Lupus erythematosus tumidus vs Jessner’s lymphocytic infiltrate of the Skin

A systematic comparison of clinical and histologic characteristics.

BY KEVIN WRIGHT, MD AND CAMILLE HENNINGER, MD

Originally reported by Hoffman,¹ and later by Gougerot and Burnier,² lupus erythematosus tumidus (LET) was the term used to describe patients with “spherical, flat disc-like red circles with a coarse texture.” The patients healed well after excision with only a “slightly noticeable whitish scar,” and histology revealed “a sharply bordered infiltrate consisting of mononuclear cells.”¹

Since this original description, the lupus classification system has been reevaluated.³ Currently, patients with similar lesions that heal with residual scarring would most likely be diagnosed with discoid lupus erythematosus (DLE). LET is now considered to be a purely dermal form of chronic cutaneous lupus erythematosus⁴ characterized by absent or minimal epidermal change and a relatively benign, non-scarring course.⁵

In 1953, Jessner and Kanof presented a group of cases depicting what they believed to be a unique entity, later to be classified as Jessner’s lymphocytic infiltration of the skin (JLIS). They summarized the clinical picture and histology as follows: “the lesions are flat, discoid, more or less elevated, pinkish to reddish brown, starting as small papules, expanding peripherally, sometimes clearing in the center, sometimes showing a circinate arrangement...They persist for weeks, months or longer and disappear without sequelae.”⁶

Since their original description, many cases that resemble both LET and JLIS have been reported and related to either disease exclusively. (See case report, next page.) Despite many shared characteristics, some investigators regard JLIS and LET as separate entities,⁷-¹¹ while many consider them excessively similar to differentiate.¹²-¹⁴

Those reporting LET and JLIS as different diseases base this opinion on clearly stated evidence (Table I). Primary evidence we define as a premise openly supported by multiple sources. Characteristics stated in articles as those unique to either disease exclusively but not as clear proof for differentiation are thus considered secondary. A systematic assessment of the literature, from original description to the present, was undertaken to clarify if this primary and secondary evidence is reproducible and consistently reported.

MATERIALS AND METHODS

A retrospective, multi-publication analysis of domestic and international peer-reviewed journals (n=37) was conducted to compare patients who have been diagnosed with either LET or JLIS based on physician opinion as well as clinical and histologic criteria.

Patients described as having a presentation suggestive of subacute cutaneous lupus erythematosus (SCLE; healing with residual depigmentation and more frequent extracutaneous disease)³ or discoid lupus erythematosus (DLE; extensive epidermal atrophy, follicular hyperkeratosis or scarring after resolution)³ were excluded in the comparison. Also excluded to the extent it was possible were patients with lesions consistent with polymorphic light eruption (extremely photosensitive lesions that both rapidly develop¹² and resolve¹⁰).

RESULTS

Epidemiology. To date, cases of LET and JLIS have been reported in patients of Caucasian, Hispanic, Asian and African origin from
geographic locations around the world. Many sources now agree that the incidence of both appears to be higher than originally reported.4,10,15 A large study in 2006 found that 7.6 percent (16/210) of JLIS patients had concurrent lupus erythematosus (LE), a disease considered moderately rare due to a prevalence of 1/50,000.16 Due to the frequency of this association, these authors believe that JLIS is in fact a dermal variant of LE.

There was no consensus as to gender predilection in either disease. For example, some authors believe that LET has either more females9 or more males affected,8 and others that they are equivalent.15 Similarly, JLIS has conflicting data on gender predominance.17,18 Ultimately, most groups report a small female predominance in LET as well as a slight majority of males with JLIS.

CLINICAL

Physical exam. Recently, LET patients have been described as having erythematous, indurated, urticaria-like plaques and those with JLIS as developing circinate or arciform, erythematous to brown papules.10 Despite this, Calnan, et al.17 describe JLIS as involving plaques while Alexiades-Armenakas, et al.19 found that all 80 patients evaluated with LET had either papules or plaques. Similarly, another source reported patients with LET and others with JLIS that exhibited papules or plaques, simultaneously or successively.13

One difference of opinion is that LET lesions can be pruritic (symptomatic),20 whereas JLIS lesions never are.21 Despite this, 53 percent (53/100) of JLIS patients enrolled in a study experienced itching in their lesions,18 while a different group following LET patients for seven years described all as having completely asymptomatic lesions.19

Laboratory. JLIS has been reported to always have negative antinuclear antibody (ANA) serology, while LET is positive in 10 percent of cases.19 Despite this, in a recent report directly comparing histologically diagnosed LET to JLIS, 30 percent (3/10) of patients with JLIS were positive for ANA as compared to only six percent (1/17) of LET patients.13 This group then went further to state that the scarcity of high titer ANA serology in both groups seemed more of a similarity than a point of distinction.

Photosensitivity. LET lesions can be caused and exacerbated by sunlight, however, some groups believe no such relationship exists in JLIS,12,22 despite these lesions occurring...
infiltrate in both LET and JLIS have been stated as being extremely similar. Similarly, the infiltration in both can be found involving both the papillary and mid-dermis (Fig 4).

Although there is consensus on the overall predominance of lymphocytes, there is still considerable debate about the other components of the cellular infiltrate in both LET and JLIS. One report found more B germinal center plasma cells in JLIS as compared to LET; however, in a later study no difference was found when using an L26 pan B-cell marker. Another group found higher percentages of plasmacytoid monocytes in tissue of patients with JLIS, yet when a more specific antibody (KiM1P) was used at a different institution, no difference could be established.

The percentage of Leu-8+ immunoregulatory T-cells was once hypothesized to be considerably higher in JLIS, but due to internal variations within the group tested, the authors concluded that no distinction could be made. Lastly, one study found no difference in the plasmacytoid dendritic cells in LET and JLIS, then went further to state that these disorders in fact shared an identical immunologic profile.

LET has been found to have a higher relative quantity of CD4+ helper T-cells than CD8+ cytotoxic T-cells in its lymphocytic infiltrate (CD4>CD8). In contrast, a few sources report that JLIS has a CD8>CD4 preponderance. One such study found mean percentages of 50 percent CD4 and 32 percent CD8 in all JLIS patients despite having 23 percent (3/13) individually show slightly higher CD8 counts. A different group found 40 percent CD4 (±3 SEM) and 49 percent CD8 (±4 SEM) in JLIS lesions, but ultimately judged the findings to be of no significance due to CD8 similarities between the patients and normal healthy controls.

In contrast, Kuo, et al. state the majority of T cells in JLIS are definitively not CD8. Supplemeting this are two separate reports by Willemze, et al. who found that 100 percent (8/8) of patients with JLIS have CD4>CD8 with specific CD4:CD8 ratios of 2:1 to 6:1.

TREATMENT

The course of disease is similarly variable in both LET and JLIS. Some patients have a cyclical course with weekly or monthly exacerbations; others have active disease continuously for years, while a few go into long-term spontaneous remission. Despite this unpredictability in clinical course, one obvious way of treating patients with any photodermatositis is routine use of sun protection. During several studies, LET and JLIS patients have reported complete resolution of lesions and remained disease free with daily use of sunscreen. Similarly, patients with JLIS discovered that lesions lighten and flatten under the use of sunscreens alone.
In a double blind, randomized prospective trial, 76 percent (19/25) of JLIS patients receiving thalidomide were in complete remission (CR) after two months, in contrast to only 16 percent (4/25) from the placebo group. In a comparison study, 66 percent (2/3) of patients with JLIS and 83 percent (5/6) of patients with LET given thalidomide achieved an initial CR.

In addition, Weber, et al. reported that 56 percent (5/9) of JLIS patients achieved CR within two to three weeks of starting hydroxychloroquine therapy. Recently, in a head-to-head study comparing these diseases, 8/10 (80 percent) of LET and 16/25 (67 percent) of JLIS patients established initial CR with the use of antimalarial treatment.

DISCUSSION

After all the evidence for separation of LET and JLIS is identified and individually examined, the similarities between...
these chronic diseases appear numerous and the distinctions far less clear. Clinically, both processes can present with papules or plaques that have minimal to absent surface changes. Frequently, but not always, lesions appear on sun-exposed surfaces and can be induced or aggravated by light exposure. Patients can be completely asymptomatic or have associated pruritus, and lesions always resolve without residual scarring. Histologically, tissue from LET and JLIS patients infrequently have minimal epidermal and dermo-epidermal junction change, but often have mucin deposition within the dermis. Lastly, although the evaluation of therapy in a condition prone to spontaneous resolution is admittedly difficult, both processes seem responsive to sun protection, thalidomide and antimalarials.

It is of interest to note several cases of long-standing LET and JLIS that have been reported to progress into DLE and SCLE.2,4,20 If the male dominant JLIS was in actuality the earliest and most benign version of LET,24,34-36 it might explain the gender disparity between them, especially if recognized as a continuum of disease with the rare capacity of evolving into DLE or SCLE, two diseases with a marked female predominance.3 Thus, if gender is indeed a risk indicator for more serious forms of these cutaneous diseases, what exactly are the differences between the women who transform to scarring types and those who have a benign course for life?

After a thorough review of the literature, the similarities between LET and JLIS strongly predominate over the differentiating features. It is our opinion, and one shared by others,19,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37 that any subtle differences between the classic descriptions of LET and JLIS represent separate points of evolution along a singular disease spectrum. Supporting this conclusion are some observations made at other institutions. Jessner and his research group originally noticed that fresh JLIS lesions had increased dermal edema, whereas older ones consistently had none.6 Two separate studies observed that photosensitivity in both diseases gradually decreased over time,13,18 while another found that early lesions of JLIS healed spontaneously but became gradually more permanent as the patient aged.33 Furthermore, Viera, et al.4 believe that the appearance of epidermal and DEJ changes in LET may represent an evolution of the disease.

In conclusion, lupus erythematosus tumidus and Jessner’s lymphocytic infiltrate should be considered as a single disease process with flexible and inclusive diagnostic criterion, considering clinical and histologic findings along the disease spectrum. Only then can prospective studies be initiated to evaluate the risks and protective factors influencing disease progression along the continuum, with the ultimate goal of identifying specific targets for focused therapy.

16. Lipshitz D. Classification of specific cutaneous manifestations in patients with lupus erythematosus: a time for change? Dermatology 2006;212:324-326
28. Clark WH, Minns NC, Reed RJ, Arnsworth AM. The lymphocytic infiltrates of the skin. Hum Pathol 1974;5:25