment of rheumatoid arthritis.

**REPORT OF A CASE**

A 66-year-old woman was initially seen in August 2009 with a 6-week history of a pruritic stinging eruption on her upper extremities and upper trunk. She reported having experienced a similar eruption approximately 8 years previously that was suspected to have been caused by hydrochlorothiazide use and had resolved approximately 9 months following discontinuation of this medication, without additional therapy. She denied recent hydrochlorothiazide ingestion; her only new medication in the months before the current episode was intermittent furosemide use for lower extremity swelling. Her medical history included hypertension, parkinsonism, rheumatoid arthritis, and anxiety and depression. Her other medications at presentation included atenolol, gabapentin, nisoldipine, carbidopa-levodopa, bupropion hydrochloride, trazodone hydrochloride, citalopram hydrobromide, duloxetine hydrochloride, ziprasidone hydrochloride, and oxycodone hydrochloride–acetaminophen, as well as multivitamins, ω-3 fish oil, and calcium supplementation.

Physical examination revealed scaly, annular, erythematous plaques in a photodistribution on the arms, legs, and upper trunk. A punch biopsy specimen was obtained, demonstrating increased dermal mucin, thickened basement membrane, and vacuolar interface dermatitis with an associated perivascular and perifollicular lymphohistiocytic infiltrate. Rare tissue eosinophils were noted. The results of her complete blood cell count with differential cell count and comprehensive metabolic profile with liver function studies were normal, except for a marginally elevated serum creatinine level of 1.2 mg/dL (reference range, 0.6-1.0 mg/dL) (to convert creatinine level to micromoles per liter, multiply by 88.4). Serological test results showed a positive antinuclear antibody (ANA) (titer and pattern not reported), an elevated antihistone antibody level at 1.3 U (reference range, 0.0-0.9 U), an elevated anti-La/SS-B antibody level at 5.5 arbitrary units (AU) (reference range, 0.0-0.9 AU), and an elevated anti-Ro/SS-A antibody level exceeding 8.0 AU (reference range, 0.0-0.9 AU). Test results for anti-Smith antibodies, anti-ribonucleoprotein antibodies, and anti–double-stranded DNA antibodies were normal. To our knowledge, urinalysis was not performed. She was diagnosed as having SCLE exacerbated by furosemide use, and her disease gradually resolved 2 months after discontinuation of the drug using photoprotection and twice daily triamcinolone acetonide, 0.1%, cream.

In January 2011, the patient was seen with a 1-month history of a similar pruritic, burning eruption on her upper trunk and upper extremities. Her skin disease had begun 2 to 3 weeks after receiving an initial subcutaneous injection of golimumab for the treatment of rheumatoid arthritis. Her medications were otherwise unchanged from her previous presentation, and she denied having received other new medications during the preceding 3 months. Her medical history was unchanged, except for the development of dry mouth and dry eyes suggestive of Sjögren syndrome during the interval. Physical examination revealed scaly, annular, erythematous plaques photodistributed on the arms, legs, and upper trunk (Figure 1). A punch biopsy specimen from the back showed a thickened basement membrane zone, an atrophic epidermis with scattered dyskeratotic keratinocytes, and vacuolar interface dermatitis with an associated superficial and mid dermal lymphohistiocytic perivascular inflammatory infiltrate (Figure 2 and Figure 3). Tissue eosinophils were not present. Increased dermal mucin deposition was noted on colloidal iron staining (Figure 4).
discontinued, and she was noted to have a mild flare in her atenolol, bupropion, and nisoldipine medications were continued over 6 weeks. In July 2011, the patient was restarted on golimumab, 21 mg (200 mg twice daily), and oral prednisone (40 mg/d) to control her male erythema and photosensitivity. Despite this regimen, her skin disease persisted. In August 2011, the patient was diagnosed with SCLE exacerbation by golimumab use and was treated with desonide lotion, photoprotection, hydroxychloroquine sulfate (200 mg twice daily), and oral prednisone (40 mg/d) tapered over 6 weeks.

Her leukopenia and renal insufficiency improved with this regimen, but her skin disease persisted. In July 2011, her atenolol, bupropion, and nisoldipine medications were discontinued, and she was noted to have a mild flare in her disease when diltiazem hydrochloride was started by her primary care physician to control her hypertension. At this time, diltiazem was replaced with losartan potassium, and additional treatment with methotrexate sodium (7.5 mg/wk) was initiated. Her methotrexate dosage was gradually escalated to 12.5 mg/wk, which led to complete resolution of her skin disease. After 6 months of therapy, the hydroxychloroquine was discontinued, and her methotrexate dosage has been lowered to 10 mg/wk.

The use of TNF inhibitors has been associated with infusion-site or injection-site reactions and with various adverse cutaneous effects, including psoriasis or psoriasiform lesions, eczematous eruptions, lichenoid eruptions, vasculitis, sarcoidosis, granuloma annulare, and cutaneous infections. Multiple reports document TNF inhibitor–induced systemic lupus erythematosus syndrome and SCLE, which have significantly different clinical and serological characteristics, as discussed herein. Tumor necrosis factor inhibitor–induced systemic lupus erythematosus syndrome has systemic involvement (fever, serositis, weight loss, polyarthritis, and hematologic abnormalities), and is associated with the induction of ANA and anti–double-stranded DNA antibodies and with various nonspecific cutaneous manifestations (malar erythema, photosensitivity, purpuric lesions, and morbilliform eruption). In contrast, DISCLE is characterized by a lack of systemic involvement, by annular or papulosquamous lesions, and by anti-Ro/SS-A antibody level elevation. While etanercept, adalimumab, and infliximab have previously been reported to induce SCLE, the patient described herein represents the first reported case of golimumab-exacerbated SCLE to our knowledge.

As previously mentioned, idiopathic and drug-induced or drug-exacerbated SCLE can manifest similar features, rendering them difficult to differentiate. From a histopathological perspective, biopsy specimens of our patient’s furosemide-exacerbated SCLE in 2009 showed rare eosinophils, while those of her golimumab-exacerbated disease failed to demonstrate tissue eosinophils. This supports previous findings by our group that tissue eosinophilia is not a reliable differentiating histopathological feature of DI-SCLE. From a clinical perspective, prior work by Marzano et al has correlated DI-SCLE with more widespread cutaneous disease, as well as the presence of bullae, malar erythema, and vasculitic lesions. Our experience with DI-SCLE has not demonstrated that these types of lesions are more common, and the patient described herein had no such features.

Although the pathogenesis of DI-SCLE is unknown, many potential mechanisms have been proposed. In their initial report on SCLE, Reed el al’ postulated that the use of offending medications may mediate epidermal cytotoxic effects by causing direct phototoxic effects, promoting Ro/SS-A antigen expression, or inducing anti-Ro/SS-A antibody production. Others have suggested the induction of a photosensitive drug reaction, but the fact that many offending medications are not known photo-

Pertinent laboratory findings included the following: serum creatinine level of 1.5 mg/dL (reference range, 0.6-1.2 mg/dL), white blood cell count of 3700/µL (reference range, 3800-10,800/µL) (to convert white blood cell count to ×10^9/L, multiply by 0.001), serum sodium level of 148 mEq/L (reference range, 135-146 mEq/L), and serum potassium level of 6.5 mEq/L (reference range, 3.5-5.3 mEq/L) (to convert sodium and potassium levels to millimoles per liter, multiply by 1.0). Urinalysis showed an elevated urine protein level. Serological testing revealed a positive ANA at a titer of 1:640 in a speckled pattern, an elevated anti-La/SS-B antibody level at 6.4 AU, and an elevated anti-Ro/SS-A antibody level exceeding 8.0 AU. Antihistone antibody testing was not performed. The patient was diagnosed as having SCLE exacerbated by golimumab use and was treated with desonide lotion, photoprotection, hydroxychloroquine sulfate (200 mg twice daily), and oral prednisone (40 mg/d) tapered over 6 weeks.

Her leukopenia and renal insufficiency improved with this regimen, but her skin disease persisted. In July 2011, her atenolol, bupropion, and nisoldipine medications were discontinued, and she was noted to have a mild flare in
sensitizers renders this mechanism less likely.24 Given the variety of drug classes associated with the development of SCLE, it is possible that DI-SCLE may occur via varying mechanisms depending on the offending agent.

Regardless of the exact mechanism, it seems plausible that DI-SCLE occurs when patients with an inherent predisposition to the reaction are exposed to an offending medication. In 2010, doxorubicin hydrochloride–induced SCLE was reported in 2 patients, one with a history of Sjogren syndrome (positive for anti-Ro/SS-A and anti-La/SS-B antibodies) and the other with a history of SCLE (positive for anti-Ro/SS-A antibodies), suggesting their predisposition to the disease.25 Furthermore, a 2003 study by Arbuckle et al26 demonstrated that autoantibodies associated with systemic lupus erythematosus are often present in patients’ serum samples many years before clinical diagnosis, implying a potential hidden predisposition in patients without a correlative medical history. Our patient’s history of anti-Ro/SS-A antibody elevation and gradual development of symptoms suggestive of Sjogren syndrome introduces the possibility that she may have had subclinical Sjogren syndrome and a predisposition to developing SCLE before her initial DI-SCLE reaction associated with hydrochlorothiazide use. Her clinical course fits this paradigm, and her subsequent reactions to furosemide and golimumab use suggest that offending medications are, by an unknown mechanism, activating her underlying predisposition to develop SCLE.

Typically, DI-SCLE resolves within weeks to a few months after the offending medication is discontinued. A unique aspect of the present case is that our patient demonstrated variable times to the resolution of SCLE with the use of different medications. Her most recent flare required 9 months and the use of systemic and topical therapy to resolve, despite the receipt of only one golimumab injection. Her prior exacerbation following furosemide use resolved within 2 months using topical therapy alone, while her initial eruption after hydrochlorothiazide use persisted for roughly 9 months after discontinuation, without topical or systemic therapy.

A potential explanation for this phenomenon may be the different half-lives of the offending medications. The half-life of golimumab is 2 weeks, while that of furosemide is 30 to 60 minutes. Although this could explain the longer course of disease associated with golimumab use, it does not account for the prolonged eruption associated with the use of hydrochlorothiazide, which has a half-life of 6 to 16 hours, even in the absence of additional therapy. Therefore, while medication half-life may contribute to the duration of SCLE, it is unlikely to be the only factor because a 2-week half-life would not be expected to result in significant drug levels many months after discontinuation.

Other confounding aspects exist in this case that may have affected the golimumab-exacerbated disease duration. The fact that our patient was taking other long-term medications known to induce or exacerbate SCLE may have contributed to the duration of SCLE. Bupropion has previously been reported to induce SCLE,2 and although atenolol and nisoldipine use has not specifically been associated with the disease, other calcium channel blockers20 and β-blockers20 have been implicated. It is possible that the use of these medications may have prolonged our patient’s course of SCLE after initiation of the disease process by golimumab. In addition, the duration of the most recent episode was, to some degree, adversely affected by the inadvertent addition of diltiazem, a known inducer of SCLE, which temporally resulted in a flare of her disease.

To our knowledge, this is the first reported case of golimumab-exacerbated SCLE, indicating that golimumab should be added to the growing list of medications capable of inducing or exacerbating SCLE. Although the exact mechanisms underlying the development of DI-SCLE remain elusive, our patient’s history of anti-Ro/SS-A antibody elevation, gradual development of Sjogren syndrome symptoms, and prior disease induced by hydrochlorothiazide and furosemide use suggest that offending medications are somehow activating an underlying predisposition to develop SCLE. Furthermore, the variable times to the resolution of her disease exacerbations imply that the different half-lives of the agents administered may be a contributing factor. Finally, this case highlights the importance of taking an accurate medication history at each visit and communicating with other physicians involved in the care of patients with DI-SCLE to ensure that the use of potentially aggravating medications is avoided.

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