Sclerodermiform Lupus Erythematosus: A Case Report of an Overlap Syndrome of Lupus Profundus and Morphea

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ABSTRACT:

Sclerodermiform lupus erythematosus is a rare type 3 overlap syndrome between chronic cutaneous lupus erythematosus (CCLE) and morphea. The diagnostic criteria are shared histopathologic features of both CCLE and morphea. Here we reported a 49-year-old female presented with an indurated mass with intermittent pain on the left inner thigh for 3 years. Dermatological examination showed ill-defined hyperpigmented, indurated plaque with bound-down skin on the inner side of the left thigh. Skin biopsy revealed subcutaneous lobular lymphocytic infiltrate with lipomembranous and hyalinized fat necrosis mixed with thickened collagen. Alcian blue pH2.5 revealed an increase in dermal and subcutaneous mucin. Immunohistochemistry for CD123 was positive plasmacytoid dendritic cells in clusters. Serological studies showed positive antinuclear and anti-ds DNA antibodies. A diagnosis of sclerodermiform lupus erythematosus was made. Administration of prednisolone, methotrexate, and chloroquine resulted in gradually improved in 5 months. Previous reports of sclerodermiform lupus and morpheaform lupus were summarized.

Key words: Lupus profundus, Lupus panniculitis, Morphea-like lesion, Morpheaform lupus, Sclerodermoid lupus, Sclerodermiform lupus erythematosus

Case report

A 49-year-old Thai female attended the dermatology clinic with a three-year history of an indurated mass with intermittent pain in her left inner thigh. She claimed to be in good health and denied ever having a fever, weight loss, joint discomfort, or other photosensitive symptoms. There have been no previous traumatic events or medication injections in this area. There was no mention of any current medications. Over time, the lesion thickened and grew unpleasant. A large, ill-defined hyperpigmented, indurated plaque with bound-down skin and superficial vein dilatation on the inner side of the left leg, was identified on examination. (Figure 1A).

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Received: 14 August 2023 Revised: 16 October 2023 Accepted: 4 January 2024

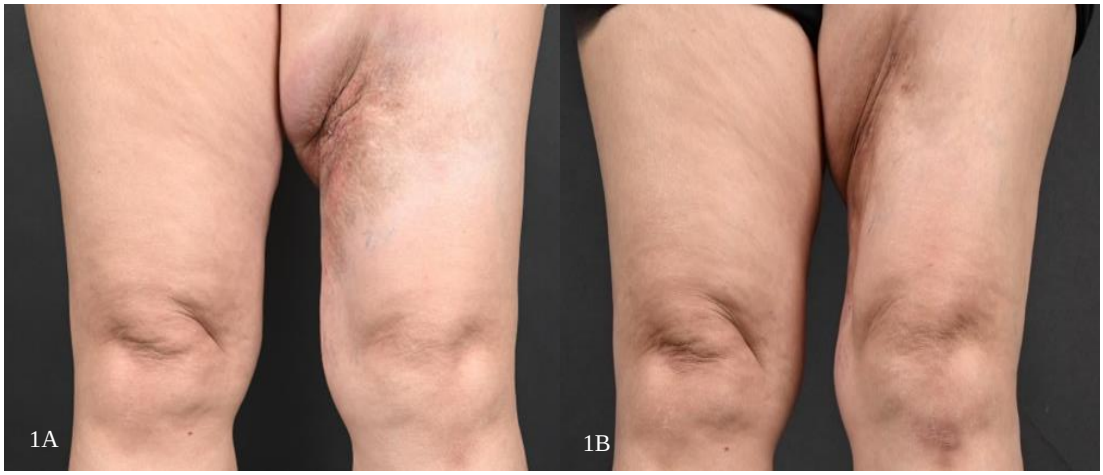

Figure 1A A large, poorly circumscribed, hyperpigmented, indurated plaque on the inner aspect of left thigh
Figure 1B A 12-month follow-up on the left thigh lesion

Morphea profundus, lupus panniculitis/profundus, cutaneous T-cell lymphoma, and deep fungal infection were included in the preliminary diagnoses. A skin biopsy from the left thigh was performed. Epidermis demonstrated hyperkeratosis and irregular acanthosis with focal basal vacuolization and melanin incontinence (Figures 2A-B). Superficial and deep perivascular and peri-adnexal lymphoplasmacytic infiltrates with extravasated erythrocytes were observed (Figure 2D). Thickened collagen bundles with sclerotic changes were detected in the dermis. Subcutaneous tissue demonstrated lobular lymphocytic infiltrate with lipomembranous and focal hyalinized fat necrosis (Figure 2C). Alcian blue pH 2.5 stain revealed increased dermal and subcutaneous mucin (Figure 2E). Immunohistochemistry for CD123 highlighted clusters of plasmacytoid dendritic cells (Figure 2F). Direct immunofluorescence revealed C3, IgG, and focal IgM deposition in a granular pattern at the dermo-epidermal junction (Figures 2G-I) Laboratory studies revealed normal ranges of complete blood count, liver, and renal functions. Serological testing revealed a positive antinuclear antibody (titer 1:320, fine-speckled pattern) and a positive anti-ds DNA antibody. Anti-Sm IgG, Anticardiolipin IgM, Anti-Beta-2-GP1 IgG, and Anti-Beta-2-GP1 IgM were all negative. Immunoglobulin C3c and C4 levels were normal. Clinical, histologic, and laboratory findings led to the diagnosis of sclerodermiform lupus erythematosus (SDLE).

Prednisolone 40 mg/day (0.6 mg/kg/day) was started and gradually tapered off over a four-month period. Chloroquine 250 mg/day was administered in conjunction with baseline screening for maculopathy. Methotrexate 10-12.5 mg/week was administered throughout prednisolone tapering, and the lesion gradually improved with less erythema, pain, and induration. Treatment response increased dramatically after 5 months and continued to improve till 12 months. The lesion progressively healed without tenderness or inflammation. (Figure 1B)

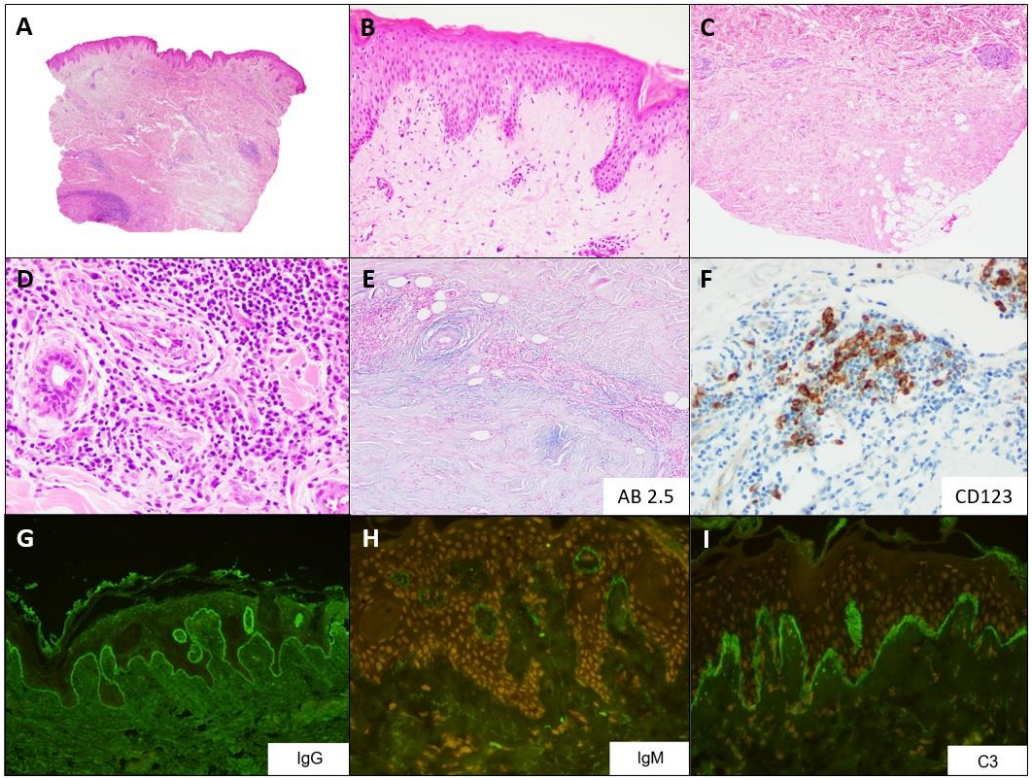

Figure 2 The skin biopsy showed hyperkeratosis and irregular acanthosis of the epidermis (A: H&E, 40x), with focal basal vacuolization and melanin incontinence (B: H&E, 100x). Subcutaneous lobular lymphocytic infiltrate with lipomembranous and hyalinized fat necrosis (C: H&E, 100x). Peri-adnexal lymphoplasmacytic infiltrate and extravasated erythrocytes in the dermis (D: H&E, 400x). Alcian blue pH 2.5 (AB 2.5) highlighted increased dermal and subcutaneous mucin (E). Clusters of plasmacytoid dendritic cells with CD123 positivity (F). Direct immunofluorescent study demonstrated granular deposits of IgG, focal IgM and C3 at a dermo-epidermal junction (G, H, I).

Discussion

Sclerodermiform lupus erythematosus (SDLE) is a rare type 3 overlap syndrome between chronic cutaneous lupus erythematosus (CCLE) and morphea. CCLE can present with discoid lupus erythematosus (DLE) or lupus panniculitis/profundus (LEP)[1]. The diagnostic criteria of SDLE are shared histopathologic features of both CCLE and morphea. In 1976, Umbert et al. first introduced the term "sclerodermiform linear lupus erythematosus"[2]. SDLE is a very rare condition. It has been reported in young adults and women. However, incidences in men have also been documented[1]. Most cases of SDLE demonstrate a morphea-like appearance. The upper extremity is the most frequent location, followed by the face and scalp, trunk, buttocks, and thighs. The histopathology of SDLE displays both characteristics of CCLE and morphea. Typical findings are interface dermatitis, thickening of the basement membrane zone, perivascular inflammation, increased dermal mucin which are characteristics of CCLE, and excessive collagen deposition that thickens the dermis or subcutaneous tissues, which is a characteristic of morphea[1].

Our present case demonstrated overlapping features of lupus profundus and morphea in both clinical and histopathologic characteristics. (Figures 1, 2) We found a large hyperpigmented, indurated plaque with bound-down skin on the left thigh, corresponding to the histopathology of epidermal and interface changes with superficial and deep perivascular and peri-adnexal lymphoplasmacytic infiltrates. Importantly, thickened collagen bundles with sclerotic changes compatible with morphea were detected in the dermis. Subcutaneous tissue demonstrated lobular lymphocytic infiltrate with lipomembranous and focal hyalinized fat necrosis, characteristics of LEP. Increased dermal and subcutaneous mucin was also detected with Alcian blue pH 2.5. We found positive CD 123 in plasmacytoid dendritic cells. CD 123 immunohistochemical staining is a plasmacytoid dendritic cell marker and can help distinguish cutaneous lupus from other inflammatory diseases[3].

Lupus profundus is a subcutaneous inflammatory disease associated with overlying DLE lesions[4]. Rangel et al. published a large study of 61 LEP patients and reported that active erythematous nodules or plaques were the most frequent lesions (77%), followed by atrophy or contour change (63%)[4]. However, no morpheaform lesion was noted[4]. The majority of patients had DLE or systemic lupus erythematosus before developing lupus profundus[4]. Upper arms and legs, as well as the face and breasts, are the most commonly involved areas in LEP[4]. Histopathological findings in LEP include hyaline necrosis of the subcutaneous fat along with lymphocytic infiltration of fat lobules. Mucin deposition along with epidermal changes can be seen. Direct immunofluorescence might show granular staining of IgG, IgM and C3 at the dermal-epidermal junction. The healing phase of LEP can result in ulcerations, atrophic scars, and/or calcification of the lesions[1].

Table 1 Case reports of sclerodermiform/morpheaform lupus erythematosus

	Age	Clinical	Systemic involvement	Location	Histology	Direct immunofluorescence	Treatment	Outcome
Stork, 1994[6]	A 22-year-old white female	-Irregular indurated plaques -Deep subcutaneous nodules for 11 months	No	Breasts, buttocks, and face	-Normal epidermis, hyalinization of connective tissue around cutaneous adnexa in the deep dermis and within broadened fibrous septa separating fat lobules -Lymphocytic panniculitis with hyaline necrosis of fat cell -Lymphocytic panniculitis with hyaline necrosis of the fat cells and a sparse lymphocytic infiltrate	Patchy granular deposits of IgM at the dermo-epidermal junction and deposits of fibrinogen in vessel walls in the upper part of the dermis	Chloroquine	Complete resolution of subcutaneous nodules leaving depressed area
Morgan, 2011[7]	A 12-year-old Philippine male	Bilateral indurated swelling for 2 years	No	Cheeks	-Full thickness mixed inflammation with prominent panniculitis	Positive lupus band pattern	Oral corticosteroid and hydroxychloroquine	Symmetric sunken cheek appearance similar to lipoatrophy
Elbendary, 2016[8]	A 9-year-old girl	Linear arrangement of subcutaneous nodules	No	Left forearm and arm	-Superficial and deep perivascular and peri-adnexal lymphocytic infiltrate with areas of collagen sclerosis -Deep peri-eccrine lymphoplasmacytic infiltrate with morphea-like changes -Loss of CD34 in the area with morphea-like changes	Negative for lupus	Subcutaneous methotrexate and pulsed intravenous methylprednisolone	Minimal residual discoloration, and slightly residual firmness overlying lesion
Cheng, 2021[10]	A 43-year-old female	Brownish indurated plaque with peripheral erythema and epidermal atrophy	No	Posterolateral aspect of right thigh	-Melanin incontinence, dense compact sclerosis of the dermis, peri-adnexal and perivascular lymphocytic infiltration -Marked septal fibrosis with lymphocytic infiltration in subcutaneous tissue	Lupus band test: positive	Oral prednisolone, hydroxychloroquine and clobetasol ointment	Skin lesion improved with post inflammatory hyperpigmentation

Table 1 Case reports of sclerodermiform/morpheaform lupus erythematosus

	Age	Clinical	Systemic involvement	Location	Histology	Direct immunofluorescence	Treatment	Outcome
Pinyowiwat, 2023[9]	A 44-year-old Thai female	Solitary indurated erythematous plaque with firm to hard consistency	No	Left lateral side of the neck	-Vacuolar interface dermatitis, superficial and deep perivascular lymphoplasmacytic infiltrate, lobular panniculitis and thickened homogenized collagen	Not done	Intralesional steroid and hydroxychloroquine	Improved with some indentation
Hobbs, 2023[1]	A 57-year-old male	Bound-down hyperpigmented plaques	N/A	Left anterior proximal upper arm	-Superficial and deep, perivascular and periadnexal lymphohistiocytic infiltrate with scattered plasma cells extending deep into the subcutis. -Sclerosis of the superficial and deep dermis and early adipose tissue. -No increase in mucin deposition with colloidal iron. The elastic stain highlights a loss of elastic fibers in the area of sclerosis.	N/A	Intralesional triamcinolone	Moderate improvement
	A 38-year-old Black male	Well-demarcated erythematous to hyperpigmented scarred coin shaped plaques with mild scale	N/A	Face and scalp	"Squared off" biopsy which consists of marked hyalinization extending into the subcutaneous fat with appendageal dropout and associated chronic inflammation. Most of the epidermis is denuded.	N/A	Topical clobetasol and hydroxychloroquine	Significant improvement, no recurrence after hydroxychloroquine taper
	A 32-year-old Black female	Hyperpigmented, dry, nodular eruption	N/A	Lower extremities	-Irregularly acanthotic with no evidence of interface changes. -Marked dermal sclerosis that extends into the superficial subcutis. Highly placed atrophic eccrine sweat gland coils. -Unusual prominent plasma cell infiltrate. Focal increase in mucin deposition seen with colloidal iron -Focal nodular lympho-plasmocytic aggregate in subcutis	N/A	Topical tacrolimus And topical clobetasol	Some improvement
	A 56-year-old White male	Red scaly, slightly indurated plaque	N/A	Right chest	-Interface and lichenoid changes are present. The CD123 immunostaining highlights numerous clusters of plasmacytoid dendritic cells, particularly at the dermoepidermal junction -Superficial and deep, perivascular, periadnexal and interstitial infiltrate consisting of numerous plasma cells. -Diffuse dermal sclerosis confirmed by an elastic stain. The inflammation extends into the adipose tissue in the form of a lobular panniculitis. A colloidal iron shows no significant increased dermal mucin.	N/A	Not provided	Not provided
	A 40-year-old Black female	-Dermal to subcutaneous indurated plaque with “bound down” skin on hip - Hyperpigmented dermal plaque on arm	N/A	Left hip and right arm	-Mild vacuolar changes of the basal keratinocytes -Superficial and deep perivascular lymphocytic infiltrate rich in plasma cells that is more prominent at the interface between the deep dermis and subcutaneous tissue. -The mid to deep reticular dermis shows extensive sclerosis. - Markedly increased mucin deposition seen with colloidal iron staining. An elastic stain highlights loss of elastic fibers in the areas of sclerosis. -A CD123 immunostaining shows rare clusters of plasmacytoid dendritic cells.	N/A	Intralesional triamcinolone, prednisone, hydroxychloroquine, topical clobetasol and methotrexate	Significant improvement

Table 1 Case reports of sclerodermiform/morpheaform lupus erythematosus

	Age	Clinical	Systemic involvement	Location	Histology	Direct immunofluorescence	Treatment	Outcome
The present case	A 49-year-old Thai female	Indurated mass with bound-down skin for 3 years	No	Left inner thigh	-Focal basal vacuolization and melanin incontinence -Increased interstitial mucin, perivascular and peri-adnexal lymphoplasmacytic infiltrates in the dermis mixed with thickened collagen -Subcutaneous lobular lymphocytic infiltration with lipomembranous and hyalinized fat necrosis -CD123 and alcian blue 2.5 staining: positive	C3, IgG, and focal IgM deposition in a granular pattern at a dermo-epidermal junction	Oral corticosteroid, methotrexate, and chloroquine	Improved with some depressed area

N/A: not available

Our patient had a three-year history of indurated plaque prior to starting treatment. The chronic inflammatory process may result in sclerotic changes in the histopathology. Dermal sclerosis can be the feature of the overlap morphea. However, the pathogenesis of sclerosis and fibrosis in SDLE is still unclear. Current data indicate that B lymphocytes may be involved in late DLE features, as evidenced by their presence in long-lasting inflammatory DLE and scar DLE lesions. B cells release cytokines that increase the synthesis of fibroblasts and collagen in a transforming growth factor (TGF)-β dependent pathway, which can lead to skin fibrosis. Additionally, the development of B cell autoantibodies, such as antibodies against platelet-derived growth factor receptor, has been linked to fibrosis[5].

According to the literature review of LEP coexisting with the terms morphea-like, morpheaform, sclerodermoid, scleroderma, sclerodermiform. All cases are demonstrated in Table 1. There were 6 women and 4 men[1, 6-10]. The cases onset ages range from 9 to 57 years. The key features of SDLE lesions include female and upper body distribution, as well as skin lesions that are cured with localized dystrophy. According to reports, the head, face, breast, upper extremities, hip, and lower limbs were all affected by the SDLE. No systemic involvement or coexisting systemic lupus erythematosus found in all cases[1, 6-10].

In LEP the first-line treatment is antimalarial (chloroquine and hydroxychloroquine),[4] which is usually well-tolerated. Patients should undergo an ophthalmic examination for maculopathy every 6-12 months. Methotrexate is another option for treating LEP[4]. Thalidomide has been shown to be effective in treating refractory LEP. The most concerning adverse effect is teratogenicity. In severe inflammatory lesions, oral corticosteroids might be implemented before starting any other treatment, such as antimalarials or immunosuppressants. Optional therapy for refractory LEP includes cyclosporine, cyclophosphamide, and the monoclonal antibody rituximab. For treatment of deep morphea, various drugs were administered include systemic corticosteroids, methotrexate, cyclosporine, D-penicillamine, mycophenolate mofetil, tocilizumab, ruxolitinib, infliximab, phototherapy and extracorporeal photochemotherapy. In the present patient, an oral corticosteroid was originally provided, and for long-term therapy, methotrexate and chloroquine were then given. Clinical signs of indurated plaques and discomfort improved in conjunction with lipoatrophy and alterations in the color of the residual lesion. The patient refused cosmetic lipoatrophy therapy such autologous fat transfer or filler injection.

In conclusion, SDLE is rare and should be distinguished from other sclerotic disorders. Clinical manifestation, histopathology, immunohistochemistry, and direct immunofluorescence help in the diagnosis of SDLE. Our patient had SDLE with signs of LEP and morphea overlap, and she responded effectively to systemic corticosteroids,

methotrexate, and chloroquine, leaving behind lipoatrophy and a change in pigmentation.

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