Lupus Erythematosus Tumidus Clinical Characteristics and Treatment: A Retrospective Review of 25 Patients

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PRACTICE **POINTS**

- Approximately 20% of patients with lupus erythematosus tumidus (LET) will have positive antinuclear antibody titers.
- Along with cutaneous manifestations, approximately 50% of patients with LET also will have pruritus, tenderness, and photosensitivity.
- If LET is resistant to hydroxychloroquine, consider using quinacrine, methotrexate, or thalidomide.

Lupus erythematosus tumidus (LET) is a rare photosensitive dermatosis that was considered a subtype of chronic cutaneous lupus erythematosus (CLE); however, its clinical course and favorable prognosis led to its reclassification into another category called *intermittent CLE*. Although known for more than 100 years, LET's association with systemic lupus erythematosus (SLE), autoantibody profile, and disease prognosis is not well characterized. The purpose of this study was to describe the demographics, clinical characteristics, autoantibody profile, comorbidities, and treatment of LET.

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Lupus erythematosus tumidus (LET) is a rare photosensitive dermatosis[1] that previously was considered a subtype of chronic cutaneous lupus erythematosus; however, the clinical course and favorable prognosis of LET led to its reclassification into another category, called *intermittent cutaneous lupus erythematosus*.[2] Although known about for more than 100 years, the association of LET with systemic lupus erythematosus (SLE), its autoantibody profile, and its prognosis are not well characterized. The purpose of this study was to describe the demographics, clinical characteristics, autoantibody profile, comorbidities, and treatment of LET based on a retrospective review of patients with LET.

Methods

A retrospective review was conducted in patients with histologically diagnosed LET who presented to the Department of Dermatology at the Wake Forest School of Medicine (Winston-Salem, North Carolina) over 6 years (July 2012 to July 2018). Inclusion criteria included males or females aged 18 to 75 years with clinical and histopathology-proven LET, which was defined as a superficial and deep lymphocytic infiltrate with abundant mucin deposition in the reticular dermis and absent or focal dermoepidermal junction alterations. Exclusion criteria included males or females younger than 18 years or older than 75 years or patients without clinical and histopathologically proven LET. Medical records were evaluated for demographics, clinical characteristics, diagnoses, autoantibodies, treatment, and recurrence.

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The authors report no conflict of interest.

The eTable is available in the Appendix online at www.mdedge.com/dermatology.

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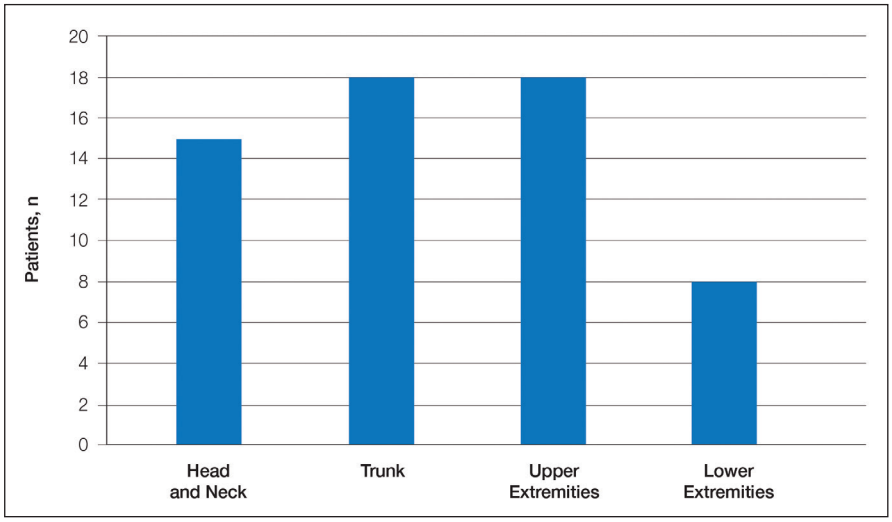

FIGURE 1. The most common anatomical distributions in patients with lupus erythematosus tumidus (N=25).

Photosensitivity was confirmed by clinical history. This study was approved by the Wake Forest School of Medicine institutional review board.

Results

Twenty-five patients were included in the study (eTable). The mean age (SD) at diagnosis was 46 (10.9) years, with a male to female ratio of 1:4. Twenty-two (88%) patients were White non-Hispanic, whereas 3 (12%) were Black. Lupus erythematosus tumidus most commonly affected the trunk (18/25 [72%]) and upper extremities (18/25 [72%]), followed by the head and neck (15/25 [60%]) and lower extremities (8/25 [32%])(Figure 1). The most common morphologies were plaques (18/25 [72%]), papules (17/25 [68%]), and nodules (6/25 [24%]) (Figures 2 and 3). Most patients experienced painful (14/25 [56%]) or pruritic (13/25 [52%]) lesions as well as photosensitivity (13/25 [52%]). Of all measured autoantibodies, 5 of 22 (23%) patients had positive antinuclear antibody (ANA) titers greater than 1:80, 1 of 14 (7%) patients had positive anti-Ro (anti-SSA), 1 of 14 (7%) had positive anti-La (anti-SSB), 2 of 10 (20%) had positive anti–double-stranded DNA, and 0 of 6 (0%) patients had positive anti-Smith antibodies. Four (16%) patients with SLE had skin and joint involvement, whereas 1 had lupus nephritis. One (4%) patient had discoid lupus erythematosus (DLE). Seventeen (68%) patients reported recurrences or flares. The mean duration of symptoms (SD) was 28 (44) months.

Topical corticosteroids (21/25 [84%]) and hydroxychloroquine (20/25 [80%]) were the most commonly prescribed treatments. Hydroxychloroquine monotherapy achieved clearance or almost clearance in 12 (60%) patients. Four patients were prescribed thalidomide after hydroxychloroquine monotherapy failed; 2 achieved complete clearance with thalidomide and hydroxychloroquine, 1 achieved complete clearance with thalidomide monotherapy, and 1 improved but did not clear. Four patients were concurrently started on quinacrine (mepacrine) after hydroxychloroquine monotherapy failed; 1 patient had no clearance, 1 discontinued because of allergy, 1 improved, and 1 cleared. Four patients had short courses of prednisone lasting 1 to 4 weeks. Three of 4 patients treated with methotrexate discontinued because of adverse effects, and 1 patient improved. Other prescribed treatments included topical calcineurin inhibitors (10/25 [40%]), dapsone (1/25 [4%]), and clofazimine (1/25 [4%]).

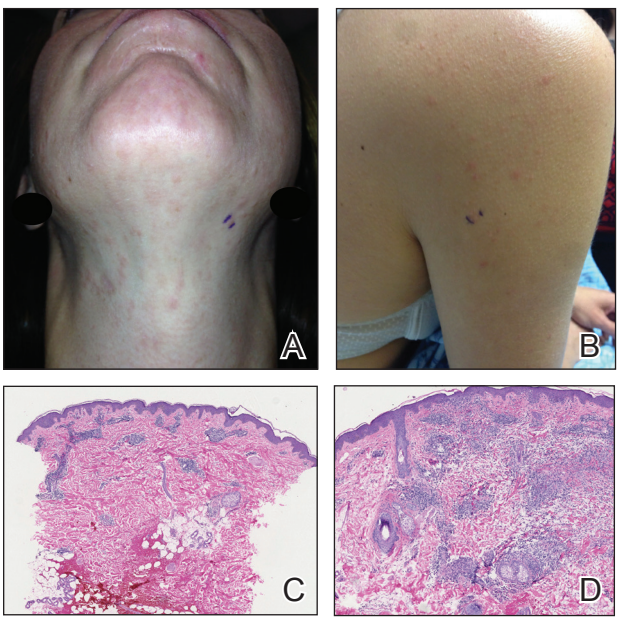

FIGURE 2. A, A patient with erythematous macules and papules involving the neck and face was diagnosed with lupus erythematosus tumidus. B, The patient also had similar morphology involving the posterior right shoulder and upper arm. C and D, A punch biopsy of both areas revealed a basket-weave stratum corneum and an unremarkable epidermis without any major interface changes (H&E, original magnifications ×4 and ×10). A pronounced perivascular and periadnexal lymphoplasmacytic infiltrate was seen in the superficial to mid dermis with focal mucin dissecting through collagen bundles.

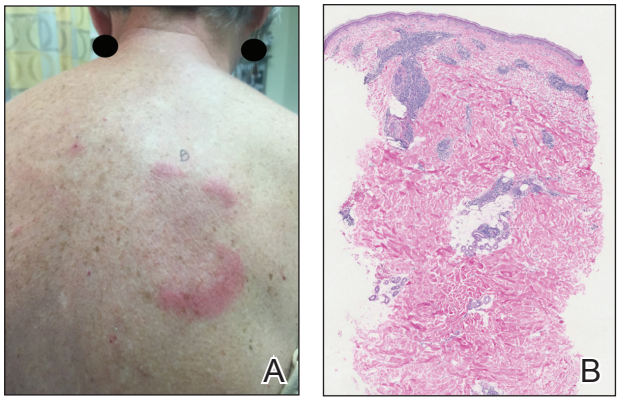

FIGURE 3. A, A patient was diagnosed with lupus erythematosus tumidus involving the back. B, A punch biopsy revealed a basket-weave stratum corneum and an unremarkable epidermis without any major interface changes (H&E, original magnification ×4). A pronounced perivascular and periadnexal lymphoplasmacytic infiltrate was seen in the superficial to mid dermis with focal mucin dissecting through collagen bundles.

Comment

Prevalence of LET—Although other European LET case series reported a male predominance or equal male to female ratio, our case series reported female predominance (1:4).[1,3-5] Our male to female ratio resembles similar ratios in DLE and subacute lupus erythematosus, whereas relative to our study, SLE male to female ratios favored females over males.[6,7]

Clinical Distribution of LET—In one study enrolling 24 patients with LET, 79% (19/24) of patients had facial involvement, 50% (12/24) had V-neck involvement, 50% (12/24) had back involvement, and 46% (11/24) had arm involvement,[2] whereas our study reported 72% involvement of the trunk, 72% involvement of the upper extremities, 60% involvement of the head and neck region, and 32% involvement of the lower extremities. Although our study reported more lower extremity involvement, the aforementioned study used precise topographic locations, whereas we used more generalized topographic locations. Therefore, it was difficult to compare disease distribution between both studies.[2]

Presence of Autoantibodies and Comorbidities—Of the 22 patients tested for ANA, 23% reported titers greater than 1:80, similar to the 20% positive ANA prevalence in an LET case series of 25 patients.[5] Of 4 patients diagnosed with SLE, 3 had articular and skin involvement, and 1 had renal involvement. These findings resemble a similar LET case series.[2] Nonetheless, given the numerous skin criteria in the American College of Rheumatology SLE classification criteria, patients with predominant skin disease and positive autoantibodies are diagnosed as having SLE without notable extracutaneous involvement.[2] Therefore, SLE diagnosis in the setting of LET could be reassessed periodically in this population. One patient in our study was diagnosed with DLE several years later. It is uncommon for LET to be reported concomitantly with DLE.[8]

Treatment of LET—Evidence supporting efficacious treatment options for LET is limited to case series. Sun protection is recommended in all patients with LET. Earlier case series reported a high response rate with sun protection and topical corticosteroids, with 19% to 55% of patients requiring subsequent systemic antimalarials.[3,4] However, one case series presented a need for systemic antimalarials,[5] similar to our study. Hydroxychloroquine 200 to 400 mg daily is considered the first-line systemic treatment for LET. Its response rate varies among studies and may be influenced by dosage.[1,3] Second-line treatments include methotrexate 7.5 to 25 mg once weekly, thalidomide 50 to 100 mg daily, and quinacrine. However, quinacrine is not currently commercially available. Thalidomide and quinacrine represented useful alternatives when hydroxychloroquine monotherapy failed. As with other immunomodulators, adverse effects should be monitored periodically.

Conclusion

Lupus erythematosus tumidus is characterized by erythematous papules and plaques that may be tender or pruritic. It follows an intermittent course and rarely is associated with SLE. Hydroxychloroquine is considered the first-line systemic treatment; however, recalcitrant disease could be managed with other immunomodulators, including methotrexate, thalidomide, or quinacrine.

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APPENDIX

eTABLE. Patient Demographics, Clinical Characteristics, and Treatment of Lupus Erythematosus Tumidus (N=25)

Characteristic	Patients
Mean age (SD), y	46 (10.9)
Sex, n (%)	
Female	20 (80)
Male	5 (20)
Race, n (%)	
Black	3 (12)
White non-Hispanic	22 (88)
Topography, n (%)	
Head and neck	15 (60)
Lower extremities	8 (32)
Trunk	18 (72)
Upper extremities	18 (72)
Morphology, n (%)	
Macules/patches	10 (40)
Nodules	6 (24)
Papules	17 (68)
Plaques	18 (72)
Symptoms, n (%)	
Pain/tenderness	14 (56)
Photosensitivity	13 (52)
Pruritus	13 (52)

Characteristic	Patients
Autoantibodies, n (%)	
Anti–double-stranded DNA	2/10 (20)
Anti-La/SSB	1/14 (7)
Antinuclear antibodies >1:80	5/22 (23)
Anti-Ro/SSA	1/14 (7)
Anti-Smith	0/6 (0)
Autoimmune comorbidities, n (%)	
Discoid lupus erythematosus	1 (4)
Hypothyroidism	2 (8)
Systemic lupus erythematosus	4 (16)
Treatment, n (%)	
Hydroxychloroquine	20 (80)
Methotrexate	4 (16)
Oral corticosteroids	4 (16)
Quinacrine	4 (16)
Thalidomide	4 (16)
Topical calcineurin inhibitors	10 (40)
Topical corticosteroids	21 (84)