Golimumab-Exacerbated Subacute Cutaneous Lupus Erythematosus

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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 Sjögren 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.


UBACUTE 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 non-scarring, 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, nisoldpine, 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).

![Figure 1](https://example.com/figure1.png)  
**Figure 1.** Photodistributed scaly, annular, erythematous plaques on the upper chest (A) and arm (B).

![Figure 2](https://example.com/figure2.png)  
**Figure 2.** A punch biopsy specimen from the upper back showing 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 (hematoxylin-eosin, original magnification ×40).
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 documented 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, DI-SCLE 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 et 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-

**Comment**

**Figure 3.** Higher magnification showing dyskeratotic keratinocytes, a thickened basement membrane zone, and vacuolar interface dermatitis with associated squamatization of the basal layer (hematoxylin-eosin, original magnification ×100).

**Figure 4.** Colloidal iron–stained specimen showing increased dermal mucin deposition (original magnification ×400).
suggesting their predisposition to the disease. Further-

sensitizers renders this mechanism less likely. Given the

Regardless of the exact mechanism, it seems plausible

suggestion that DI-SCLE occurs when patients with an inher-

and anti-La/SS-B antibodies) and the other with a

sible that DI-SCLE occurs when patients with an inher-

teresting the golimumab-exacerbated disease dura-

the only factor because a 2-week half-life would not be

A potential explanation for this phenomenon may be

Typically, DI-SCLE resolves within weeks to a few

variable times to the resolution of her disease exacerbated

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Another confounding aspect exists in this case that may

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It is possible that the use of these medications may have

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