Subacute cutaneous lupus erythematosus versus discoid lupus erythematosus: A challenging diagnosis

Julianne Kleitsch, BA,[a,b] Darosa Lim, MD,[a,b] Rachita Pandya, BA,[a,b] and Victoria P. Werth, MD[a,b]

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INTRODUCTION

Cutaneous lupus erythematosus (CLE) is an autoimmune skin disease that can occur with or without systemic involvement. CLE can be classified into 3 main subtypes: acute CLE, subacute CLE (SCLE), and chronic CLE. The most common type of chronic CLE is discoid lupus erythematosus (DLE). Each subtype has distinctive morphology, and diagnosis is made on the basis of clinical features, laboratory studies, histology, and antibody serology.[1]

Current treatment options for CLE are limited. Furthermore, CLE can be refractory to treatments with variable and unpredictable response, with only a 50% response to first-line therapy hydroxychloroquine.[2] Numerous CLE-specific clinical trials are currently in progress; however, they sometimes require patients have a specific subtype of CLE, most often DLE.[3] Classifying patients by subtype can be challenging because there can be many overlapping features and at least 20% of patients have more than 1 CLE subtype. Although efforts have been made to improve classification criteria for DLE, it can still be difficult to distinguish DLE from other subtypes.[4,5] In this report, we present 2 patients with a challenging diagnosis of DLE versus SCLE.

Abbreviations used:

CLE:	cutaneous lupus erythematosus
DLE:	discoid lupus erythematosus
SCLE:	subacute cutaneous lupus erythematosus

CASE SERIES

Case 1

Patient 1 is a 43-year-old White woman who presented to the autoimmune dermatology clinic with a 3-year history of CLE. At the time of the visit, she was being treated with hydroxychloroquine (200 mg/d) and topical tacrolimus and mometasone, without significant improvement. Previous laboratory test results were positive for anti−Sjögren's-syndrome-related antigen A (3.2 AI, normal 0.0-0.9)/anti−Sjögren's-syndrome-related antigen B (3.1 AI, normal 0.0-0.9), anti-double stranded DNA (7 IU/mL, normal <5), and rheumatoid factor (19 IU/mL, normal <14), and slightly decreased C3 (83 mg/dL, normal 88-201) and C4 (12 mg/dL, normal 13-39). She was negative for antinuclear antibodies, anti-Sm, and anti-Sm/RNP. Despite laboratory test results consistent with possible systemic lupus erythematosus, she did not meet 2019 European Alliance of

From the Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania[a]; and Corporal Michael J. Crescenz VAMC, Philadelphia, Pennsylvania.[b]

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Correspondence to: Victoria P. Werth, MD, Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, 211B Clinical Research Building, 415 Curie Boulevard, Philadelphia, PA 19104. E-mail: werth@pennmedicine.upenn.edu.

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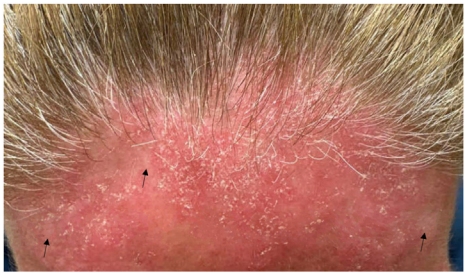

Fig 1. Forehead and scalp: erythematous and scaly coalescing plaques with areas of mild hypopigmentation without scarring (*black arrows*) (patient 1).

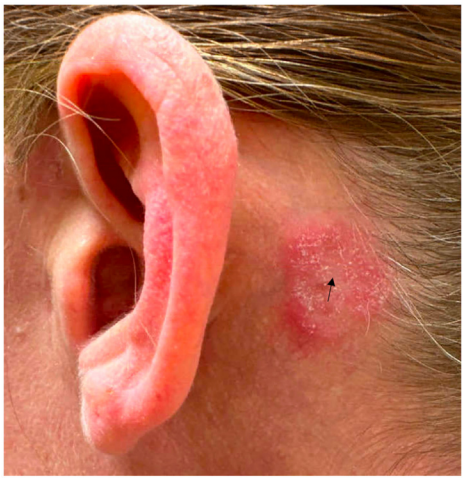

Fig 2. Well-demarcated round and scaly erythematous plaque with areas of hypopigmentation (*black arrow*) involving the scalp, posterior to the ear (patient 1).

Associations for Rheumatology/American College of Rheumatology criteria for systemic lupus erythematosus. Physical examination showed erythema of the forehead, erythematous papules on the arms with hypopigmented macules, atrophic areas on the upper portion of the back with surrounding erythema, erythema with scale on the posterior aspect of the neck, and erythema in her ears. Skin biopsy of the upper portion of the back revealed a lymphocytic infiltrate of the epidermis and dermis, interface changes, and follicular plugging, changes that can be seen in both SCLE and DLE. Therapeutic management included increasing hydroxychloroquine to 300 mg per day, a dosage of 5 mg/kg per day, and 5 mg/mL intralesional triamcinolone and topical clobetasol for the scalp. At the 6-month follow-up appointment, the patient saw minor improvement in disease activity. She had activity in sun-exposed areas, including the posterior aspect of the neck and upper portion of the back and arms, as well as other areas, including her scalp and ears. The lesions

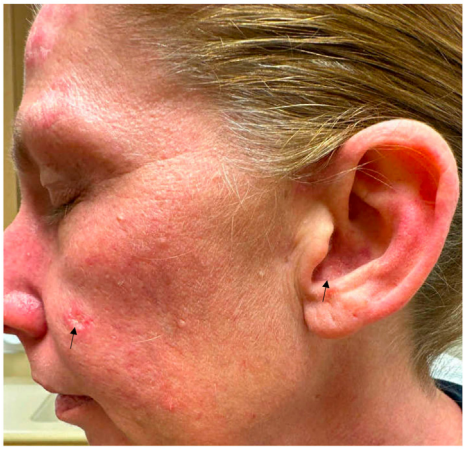

Fig 3. Erythematous papules, with areas of hypopigmentation and atrophic scarring (*black arrows*) involving the face and ear, including the conchal bowl (patient 1).

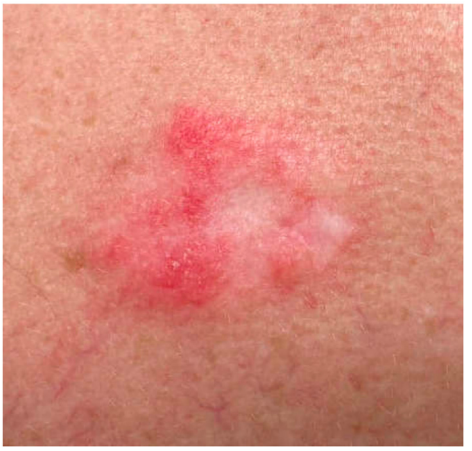

Fig 4. Indurated erythematous plaque with hypopigmentation and scarring involving the upper portion of the back (patient 1).

on her face and scalp were coalescing, whereas lesions on her back, arms, ears, and face were well demarcated. She also had areas of postinflammatory hypopigmentation without scarring on her forehead and scalp (Figs 1 and 2) and areas of resolving pigmentation, consistent with SCLE, and other areas of hypopigmentation with atrophic scarring on her face, ear, and back, consistent with DLE (Figs 3 and 4).

Case 2

Patient 2 is a 52-year-old White woman with a 24-year history of biopsy-supported CLE. Her CLE has been poorly controlled since diagnosis, and she has not been on regular treatment. She has been

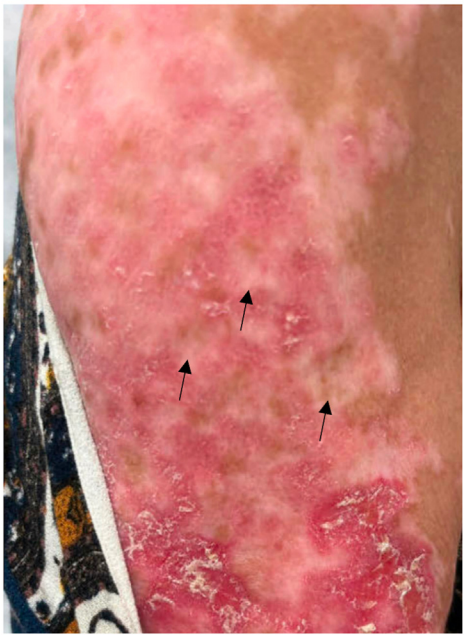

Fig 5. Erythematous coalescing plaques with hyperkeratotic scale and areas of hypopigmentation and atrophy (*black arrows*) over the arm (patient 2).

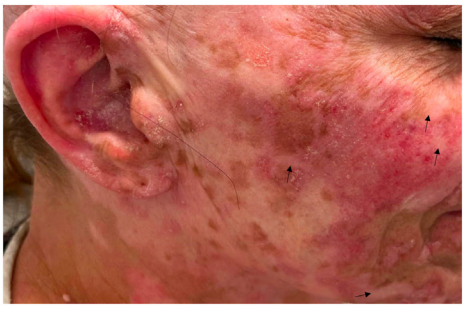

Fig 6. Erythematous and scaly plaques, with areas of hypopigmentation without scarring (*black arrows*) involving the ear, including the conchal bowl and face (patient 2).

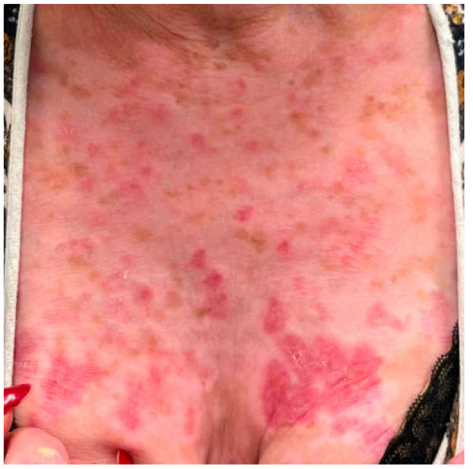

Fig 7. Erythematous, scaly papules and plaques, with areas of hypopigmentation and atrophy involving the chest (patient 2).

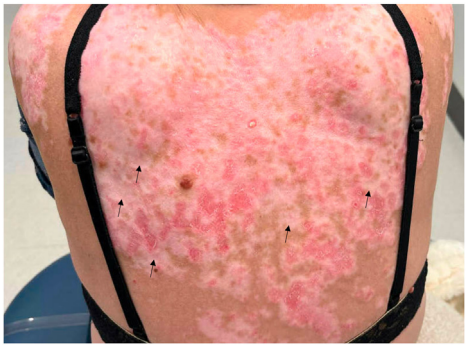

Fig 8. Erythematous and scaly coalescing papules and plaques with diffuse areas of hypopigmentation and atrophy (*black arrows*) involving the back (patient 2).

intermittently on hydroxychloroquine and prednisone for flares and failed a trial of methotrexate because of nausea. She recently restarted hydroxychloroquine (400 mg/d) but only takes it intermittently. She reported new symptoms of joint pain in the morning for the last 2 to 3 years, patchy hair loss for the last year, Raynaud's phenomenon, and muscle soreness of her legs. Previous laboratory test results showed a weakly positive anti-double stranded DNA antibody (10 IU/mL, normal 0-9), elevated sedimentation rate (48 mm/h, normal 0-40) and normal C3, C4, C-reactive protein, and white blood cell count levels. On physical examination, the patient had areas of erythematous scaly plaques and papules diffusely on her face, scalp, chest, arms, hands, and back, and well-demarcated lesions on her face and ears. She also had involvement of her palatal mucosa. She had areas of postinflammatory hypopigmentation without scarring over her face, arms, chest, and back, as well as areas of atrophy on her arms, chest, and back (Figs 5-8). The patient was started on prednisone (10 mg/d) and topical triamcinolone 0.1% and continued on hydroxychloroquine (400 mg/d). Additional laboratory test results showed a positive anti—Sjögren's-syndrome-related antigen A (1.2 IU/mL, normal 0.0-0.9) and antinuclear antibodies (1:5120, normal <1:160) as well as proteinuria. The patient was followed up 4 weeks later with resolving erythematous papules and plaques with a mix of postinflammatory hypopigmentation without scarring and areas of resolution with resolving pigmentation, consistent with SCLE, and other areas of hypopigmentation with atrophy over

her face, arms, scalp, chest, and back, consistent with DLE.

DISCUSSION

In both these patients, there were overlapping features of both SCLE and DLE. Distinguishing between SCLE and DLE can be a challenging diagnosis; however, there are several characteristic features to consider — distribution, active lesion morphology, and scarring.

Photosensitivity can be seen in all subtypes of CLE, and the reported incidence by subtype varies widely − 27% to 100% in SCLE and 25% to 90% in DLE.[6] Unsurprisingly, SCLE and DLE lesions are often found on sun-exposed skin. SCLE tends to appear on the upper thorax ("V" distribution), upper portion of the back, and extensor surfaces of the arms and forearms, sparing the central portion of the face, scalp, and below the waist.[1] In drug-induced SCLE, accounting for up to 38% of cases,[7] lesions can also be found in sun-protected areas. DLE predominantly involves the head and neck regions, particularly the scalp and ears, but it can also involve the extensor arms and hands in generalized DLE. DLE can affect mucosal surfaces as well.[1] Both patients had lesion distribution in sun-exposed areas, as seen in both SCLE and DLE. Additionally, they both had face, scalp, and ears involvement, and patient 2 had mucosal surface involvement. Although these specific areas may be more characteristic of DLE, they do not rule out SCLE.

Another helpful characteristic in distinguishing SCLE from DLE is the morphology of active lesions. The 2 morphologic variants of SCLE include annular and papulosquamous, with approximately 42% of patients with SCLE having annular, 39% with papulosquamous, and 16% with features of both.[8] As these lesions typically involve a superficial dermal inflammatory infiltrate, they are usually minimally palpable. This differs from DLE, which more frequently involves a denser infiltrate that extends to the reticular dermis as well.[9] DLE lesions are characterized by well-demarcated, erythematous, scaly papules that can develop into infiltrated discoid plaques, less commonly, they can be hypertrophic or verrucous.[1] DLE commonly involves follicular plugging.[5] Patient 1 had erythematous, scaly papules and plaques on her arms and face as well as well-demarcated, indurated, discoid lesions on her ears and upper portion of the back. Patient 2 had areas on her back and arms with papules coalescing into plaques, with some hypertrophic scales. On her face, she had well-demarcated, indurated, discoid lesions. Both patients had morphologic features of papulosquamous SCLE, but also with discoid lesions consistent with DLE. Additionally, many of patient 2's lesions had hyperkeratotic scale, which would be more consistent with DLE.

Damage after lesion resolution can be particularly helpful in distinguishing SCLE from DLE. SCLE typically resolves without scarring, but dyspigmentation may occur.[1] In DLE, lesions typically lead to scarring and atrophy, in addition to dyspigmentation.[1] Early lesions can be difficult to distinguish from SCLE, before a pattern of damage can be appreciated. Patient 1 had some mild hypopigmented macules on her arms and face, but also presented with areas of atrophy and scarring on her upper portion of the back and ears. Patient 2 presented with extensive areas of damage. On her arms and back, lesions resolved with diffuse hypopigmentation and atrophy, but with intact skin markings. Her face had areas of atrophic scarring and other areas of hypopigmentation. Despite both patients having CLE for many years, a consistent and clear picture of scarring after active lesion resolution could not be appreciated, as resolution both with and without scarring could be appreciated.

In both patients, there were overlapping features of SCLE and DLE. Furthermore, neither patient can be classified as SCLE or DLE alone. Although treatment recommendations for SCLE and DLE are similar,[10] uncertainty in diagnosis between both subtypes can create difficulty when enrolling for clinical trials. Some CLE trials will allow both patients with SCLE and DLE to participate, whereas others require that patients have DLE.[3] As seen in our patients, even after many years with a diagnosis of CLE and features of DLE, the diagnosis is not always clear. This could be because of an overlap of DLE and SCLE in these patients or, alternatively, the patients have not fully developed a specific subtype yet. In trials that require a diagnosis of DLE, it may be challenging to properly assign patients to one diagnosis, and this may result in the exclusion of patients who would otherwise be willing and eligible to enroll. Further, this may eventually exclude patients from valuable treatment options approved specifically for patients with DLE.

Conflicts of interest

Dr Werth has grants from Pfizer, Corbus and CSL Behring, Priovant and has consulted for Pfizer, Janssen, Bristol Myers Squibb, Octapharma, CSL Behring, Corbus, Galderma, Novartis, Rome Pharmaceuticals. Authors Kleitsch, Lim and Pandya have no conflicts of interest to declare.

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