SKIN

BRIEF ARTICLE

Unveiling Multiple Chronic Relapsing Plaques and Ulcerations in a Healthy Individual

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ABSTRACT

Lupus erythematosus panniculitis (LEP) is an uncommon variant of chronic cutaneous lupus erythematosus. The lesions are characterized by the involvement of subcutaneous tissue, typically presented with tender erythematous or purplish subcutaneous nodules or plaques with different overlying skin appearances, rarely skin ulceration. The clinical course of LEP is typically chronic and relapsing with periods of exacerbations which can be triggered by trauma. Most LEP patients have a favorable prognosis in SLE patients. We report a 60-year-old Southeast Asian female who presented with reddish ulcerated plaques on the face and left arm for 2 months. Histopathological findings showed peri-adnexal and subcutaneous fat lobule inflammation consisted of lymphocytes, plasma cells, and some histiocytes. Focal hyaline necrosis of fat cells was also identified. Although DIF tests showed negative results, CD123+ immunohistochemical staining was found positive. Other blood investigations were unremarkable. She did not fulfill the criteria for systemic lupus erythematosus. She was successfully treated with hydroxychloroquine, oral prednisolone, and a topical potent corticosteroid. Her ulcers healed with post-inflammatory hyperpigmentation and scars.

INTRODUCTION

Lupus erythematosus panniculitis (LEP), also known as lupus profundus, is a rare variant of chronic cutaneous lupus erythematosus, which can have distinctive manifestations and are associated with DLE or systemic lupus erythematosus (SLE).[1-3] The rate of LEP association with SLE has been described with variable proportions from 10% to 42%. On the other hand, LEP is an uncommon dermatological manifestation of SLE with an incidence of 2-4.5%.[16,17] The lesions of LEP are typically presented with solitary or multiple, tender erythematous or purplish subcutaneous nodules and/or plaques with varying overlying skin appearances, from normal skin to discoid lupus erythematosus, rarely skin ulceration.[1-3] We report a 60-year-old Southeast Asian female was admitted to the outpatient department due to reddish ulcerated plaques on her face and left arm for 2 months.

CASE DESCRIPTION

A healthy 60-year-old Southeast Asian woman presented with progressive pruritic, indurated reddish rashes on the face and left arm for 2 months. Over a year, they had been

presented on her chest wall, hip, and both arms in a waxing-and-waning pattern--spontaneously resolved to hyperpigmented rashes. However, the lesions on the face and left arm became more tender and edematous regardless of sun exposure. Some lesions on the arm were ulcerated. She reported no fever, malaise, arthralgia, oral ulcer, or breathing difficulty. She denies a history of trauma.

On dermatological examination, multiple well-defined tender edematous erythematous plaques were observed on the left arm, face, and both buttocks. Some lesions contained necrotic vegetative ulcers on erythematous-base plaques (**Figure 1A-1D**). Her nails and oral mucosa were unremarkable.

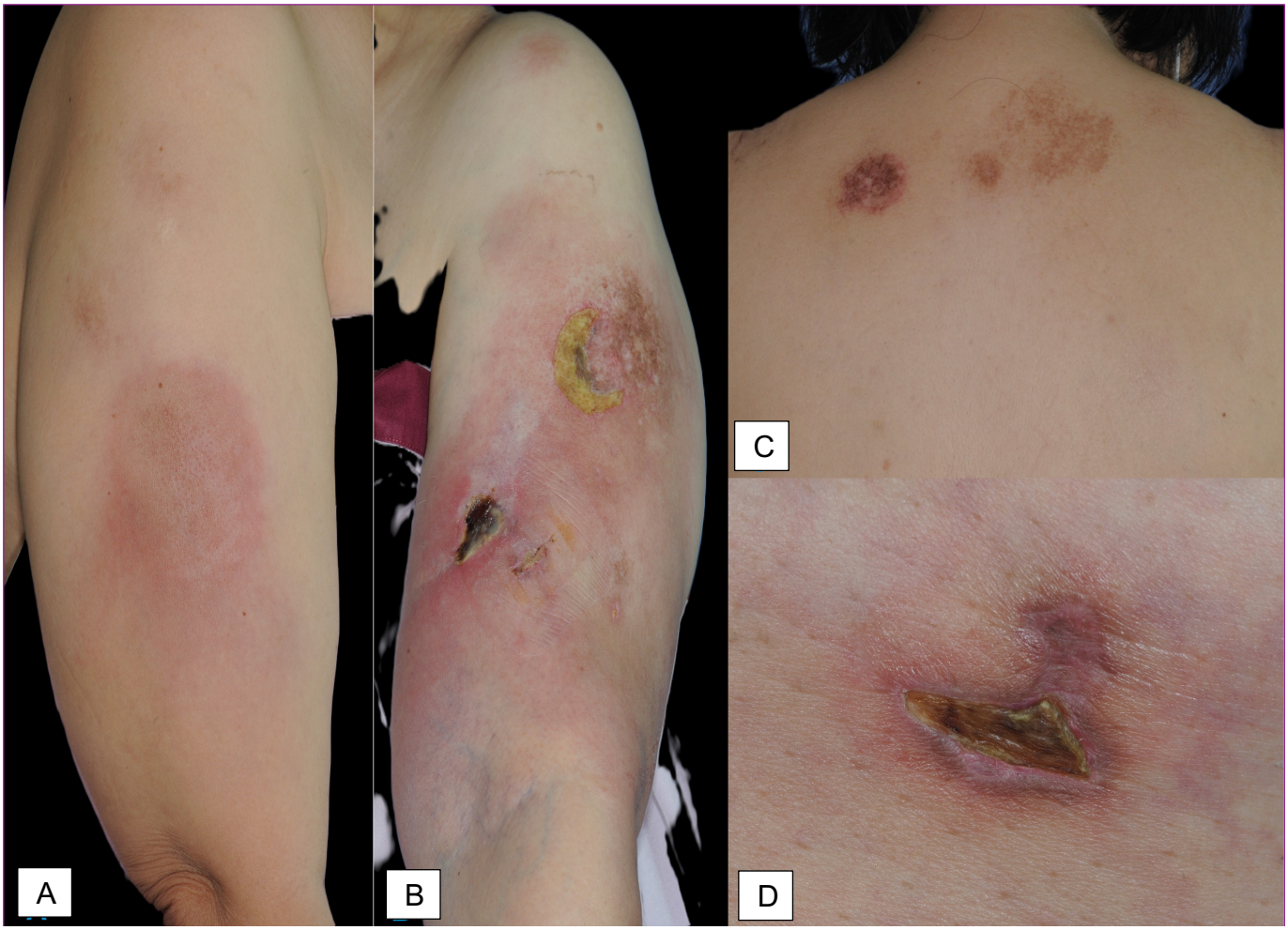

Figure 1. Multiple well-defined edematous erythematous plaques on both arms (A, B) and trunk (C). Some lesions show necrotic vegetative ulcered plaques on erythematous base plaques (B,D).

An incisional skin biopsy was performed on a lesion from the left arm to establish the diagnosis. Histopathological findings demonstrated unremarkable epidermis; nonetheless, peri-adnexal inflammation was evident. There was an inflammation of subcutaneous fat lobules. The inflammation consisted of lymphocytes, plasma cells, and some histiocytes. Focal hyaline necrosis of fat cells was noted. No distinct vasculitis was

observed (**Figure 2A-2C**). Direct immunofluorescence (DIF) was negative for C3, IgA, IgG, IgM, and Fibrinogen. Immunohistochemical staining of CD123+ was positive, highlighting plasmacytoid dendritic cell clusters.

Her complete blood count, blood chemistries, erythrocyte sedimentation rate (ESR), and urinalysis results were normal. Antinuclear antibody (ANA) was positive at 1:80 with a homogeneous pattern. Additional investigations including anti-dsDNA, anti-Sm, C3, and C4 levels were unremarkable. Her clinical manifestations and histopathological findings in conjunction with immunohistochemical staining were compatible with lupus erythematosus panniculitis. However, she did not meet the ACR/EULAR 2019 diagnostic criteria for SLE.

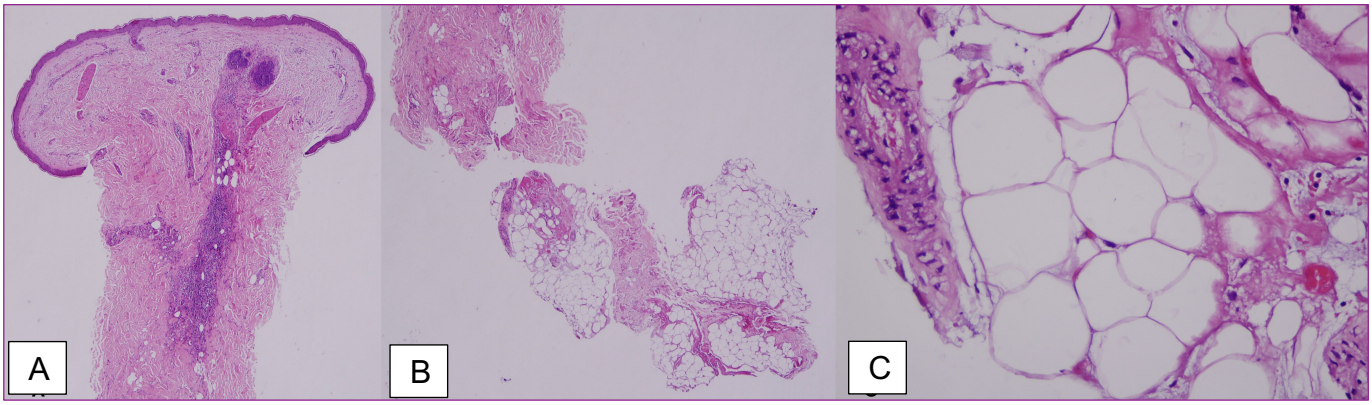

Figure 2. Skin biopsy (H&E)-histopathological examination showed peri-adnexal inflammation (A) and inflammation of subcutaneous fat lobules (B). The inflammation consisted of lymphocytes, plasma cells, and some histiocytes. As well, focal hyaline necrosis of fat cells was identified.

She received hydroxychloroquine in combination with oral prednisolone after baseline ophthalmological examination. Hydroxychloroquine was initially given at 400 mg/day for 2 weeks then decreased to 200 mg/day due to transaminitis. Prednisolone was initiated at 20 mg/day for 4 weeks and titrated up to 30 mg/day the lesions showed very minimal improvement. Other than systemic treatment, she also received a topical potent corticosteroid and emollient.

DISCUSSION

Lupus erythematosus panniculitis **(**LEP**)** was first described by Kaposi in 1883 and termed lupus erythematosus profundus by Irgang in 1940.[4,5] LEP is a rare variant of chronic cutaneous lupus erythematosus, a distinctive manifestation associated with DLE or SLE. The rate of LEP in association with SLE has been described with variable proportions, from 10**%** to 42**%.** On the other hand, LEP is an uncommon dermatological manifestation of SLE with a frequency of occurrence at about 2**-**4**.**5**%**.[1]

The Pathogenesis of LEP is not yet fully understood, but some reports suggest that LEP is associated with injection or trauma.[2] Like other cutaneous lupus erythematosus, women are more affected than men--two to nine times more frequently than men.[1-8] LEP appears to be predominant in middle**-**aged women, in the 3rd to 4th decade of life.[9] The

clinical course of LEP is typically chronic and relapsing with periods of exacerbations which can be triggered by trauma. Most LEP patients have a favorable prognosis in SLE patients.[2]

The lesions of lupus erythematosus panniculitis (LEP) are typically presented with solitary or multiple, tender erythematous or purplish subcutaneous nodules and/or plaques with varying overlying skin appearances, ranging from normal skin to discoid lupus erythematosus, also known as lupus profundus, or rarely skin ulceration. As in our case, ulceration has been reported to occur in 28%. A proposed pathogenesis of the ulceration in LEP was secondary to impaired circulation due to fibrin thrombus or extensive tissue hyaline necrosis of fat. The lesions often resolve with atrophy of skin and hypodermis as well as lipoatrophy or scarring. Most lesions are localized to the face, proximal arms, shoulder, thigh, and buttocks, areas abundant in subcutaneous fat.[10-12] Elevated ANA titer was found in 27%-95.4% of LEP patients with a higher probability of developing systemic involvement or SLE.[11]

LEP should be differentiated from other inflammatory diseases of subcutaneous fat which may present in similar patterns such as erythema nodosum, erythema induratum of Bazin, and, particularly, subcutaneous panniculitis-like T-cell lymphoma (SPTCL), which is difficult to diagnose.[11] The key feature that differentiates lupus erythematosus panniculitis from SPTCL, one of the most common differential diagnoses of LEP, is its discriminative histological feature. The presence of plasma cells is found exclusively in lupus panniculitis.[13]

To establish the diagnosis, a histopathological examination is required. A typical feature is predominantly lymphocytic lobular or mixed panniculitis, with frequent plasma cells and sometimes eosinophils. The dermis is infiltrated with inflammatory cells such as lymphocytes, histiocytes, and plasma cells. Intralobular septa is hyalinized and thickened with the presence of hyaline fat necrosis. Other features include pathological characteristics of discoid lupus erythematosus, dermo-epidermal changes, such as thickening of the basement membrane, mucin deposition, calcifications, and vascular changes such as lymphocytic vasculitis, fibrin thrombosis, and perivascular fibrosis.[1,11,14]

A recent study found that DIF-positive at the basement membrane and blood vessels in the dermis was found in 36.0%-90.5% and 85.7% of LEP patients respectively. A positive DIF test solidifies the histopathological diagnosis of LEP. However, because of some overlapping histopathological features between LEP and SPTCL, an additional tool to establish the diagnosis is crucial. CD123+ plasmacytoid dendritic cells are typically increased and found as plasmacytoid dendritic cell clusters in LEP. Accordingly, CD123+ immunohistochemical staining is utilized in such cases to conclude the diagnosis in conjunction with clinical manifestation and histopathological findings.[14]

The first-line therapy option for LEP is hydroxychloroquine or chloroquine.[15] LEP is well controlled with an antimalarial agent alone in most patients. These medications should be continued until the lesions resolve, followed by a maintenance suppressive dose for 6 to 24 months. Regular ophthalmologist consultation for retinopathy surveillance is recommended. Systemic corticosteroids are often beneficial in severe cases accompanied by SLE. The combination of antimalarial and systemic corticosteroids should be considered in recurrent and

recalcitrant cases. Other medications include thalidomide, dapsone, cyclosporine, intravenous immunoglobulins, and rituximab.[11]

CONCLUSION

As there can be normal or varying overlying skin changes in LEP, the diagnosis is often mistaken for other inflammatory skin diseases. Histopathology often shows inflammatory cells deep to subcutaneous. Positive immunohistochemical staining of CD 123, which denotes plasmacytoid dendritic cells, is a clue to the definite diagnosis. Long-term follow-up may be required due to its chronic and relapsing courses, regardless of SLE association which occurs in only a small number of patients.

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