Lupus Erythematosus and Localized Scleroderma Coexistent at the Same Sites: A Rare Presentation of Overlap Syndrome of Connective-Tissue Diseases

Anabella Pascucci, MD; Peter J. Lynch, MD; Nasim Fazel, MD, DDS

PRACTICE **POINTS**

- Discoid lupus erythematosus and localized scleroderma may rarely overlap within the same lesions.
- Cutaneous overlap syndromes tend to respond well to antimalarials, topical steroids, and systemic steroids.

Overlap syndromes are known to occur with connective-tissue diseases (CTDs). Rarely, the overlap occurs at the same tissue site. We report the case of a patient with clinical and histopathologic findings consistent with the presence of discoid lupus erythematosus (DLE) and localized scleroderma within the same lesions. Based on our case and other reported cases in the literature, the following features are common in patients with an overlap of lupus erythematosus (LE) and localized scleroderma: predilection for young women, photodistributed lesions, DLE, linear morphology clinically, and positivity along the dermoepidermal junction on direct immunofluorescence. Most patients showed good response to antimalarials, topical steroids, or systemic steroids.

Cutis. 2016;97:359-363.

Dr. Pascucci was from and Drs. Lynch and Fazel are from the Department of Dermatology, University of California Davis School of Medicine, Sacramento. Dr. Pascucci currently is from the Division of Dermatology, University of California Los Angeles.

The authors report no conflict of interest.

Correspondence: Anabella Pascucci, MD, UCLA Dermatology, 514 N Prospect Ave, Redondo Beach, CA 90277 (apascucci@mednet.ucla.edu).

Although lupus erythematosus (LE) and scleroderma are regarded as 2 distinct entities, there have been multiple cases described in the literature showing an overlap between these 2 disease processes. We report the case of a 60-year-old man with clinical and histopathologic findings consistent with the presence of localized scleroderma and discoid LE (DLE) within the same lesions. We also present a review of the literature and delineate the general patterns of coexistence of these 2 diseases based on our case and other reported cases.

Case Report

A 60-year-old man presented with a progressive pruritic rash on the face, neck, and upper back of approximately 20 to 30 years' duration. On initial evaluation, the patient was found to have indurated hypopigmented plaques with follicular plugging bilaterally on the cheeks, temples, ears, and upper back (Figure 1). Punch biopsies were performed on the left cheek and upper back. Histopathology was notable for vacuolar interface dermatitis with dermal sclerosis at both sites. Specifically, interface changes, basement membrane thickening, and periadnexal inflammation were present on histopathologic examination from both biopsies supporting a diagnosis of DLE (Figure 2A). However,

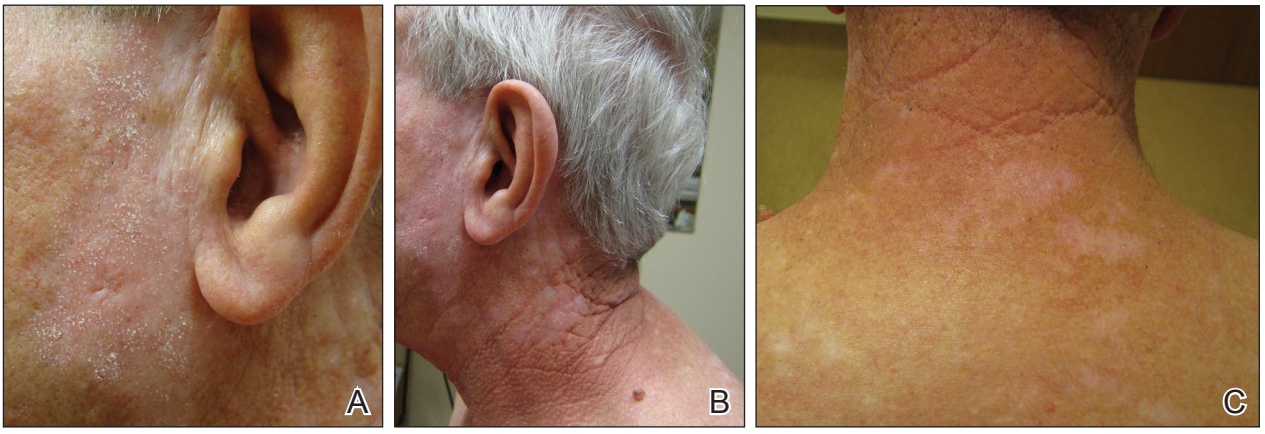

Figure 1. Indurated hypopigmented plaques with follicular plugging on the left cheek (A), lateral aspect of the neck (B), and upper back (C).

there also was sclerosis present in the reticular dermis, suggesting a diagnosis of localized scleroderma (Figure 2B). Direct immunofluorescence was negative for a lupus band. Laboratory workup was positive for antinuclear antibody (titer, 1:40; speckled pattern) and anti–Sjögren syndrome antigen A but negative for double-stranded DNA antibody, anti-Smith antibody, anti–Sjögren syndrome antigen B, and Scl-70.

The patient was started on oral hydroxychloroquine 200 mg twice daily and clobetasol ointment 0.05% twice daily to affected areas. After 2 weeks of treatment, he developed urticaria on the trunk and the hydroxychloroquine was discontinued. He continued using only topical steroids following a regimen of applying clobetasol ointment 0.05% twice daily for 2 weeks, alternating with the use of triamcinolone ointment 0.1% twice daily for 2 weeks with improvement of the pruritus, but the induration and hypopigmentation remained unchanged. Alternative systemic medication was started with mycophenolate mofetil 1 g twice daily. The patient showed remarkable clinical improvement with a decrease in induration and partial resolution of follicular plugging after 4 months of treatment with mycophenolate mofetil in combination with the topical steroid regimen.

Comment

Autoimmune connective-tissue diseases (CTDs) often occur with a wide range of symptoms and signs. Most often patients affected by these diseases can be sorted into one of the named CTDs such as LE, rheumatoid arthritis, scleroderma, polymyositis/dermatomyositis, and Sjögren syndrome. On the other hand, it is widely recognized that patients with one classic autoimmune CTD are likely to possess multiple autoantibodies, and a small number of these patients develop symptoms and/or signs that satisfy the diagnostic criteria of a second autoimmune CTD; these latter patients are said to have an overlap syndrome.[1] The development of a second identifiable CTD, hence indicating an overlap syndrome, may occur coincident to the initial CTD or may occur at a different time.[1]

Essentially all 5 of the CTDs mentioned above have been reported to occur in combination with one another. Most of the reports involving overlap among these 5 CTDs include patients with multiorgan systemic involvement without cutaneous involvement, leading to a fairly simple straightforward classification of overlap syndromes as viewed by rheumatologists.[1] However, the situation is not that simple for dermatologists based on the fact that skin involvement for 2 of these diseases—scleroderma and LE—can occur either in a setting of systemic disease or in situations where the cutaneous involvement occurs as a stand-alone process. This overlap often occurs with the localized forms of scleroderma (ie, morphea, morphea profunda, linear morphea) and those instances of LE that are primarily limited to the skin (ie, DLE, subacute cutaneous LE, lupus panniculitis). When the overlap occurs between the localized forms of scleroderma and purely cutaneous LE, the situation becomes even more complicated, as the skin lesions of the 2 diseases may occur at separate locations or coexistent disease may develop in the same location, as in our case.

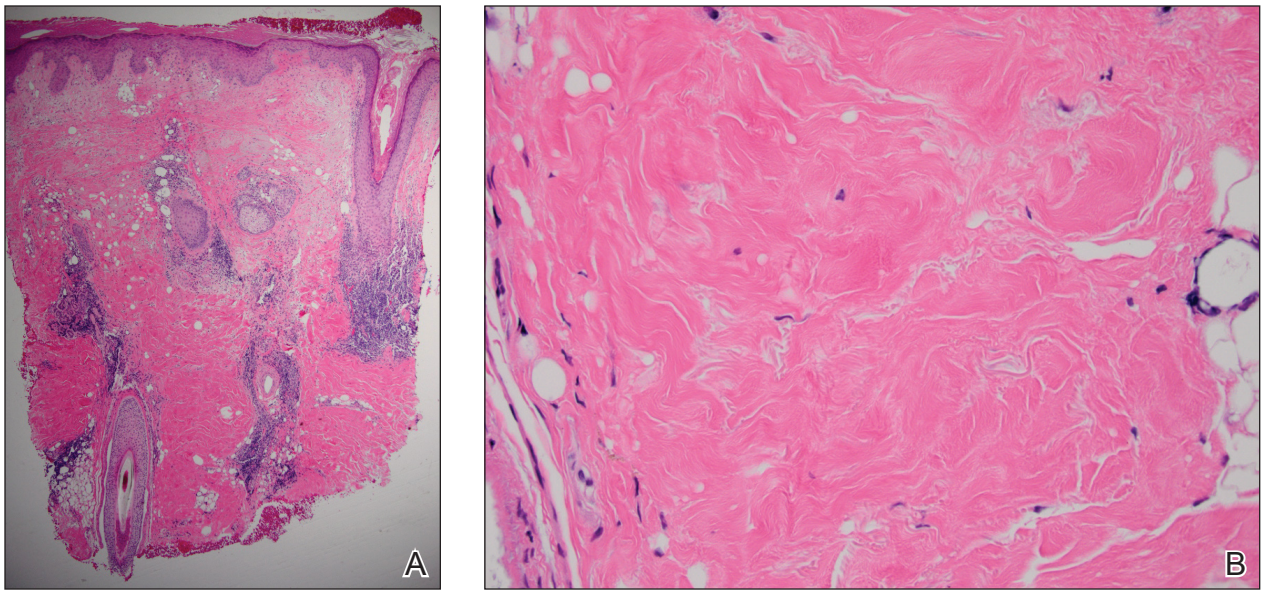

Figure 2. Interface changes, basement membrane thickening, and periadnexal inflammation supporting a diagnosis of discoid lupus erythematosus (A)(H&E, original magnification ×10). Sclerosis of the reticular dermis with thickening of collagen bundles consistent with localized scleroderma also were noted (B)(H&E, original magnification ×40).

More than 100 cases have been reported wherein LE and scleroderma coexist in the same patient.[1] Most of these cases have been examples of type 1 overlap (Table 1), though a few have been type 2 overlap, with localized scleroderma coexisting with systemic LE or vice versa.[1,2] There are rare reports of an overlap of the localized form of both of these entities (type 3 overlap), as demonstrated in our patient. According to a PubMed search of articles indexed for MEDLINE using the search terms *localized scleroderma* and *morphea* as well as *discoid lupus erythematosus*, we found 12 other cases describing type 3 overlap (Table 2).

The first case was described in 1976 as annular atrophic plaques on the face and neck of a 48-year-old man.[3] As in our case, there were overlapping features of DLE and localized scleroderma. The investigators postulated that the entity was an atypical form of DLE.[3] There were 4 more cases described in 1978, but the majority of these patients were young women with linear plaques. Instead of calling the disease a new form of DLE, the investigators considered it to be an overlap syndrome.[4] Many years passed before another similar case was described in the literature in 1990.[5] Interestingly, the investigators performed multiple biopsies on this patient over several years and observed that the pathology changed from subacute cutaneous LE to an overlap of subacute cutaneous LE and localized scleroderma to localized scleroderma, suggesting that localized scleroderma was the end result of persistent inflammation from the cutaneous LE lesions. The investigators compared the evolution of subacute cutaneous LE to localized scleroderma in the patient to the evolution of acute graft-versus-host disease

Table 1.

Dermatologic Classification of Overlap Syndromes in Connective-Tissue Diseases

Type 1	Systemic disease overlapping with systemic disease
Type 2	Cutaneous disease (eg, localized scleroderma, cutaneous LE) overlapping with systemic disease (eg, systemic LE)
Type 3	Cutaneous disease (eg, localized scleroderma) overlapping with cutaneous disease (eg, cutaneous LE); overlap may occur with distinctive lesions developing at separate sites or clinical and/or histological features of both diseases within the same site (known as coincident overlap)

Abbreviation: LE, lupus erythematosus.

Table 2.

Summary of Reported Cases of Type 3 Overlap of Connective-Tissue Diseases

Reference (Year)	Sex	Age at Onset, y	Location of Lesions	Histologic Findings	Overlap[a]	Morphology	Therapy	Positive Laboratory Test Results	Systemic Involvement	DIF	Evolution
Chorzelski et al[3] (1976)	M	48	Face, neck	DLE, atrophic appendages	Yes	Annular plaques	Unknown	None	No	IgG, C3 at DEJ	Unknown
Umbert and Winkelmann[4] (1978)	F	7	Arms	DLE, sclerosis	Yes	Linear plaques	Topical steroids, antimalarials	None	No	IgM, C3 at DEJ	Improvement
	F	26	Face, trunk, arms, legs	DLE, sclerosis	Yes	Annular plaques	Antimalarials	None	No	Negative	Poor response
	F	11	Scalp, face, arms	DLE, sclerosis	Yes	Linear and annular plaques	Antimalarials	Anti-DNA	No	IgG, IgM, C3 at DEJ	Improvement
	M	47	Face, back, arms	DLE, sclerosis	No	Linear	Antimalarials	None	No	IgM, fibrin at DEJ	Improvement
Rao et al[5] (1990)	F	22	Chest, arms, neck, face	SCLE initially, then morphea on repeat biopsy	Yes	Annular plaques	Topical/oral steroids	ANA, RF, low C3	Yes, oral ulcers	IgG, IgA, IgM at DEJ	Unknown
Stork and Vosmik[6] (1994)	F	22	Arms, breasts, buttocks, face	Scleroderma, lupus panniculitis	No	Plaques, nodules	Antimalarials, topical steroids	ANA	No	IgM at DEJ	Improvement
Marzano et al[7] (2005)	F	21	Scalp, forehead, face, buttocks	Lupus panniculitis	Yes	Linear	Prednisone, antimalarials	ANA, dsDNA, low C3	Yes, renal	Not reported	Improvement
	F	29	Arms	Lupus panniculitis, fibrosis	Yes	Linear, nodules	Prednisone, antimalarials	ANA, anticardiolipin antibodies	Yes, thrombocytopenia	IgM, C3 at DEJ	Improvement
Julia et al[8] (2008)	F	13	Arms, chest, back	DLE, fibrosis	Yes	Linear	Topical steroids, antimalarials	None	No	Negative	Poor response
Mir et al[9] (2011)	F	20	Arms	DLE, morphea	Yes	Plaques	Steroids, abx, antimalarials	ANA, dsDNA	No	Not reported	Poor response
Khelifa et al[10] (2011)	M	34	Forehead	DLE, morphea	Yes	Linear	Topical steroids, antimalarials	None	No	Not reported	Improvement
Current case	M	30s to 40s[b]	Face, neck, upper back	DLE, sclerosis	Yes	Plaques	Topical steroids, mycophenolate mofetil	ANA, SS-A	No	Negative	Improvement

Abbreviations: DIF, direct immunofluorescence; M, male; DLE, discoid lupus erythematosus; DEJ, dermoepidermal junction; F, female; SCLE, subacute cutaneous lupus erythematosus; ANA, antinuclear antibody; RF, rheumatoid factor; dsDNA, double-stranded DNA; abx, antibiotics; SS-A, anti–Sjögren syndrome antigen A.

[a]Overlap occurs in same anatomic location/same clinical site.

[b]Patient was aged 60 years at presentation, but age of onset was 20–30 years prior, according to the patient.

(GVHD) to chronic GVHD. Acute GVHD has a lichenoid tissue reaction that develops into sclerosis in the chronic form.[5]

Additionally, there were 3 cases in the literature showing an overlap of lupus panniculitis with localized scleroderma.[6,7] Stork and Vosmik[6] described a case of a 22-year-old woman with lesions clinically suspicious for localized scleroderma, with lupus panniculitis demonstrated on histopathology. They discussed the difficulty in differentiating between lupus panniculitis and localized scleroderma but did not specify whether they believed the case represented a distinct entity or an overlap syndrome.[6] Alternatively, Marzano et al[7] reported 2 similar cases, which the investigators considered to be a specific new variant called sclerodermic linear lupus panniculitis.

In the last 10 years, there were 3 additional cases reported that described an overlap of DLE and localized scleroderma in the same anatomic location, similar to our patient.[8-10] Although Julia et al[8] considered their case to be an example of the distinct entity called sclerodermiform linear LE, the investigators in the other 2 cases described the possibility of an overlap syndrome.[9,10]

Based on reported cases, we found the following patterns in the overlap of cutaneous LE and localized scleroderma: predilection for young women, photodistributed lesions, DLE, linear morphology clinically, and positivity along the dermoepidermal junction on direct immunofluorescence. As in our case, the few affected men were older compared to affected women. Men ranged in age from 34 to 48 years compared to women who ranged in age from 7 to 29 years. We did not find a pattern in the laboratory findings in these patients. Most patients had a good response to antimalarials, topical steroids, or systemic steroids.

Conclusion

All 12 previously reported cases showed some form of overlap of cutaneous LE and localized scleroderma. As previously discussed, overlap syndromes are common in patients with CTDs. We postulate that our case represents a rare form of overlap syndrome, with the overlap occurring at the same clinical sites.

REFERENCES

1. Iaccarino L, Gatto M, Bettio S, et al. Overlap connective tissue disease syndromes [published online June 26, 2012]. *Autoimmun Reviews*. 2012;12:363-373.
2. Balbir-Gurman A, Braun-Moscovici Y. Scleroderma overlap syndrome. *Isr Med Assoc J*. 2011;13:14-20.
3. Chorzelski TP, Jablonska S, Blaszyczyk M, et al. Annular atrophic plaques of the face. *Arch Dermatol*. 1976;112:1143-1145.
4. Umbert P, Winkelmann RK. Concurrent localized scleroderma and discoid lupus erythematosus. *Arch Dermatol*. 1978;114:1473-1478.
5. Rao BK, Coldiron B, Freeman RG, et al. Subacute cutaneous lupus progressing to morphea erythematosus lesions. *J Am Acad Dermatol*. 1990;23(5, pt 2):1019-1022.
6. Stork J, Vosmik F. Lupus erythematosus panniculitis with morphea-like lesions. *Clin Exp Dermatol*. 1994;19:79-82.
7. Marzano AV, Tanzi C, Caputo R, et al. Sclerodermic linear lupus panniculitis: report of two cases. *Dermatology*. 2005;210:329-332.
8. Julia M, Mascaro JM Jr, Guilaber A, et al. Sclerodermiform linear lupus erythematosus: a distinct entity or coexistence of two autoimmune diseases? *J Am Acad Dermatol*. 2008;58:665-667.
9. Mir A, Tlougan B, O'Reilly K, et al. Morphea with discoid lupus erythematosus. *Dermatol Online J*. 2011;17:10.
10. Khelifa E, Masouye I, Pham HC, et al. Linear sclerodermic lupus erythematosus, a distinct variant of linear morphea and chronic cutaneous lupus erythematosus. *Int J Dermatol*. 2011;50:1491-1495.