

# Intralesional overlap syndrome: Sclerodermic lupus panniculitis and sclerodermic discoid lupus erythematosus



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**Key words:** discoid lupus erythematosus; localized scleroderma; morphea; overlap syndrome; sclerodermiform linear lupus erythematosus; sclerodermic lupus erythematosus profundus; sclerodermic lupus panniculitis.

## INTRODUCTION

Coexistence of multiple connective tissue diseases in a patient is referred to as *overlap syndrome*. The phenomenon is classified as type 1 through 3 with type 1 representing overlap between 2 systemic diseases, type 2 between cutaneous and systemic disease, and type 3 between 2 cutaneous diseases.<sup>1</sup> Moreover, a single lesion featuring multiple connective tissue diseases is uniquely rare. Here we present a case of lupus erythematosus panniculitis (LEP), also known as *lupus profundus*, with concurrent histologic evidence of localized scleroderma defining the entity of sclerodermic lupus profundus. The patient also had concomitant discoid lupus erythematosus (DLE) with a similar pattern (scleroderma-like fibrosis, ie, sclerodermic DLE). Sclerodermic LEP (SLEP), first coined by Marzano in 2005 to describe this entity, has only been noted in 4 patients. Three of these harbored a linear pattern of LEP,<sup>2,3</sup> whereas 1 presented with a nonlinear configuration.<sup>4</sup> This report describes the fourth case of linear SLEP and reviews the previously published cases.

## CASE REPORT

A 63-year-old African-American woman with history of arthralgias, scalp lesions, and recurrent lip lesions presented in November 2018 for complaints of right arm skin thickening. She noticed intermittent swelling of both hands and right shoulder stiffness in January 2018. That October she noticed skin thickening in the right medial upper arm extending into the axilla. She described

### Abbreviations used:

DLE:	discoid lupus erythematosus
LE:	lupus erythematosus
LEP:	lupus erythematosus panniculitis
SLE:	systemic lupus erythematosus
SLEP:	sclerodermic lupus erythematosus panniculitis

subcutaneous nodules coalescing into a linear area of thickened skin. Examination found thickening of the right axillary folds with extension to the back and palpable axillary adenopathy (Fig 1). Erythrocyte sedimentation rate (ESR) was 41. Negative results included antinuclear antibody, rheumatoid factor, and anticyclic citrullinated peptide antibody.

The excisional arm biopsy demonstrated an extensive fibrosing reaction involving the deeper dermis and interlobular fat septa, reminiscent of morphea profunda (Fig 2). However, there were classic features associated with LEP, namely hyalinizing alteration of the fat lobule, lymphoplasmacytic infiltrate permeating the fat lobule, and a striking subcutaneous lymphocyte-rich vasculopathy (Fig 3). There was expansion of the intima of smaller arteries and arterioles by mucin, collagen, and spindle cells with myofibroblastic features. Smaller vessels represented by capillaries and venules showed basement membrane zone thickening consistent with antecedent microvascular injury.

The lymphocytes were predominated by T cells over B cells in a 3:1 ratio while the CD4/CD8 ratio

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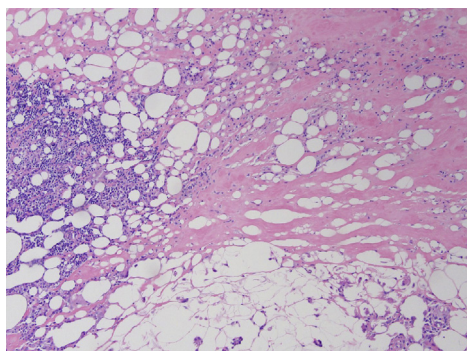
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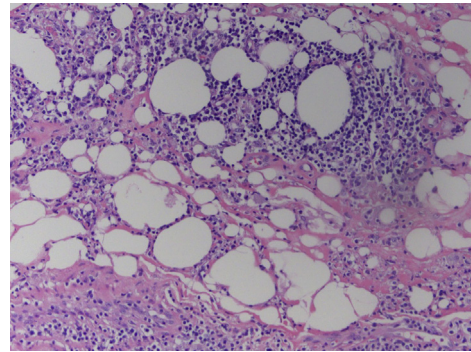


**Fig 1.** SLEP, Right axilla. A 6-cm × 3-cm linear thickening of the skin in the axilla resulting from progressive coalescence of subcutaneous nodules. Excisional biopsy was diagnosed as LEP with concurrent features resembling localized scleroderma (ie, SLEP).

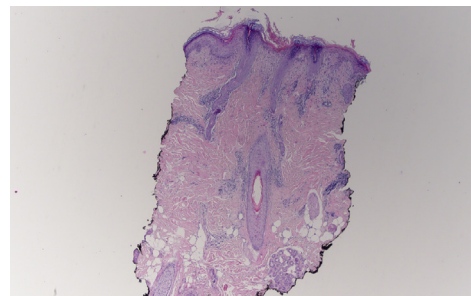


**Fig 2.** In this field, there is hyalanosis of the fat, a lymphocytic lobular panniculitis, and concomitant scleroderma-like fibrosis. At the inception of lupus profundus, one observes a brisk lymphocytic lobular panniculitis, a finding well exemplified in this photo. (Hematoxylin-eosin stain; low power.)

was within normal limits. Plasma cells were polyclonal. To explore the sclerodermic aspect of the biopsy, a CD34 preparation was conducted revealing a diminution in CD34 expression within the deeper dermis and the zone of subcuticular hyalinizing fibrosis mirroring the pattern of CD34 reduction seen in cutaneous scleroderma. Unlike scleroderma, there was no acquisition of a smooth muscle actin phenotype amidst the fibroblasts. Human myxovirus resistance protein 1 (MXA) preparation was



**Fig 3.** In this field, there is both an active lymphocytic lobular panniculitis and hyalinizing alteration of the fat. (Hematoxylin-eosin stain; high power.)



**Fig 4.** There is an atrophying interface dermatitis with both epidermal and follicular involvement accompanied by marked hyperkeratosis and deeper seated dermal sclerosis consistent with sclerodermic lupus erythematosus. (Hematoxylin-eosin stain; low power.)

significantly positive, indicating an enhanced type I interferon microenvironment corroborative of lupus erythematosus. MXA expression was strongly upregulated in the endothelium, inflammatory cells, and epithelial structures of adnexal derivation.

A revisited old scalp biopsy was diagnostic of DLE with a supervening fibrosing keloidal-like dermal response consistent with sclerodermic DLE (Fig 4). A revisited lip biopsy showed variable lichenoid to cell poor pattern with chronic microvascular changes.

The patient followed up with the rheumatology department. Repeat tests showed ESR of 9. Anti-double-stranded DNA antibody and extractable nuclear antigen antibodies panel were negative. There were no serologic signs of systemic disease. Plaquenil treatment was recommended. At 6-month follow-up, the patient had not begun treatment, and the lesion had become more prominent.

## DISCUSSION

LEP, also known as *lupus profundus*, is a variant of lupus erythematosus (LE), manifested by tender subcutaneous panniculitic nodules or plaques in a

predominantly upper body distribution.<sup>5</sup> The lesions follow a relapsing remitting course and heal with an area of lipoatrophic depression.<sup>5</sup> This rare phenomenon occurs in 1% to 3% of cutaneous LE.<sup>5</sup>

Concurrent LE and scleroderma has been reported, most often with overlap of the systemic variants of these conditions. Overlap syndrome between LEP and morphea profunda has only been described in 4 patients.<sup>2-4</sup> Even more unusual is overlap of these pathologies within the same lesion. Of the 4 SLEP patients described, 3 displayed a linear variant of LEP.<sup>2,3</sup> Intralesional overlap between DLE and morphea has been described in the literature as well.<sup>1</sup>

The clinical and histologic findings in this case are highly characteristic of SLEP. Localization to the upper arm is unsurprising given that this is the most common site for LEP. On microscopy, the patient's biopsy stained MXA positive, which would not be observed in morphea but is characteristic for LEP.<sup>6</sup> Furthermore, the phenotypic profile one expects to see in fully evolved morphea is not observed. Although there is reduction of CD34 in the zones of fibrosis typical for morphea, smooth muscle actin acquisition is not seen, thereby distinguishing this biopsy from true scleroderma. That being said it is possible that some cases of sclerodermic LE could demonstrate the classic scleroderma CD34 negative smooth muscle actin positive phenotype. One would have to study many cases of sclerodermic LE to better understand the CD34 and smooth muscle actin staining patterns. Old biopsies revealed discoid lesions with concomitant fibrosis consistent with sclerodermic DLE.

Given the very limited sample size, it is difficult to draw meaningful conclusions about progression to systemic disease. The 4 cases previously described all reported female patients, ages ranging 9 to 32. Of the 4 patients, 2 showed signs of systemic involvement, the first with diffuse membranoproliferative glomerulonephritis and the second with thrombocytopenia, anticardiolipin antibodies, and spontaneous abortion. Marzano et al<sup>2</sup> suggest that SLEP may be an aggressive variant given both their patients' systemic symptoms. The 2 other cases have not shown systemic involvement. Laboratory results have been inconsistent among the patients. Although our patient's history and biopsy results support the

hypothesis of Marzano et al,<sup>2</sup> serology including antinuclear antibody for systemic disease has been negative. Therefore, the current patient suffers from purely cutaneous disease, and no systemic progression is anticipated. All patients thus far have responded well to steroids and antimalarial medications, with all but the youngest patient reporting local lipoatrophy on resolution.

This case sheds light on the unusual phenomenon of type 3 overlap syndrome between morphea and LEP, and morphea with DLE. Coexistence of scleroderma and lupus is well documented, with shared features including positive antinuclear antibody, esophageal dysmotility, and Raynaud phenomenon. Patients with anti-RNP antibodies may exhibit overlap in the same biopsy. However, here the conditions are concurrent and not evolutionary or sequela, as evidenced by fibrotic evolution that would not be seen in lupus. This case represents the fourth report of SLEP. This case underscores the value of MXA in differentiating classic scleroderma from SLEP. Previous investigators warn of the possibility of impending SLE in SLEP. However, this finding has yet to be substantiated with follow-up on all reported patients.

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