Characterization of clinical photosensitivity in cutaneous lupus erythematosus

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Background: Photosensitivity (PS) in lupus erythematosus (LE) is frequently determined by patient report. Objective: We sought to characterize self-reported PS in cutaneous LE (CLE).

Methods: The PS survey was used to classify subject responses into 5 phenotypes: direct sun-induced CLE flare (directCLE); general exacerbation of CLE (genCLE); polymorphic light eruption–like reactions (genSkin); general pruritus/paresthesias (genRxn); and sun-induced systemic symptoms (genSys). In all, 91 subjects with CLE alone or with CLE and systemic LE were interviewed.

Results: In all, 81% ascribed to 1 or more PS phenotypes. CLE-specific reactions (direct sun-induced CLE flare or general exacerbation of CLE) were reported by 86% of photosensitive subjects. Higher CLE disease activity (measured by CLE Disease Area and Severity Index activity scores) was suggestive of direct sun-induced CLE flare reactions ($P = .09$). In all, 60% of photosensitive subjects described CLE-nonspecific reactions: polymorphic light eruption–like rash and general pruritus/paresthesias. These phenotypes often co-occurred with CLE-specific reactions and were predicted by more systemic disease activity as measured by Physicians Global Assessment (PGA) scores in regression analyses (genSkin, $P = .02$) and (genRxn, $P = .05$). In all, 36% of subjects reported systemic reactions and higher PGA scores were predictive of the sun-induced systemic symptoms phenotype ($P = .02$); a diagnosis of systemic LE was not ($P = .14$).

Limitations: PS was inferred from patient report and not directly observed.

Conclusions: Characterization of self-reported PS in LE reveals that patients experience combinations of CLE-specific, CLE-nonspecific, and systemic reactions to sunlight. Sun-induced CLE flares are associated with more active CLE disease. Polymorphic light eruption–like, generalized pruritus/paresthesias, and systemic reactions are associated with more active systemic disease. Recognition of PS phenotypes will permit improved definitions of clinical PS and allow for more precise investigation into its pathophysiology. (J Am Acad Dermatol 2013;69:205-13.)

Key words: cutaneous lupus erythematosus; dendritic cells; immunohistochemistry; photosensitivity; polymorphic light eruption; systemic lupus erythematosus.

Photosensitivity (PS) is one of the most common manifestations of systemic lupus erythematosus (SLE),¹ and is 1 of only 11 criteria used to make the diagnosis of SLE.² However, the definition of PS is vague and its pathophysiology is not well understood. There is a need to better define the clinical aspects of PS in lupus erythematosus (LE), to enhance further study of this difficult problem.
Although investigations into PS in LE have focused predominantly on cutaneous LE (CLE) induction via phototesting, most patients with LE do not undergo phototesting as part of their clinical workup. More commonly, clinicians apply the PS criterion to patients with LE based on patient history and/or physical examination findings related to sun-induced eruptions. Making the diagnosis of PS in LE is simple when patients report a history of LE exacerbation in the summer or after a tropical holiday. Most patients, however, describe a wide array of adverse reactions to sunlight, some of which may be related to LE and others not. On the differential diagnosis for CLE is the most common of all photodermatoses: polymorphic light eruption (PMLE). Early lesions of CLE may be difficult to distinguish from PMLE, both clinically and histologically. Furthermore, PMLE has been reported to occur more frequently in patients with LE than in the general population. Despite these associations, studies have failed to show any convincing pathophysiologic link between PMLE and LE, which suggests that the 2 conditions are comorbid. An alternative explanation is that PS in LE is variable and that a PMLE-like reaction may be one of many clinical phenotypes of PS in LE.

In our tertiary referral population, we found that 70% of patients with CLE reported adverse reactions to sunlight. Patient-reported adverse reactions to sunlight were classified into 1 of 5 categories based on CAPSULE SUMMARY

- According to the American College of Rheumatology, photosensitivity in lupus erythematosus (LE) is determined by clinical examination or by patient history of unusual reaction to sunlight.
- Self-reported photosensitivity in cutaneous LE comprises cutaneous LE-specific and LE-nonspecific skin reactions, pruritus/paresthesias, and systemic symptoms.
- Physicians should recognize the varied manifestations of photosensitivity in LE because these phenotypes are associated with both systemic and cutaneous disease activity.

METHODS

Subject selection

Patients with LE presenting to the outpatient autoimmune skin disease clinic at the University of Pennsylvania were enrolled in an ongoing database study of prevalence and severity of LE. All patients older than 18 years with clinical, histologic, and/or serologic evidence of CLE and/or SLE with skin manifestations were invited to participate. Subjects were categorized according to the modified Gilliam classification into the various subtypes of CLE. Subjects with SLE who met the American College of Rheumatology criteria were included if they also had a form of CLE. The protocol for the study was approved by the institutional review board of the University of Pennsylvania School of Medicine.

Study procedures

Study visits were completed at the time of subjects’ regularly scheduled clinic visit. Information was obtained by clinical interview, physical examination, medical record review, and subject questionnaires. A complete skin examination was performed and the CLE Disease Area and Severity Index (CLASI) outcome measure was completed. Whenever available, recent laboratory values, including LE serologies and/or biopsy results, were reviewed and documented in the study chart.

Clinical interview using the PS survey

The PS survey provided a framework for characterizing subjects’ experience of sun sensitivity or lack thereof (Fig 1). The PS survey was based on information gathered over 9 months, during which patients in the autoimmune skin disease clinic were interviewed about their experience with sunlight. Recurring themes of self-reported PS—relating to sun-induced reactions, morphology, characteristics, and timing—were identified and incorporated into a brief PS survey.

Subjects were instructed to “Tell me about what happens when you go in the sun.” Study personnel completed the PS survey using the subject’s free-form answer. Only after the subject was allowed to speak freely did study personnel ask questions from the PS survey to limit information bias. Any adverse reaction to sunlight described by the subject was accounted for and classified into a PS phenotype. Data collection took place from November 2009 to January 2011.
answers to the survey (Table I). In general, question 4 corresponded with direct sun-induced CLE flare (directCLE), question 3 with general exacerbation of CLE (genCLE), question 5 with genSkin, questions 6 and 7 with general pruritus/paresthesias (genRxn), and question 8 with sun-induced systemic symptoms (genSys). If a subject’s report did not correspond with the answer options provided, the study personnel could write answers in the blanks provided. This occurred almost exclusively for the genCLE phenotype. Thus, subjects reporting “yes” to question 3 or those necessitating a write-in answer, suggestive of a link between CLE and sun exposure, were classified as the genCLE phenotype. Finally, the directCLE and genCLE phenotypes were mutually exclusive, but all other PS phenotypes were not and patients could be classified as multiple PS phenotype.

Timing of PS reactions
Timing of 3 PS phenotypes was ascertained for: directCLE, genSkin, and genRxn. Subjects were asked about onset of reactions and time until resolution of cutaneous reactions after sun exposure. Reactions were labeled early, transient; early, lasting; or late, lasting (Table II).

SLE Disease Activity Index
Disease activity in SLE was assessed by the Safety of Estrogens in Lupus National Assessment (SELENA)—SLE Disease Activity Index (SLEDAI), a validated instrument used in the SELENA trials. This SLEDAI uses a weighting system to evaluate disease activity in 9 organ systems. The total SLEDAI score ranges from 0 (no activity) to 105 (maximum activity). Overall systemic disease activity is further assessed by the clinician via the Physicians Global Assessment (PGA) score, a 0-to-3 scale with 0 = none to 3 = severe systemic disease activity.

CLE Disease Area and Severity Index
The CLASI is a validated tool to assess disease severity in CLE. It quantifies disease activity (erythema, scale) and damage (dyspigmentation, scar) over 13 distinct areas of the body. Activity and damage scores range from 0 to 70 and 0 to 56 respectively, with higher scores representing more severe disease. Disease activity is classified into mild (0-9) and moderate to severe (≥10) by CLASI activity score.

Immunohistochemistry
Preliminary investigation into potential mediators of PS phenotype was undertaken by examining skin biopsy specimens from 11 patients and 5 control subjects (age and location balanced). The goal of this exploratory observation study was to generate, rather than test, hypotheses; so, power analysis to justify sample size is not presented. Punch biopsy specimens (4 mm) were taken from sun-exposed, extensor, nonlesion, forearm skin of patients with PS and LE. The biopsy specimens were formalin-fixed, paraffin-embedded, 4-mm cut sections with 3 tissue sections placed on each slide.

After slide deparaffinization and hydration, antigen retrieval was performed in Target Retrieval Solution, high pH (S3308; DAKO Corp, Carpinteria, CA) for 30 minutes using a water bath. Endogenous peroxidase activity was blocked using 3% hydrogen peroxide for 10 minutes and then protein-blocking was performed using serum-free protein-blocking solution (X0909; DAKO) for 1 hour. Tissue sections were incubated overnight at 4°C with either anti-CD3 mouse monoclonal antibody (1:50, clone LN10; Novocastra, Newcastle-upon-Tyne, United Kingdom) or anti-CD11c rabbit monoclonal antibody (1:50, clone EP1347Y; ABCAM, Cambridge, MA). Slides were then incubated at 25°C for 40 minutes with universal biotinylated linker secondary antibody (K0690; DAKO) for 1 hour. Tissue sections were incubated overnight at 4°C with either anti-CD3 mouse monoclonal antibody (1:50, clone LN10; Novocastra, Newcastle-upon-Tyne, United Kingdom) or anti-CD11c rabbit monoclonal antibody (1:50, clone EP1347Y; ABCAM, Cambridge, MA). Slides were then incubated at 25°C for 40 minutes with universal biotinylated linker secondary antibody (K0690; DAKO) for CD3 or secondary antibody specific for rabbit primary (K4010; DAKO) for CD11c. After, streptavidin-horseradish peroxidase from the Universal LSAB+ Visualization System (DAKO) was applied to tissue sections for 30 minutes. Finally sections were counterstained with hematoxylin. To serve as a negative control, 1% bovine serum albumin was included in the immunohistochemical procedures.

Abbreviations used:
CLASI: Cutaneous Lupus Erythematosus Disease Area and Severity Index
CLE: cutaneous lupus erythematosus
directCLE: direct sun-induced cutaneous lupus erythematosus flare
genCLE: general exacerbation of cutaneous lupus erythematosus
genRxn: general pruritus/paresthesias
genSkin: polymorphic light eruption-like
genSys: sun-induced systemic symptoms
LE: lupus erythematosus
mDC: myeloid dendritic cells
PGA: Physicians Global Assessment
PMLE: polymorphic light eruption
PS: photosensitivity
SELENA: Safety of Estrogens in Lupus
Erythematosus National Assessment
SLE: systemic lupus erythematosus
SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

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albunin in phosphate-buffered saline was applied to 1 tissue section of each slide.

Cell quantification was performed for CD3⁺ (T cells) and CD11c⁺ (myeloid dendritic cells [mDC]). For each specimen, 5 consecutive fixed fields in the papillary dermis and the reticular dermis were photographed using ×20 objective and ×10 eyepiece and Nikon microscopy camera (Nikon, Melville, NY). Cells were counted using ImageJ software (National Institutes of Health, Bethesda, MD). The mean number of cells per high-power field averaged across 10 high-power fields (200×) was used for analyses.

Statistical analysis
For data that were assumed normally distributed, frequencies and means ± SD were reported. Pearson χ² analysis was used to determine associations of gender or race with PS phenotypes. Simple and multivariable logistic regression analyses were performed to determine relationships between PS phenotypes (dependent variable) and CLE subtype, SLE diagnosis, SLE activity (measured by PGA), and CLE activity (measured by CLASI activity score). Non-gaussian response variables were reported as frequencies and medians ± interquartile ranges. Group differences were assessed by either Kruskal-Wallis or Mann-Whitney U tests. Reported indices of association were calculated as 2-tailed P values.

RESULTS
Subject characteristics
A total of 91 subjects were enrolled with mean age ± SD of 46 ± 13 years. Gender, race, diagnosis, and SLE manifestations are presented in Table III. The >1 CLE subtype category comprised 3 subjects with discoid LE and subacute CLE, 5 with discoid LE and acute CLE, 1 with tumid LE and subacute CLE, and 1 with tumid LE and discoid LE. Of subjects, 42% had CLE and met criteria for SLE.

Prevalence PS phenotypes in LE
Clinical interview using the PS survey revealed that 81% of subjects ascribed to at least 1 PS phenotype. There were no significant (P < .05) relationships among gender, race, SLE diagnosis, CLE diagnosis, PGA, CLASI activity, and the absence of PS.

Of those reporting PS (N = 74), 86% (64 of 74) reported PS as worsening of CLE after sun exposure: 46 subjects described specific occurrences of sun-induced CLE flare (directCLE) and 18 reported a
general association between sun exposure and CLE (genCLE). Of subjects, 60% (44 of 74) experienced cutaneous reactions that were not typical for LE: 13 subjects had a PMLE-like reaction (genSkin), 12 experienced genRxn of sun-exposed skin, and 19 experienced both genSkin and genRxn (Fig 2). Rarely did subjects experience these LE-nonspecific cutaneous reactions in the absence of CLE-specific PS: only 5 of 32 had genSkin and 2 of 31 genRxn subjects reported these reactions in the absence of directCLE or genCLE phenotypes. Of subjects reporting genSys, 52% met criteria for SLE.

Timing of PS phenotypes
The time course of 3 PS phenotypes was investigated: directCLE, genSkin, and genRxn. Of those with directCLE, 90% experienced CLE worsening, soon after sun exposure; half of these subjects reported early (within 1 week) resolution, whereas others ascribed to lasting skin reactions. Only 4 of 39 subjects described late-onset sun-induced CLE-specific skin reactions. GenSkin and genRxn groups nearly always experienced early-onset, transient (resolving within 1 week) reactions to sunlight (Fig 3).

Associations among gender, race, and PS phenotypes
Gender. Gender was significantly associated with 2 PS phenotypes: genSkin (PMLE-like reaction, \( P = .01 \)) and genSys \( ( P = .03 \)) and not with any other PS phenotype, with more female subjects than expected reporting these phenotypes.

Race. There were no significant associations between race and any PS phenotype.

Relationships among CLE subtypes, SLE diagnosis, CLASI activity, systemic disease activity, and PS phenotypes

directCLE phenotype. There was a statistically suggestive \( ( P = .094) \) trend for CLASI activity scores to predict experiencing the directCLE phenotype with more subjects with moderate-severe compared with mild CLASI activity experiencing directCLE after sun exposure. Although CLE subtype, SLE diagnosis, and systemic activity (measured by PGA) were not significantly related to directCLE, the association between CLASI activity and directCLE remained statistically suggestive \( ( P = .093) \) in the multivariable model (Tables IV and V).

genCLE phenotype. In both the simple \( ( P = .077) \) and multivariable \( ( P = .099) \) models, there was a statistically suggestive trend for subjects with timid

<table>
<thead>
<tr>
<th>Table I. Clinical photosensitivity phenotypes</th>
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<tbody>
<tr>
<td>Photosensitivity phenotypes</td>
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<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>directCLE</td>
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<tr>
<td>genCLE</td>
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<tr>
<td>genSkin</td>
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<tr>
<td>genRxn</td>
</tr>
<tr>
<td>genSys</td>
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</table>

CLE, Cutaneous lupus erythematosus; directCLE, direct sun-induced cutaneous lupus erythematosus flare; genCLE, general exacerbation of cutaneous lupus erythematosus; genRxn, general pruritus/paresthesias; genSys, sun-induced systemic symptoms; PMLE, polymorphic light eruption.

<table>
<thead>
<tr>
<th>Table II. Timing of photosensitivity reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset Time</td>
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<tr>
<td>Early</td>
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<tr>
<td>Late</td>
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LE compared with other CLE subtypes to experience a general link between CLE flares and sun exposure.

**genSkin phenotype.** Systemic disease activity as measured by PGA was predictive of the genSkin phenotype with more subjects with PGA score of 1 or higher (mild-severe, \( P = .02 \)) experiencing PMLE-like reactions compared with subjects with no systemic disease activity (PGA score 0, \( P = .05 \)).

**genRxn phenotype.** In both the simple and multivariable model, SLE diagnosis was predictive of the genRxn phenotype such that subjects with both SLE and CLE were more likely (\( P = .003 \)) to experience PMLE-like reactions compared with those with CLE alone (\( P = .04 \)). PGA scores were predictive of genRxn in the simple model, but failed to reach significance in the multivariable analysis.

**genSys phenotype.** Sun-induced systemic reactions (genSys) were predicted by PGA scores in the simple model (\( P = .021 \)) and trended toward predictive in the multivariable model (\( P = .064 \)), such that subjects with more active systemic disease (PGA score \( \geq 1 \)) experienced the genSys phenotype, whereas those with no systemic activity (PGA score 0) did not.

### Table III. Subject characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
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<td><strong>Diagnosis</strong></td>
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<td>SCLE</td>
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<td>LET</td>
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<td>&gt;1 CLE subtype</td>
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<td>ACLE</td>
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<tr>
<td>CCLE other</td>
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<tr>
<td>CLE and SLE</td>
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<tr>
<td><strong>Systemic manifestations in subjects with CLE and SLE</strong></td>
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<td>Arthritis</td>
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<td>Renal</td>
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<tr>
<td><strong>Race</strong></td>
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<td>African American</td>
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<td>Other</td>
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<td>White</td>
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<td><strong>Gender</strong></td>
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<tr>
<td>Male</td>
<td>18</td>
</tr>
<tr>
<td>Female</td>
<td>73</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>91</td>
</tr>
</tbody>
</table>

ACLE, Acute cutaneous lupus erythematosus; CCLE, chronic cutaneous lupus erythematosus; CLE, cutaneous lupus erythematosus; DLE, discoid lupus erythematosus; LET, tumid lupus erythematosus; SCLE, subacute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus.

### Fig 2. Cutaneous lupus erythematosus (CLE). Percentage of subjects with photosensitivity (PS) (N = 83) reporting each PS phenotype as captured by PS survey. Because 23 subjects reported both genSkin and general pruritus/paresthesias (genRxn) concomitantly, this overlap is listed on graph to allow for accurate percentage calculation. *directCLE*, Direct sun-induced CLE flare; *genCLE*, general exacerbation of CLE; *genSys*, sun-induced systemic symptoms.

### Fig 3. Cutaneous lupus erythematosus (CLE). Percentage of time courses for photosensitivity (PS) reactions among subjects experiencing direct sun-induced CLE flare (*directCLE*), genSkin, and general pruritus/paresthesias (genRxn). *Early*, PS symptoms occur within minutes to next day; *lasting*, PS symptoms last for weeks to months; *transient*, PS symptoms resolve same day to within 1 week; *late*, PS symptoms occurring from 1 day to 1 week after sun exposure.

### Immunohistochemistry

Immunohistochemistry for mDC and T cells was conducted using anti-CD11c and anti-CD3 monoclonal antibody, respectively. The Mann-Whitney test indicated a significant difference in mDC (CD11c) counts between subjects with versus those without genSys (\( P = .04 \)) and a statistically suggestive trend (\( P = .06 \)) toward subjects with systemic symptoms having more resident (CD3) T cells (Fig 4). There
were no significant associations between genSys and SLE diagnosis; nor were there significant differences in mDC or T-cell counts between subjects with and without SLE. Subjects with genSys tended to have lower CLASI activity scores compared with subjects denying genSys (median \(6\) interquartile range: \(5 \pm 12\) vs \(16 \pm 13\)) and SLEDAI scores were not significantly different.

**DISCUSSION**

Clinical interviews using the PS survey allowed us to carefully characterize self-reported PS among a primarily CLE population. There was tremendous variability in how patients with LE experience PS. Overall, we found that 81% of subjects report PS. Unlike previous reports suggesting that PS occurs more commonly in whites compared with other racial groups, we found no associations between any PS phenotype and race.1,26,27 Not surprisingly, most PS reactions fell in the CLE-specific category. The most common PS phenotype was directCLE with 62% of PS subjects reporting specific examples of sun-induced CLE flare. In contrast to reports describing a delay between sun exposure and CLE induction, the majority of subjects reported sun-induced CLE flares occurring early after sun exposure.1 Exacerbations were commonly described as transient as opposed to lasting (for weeks to months). Interestingly, there was a trend for subjects with higher CLASI activity scores to report directCLE phenotype. We have shown previously

### Table IV. P values for simple logistic regression analyses with photosensitivity phenotypes as dependent variables

<table>
<thead>
<tr>
<th>PS phenotypes</th>
<th>CLE subtype(^a)</th>
<th>SLE diagnosis(^b)</th>
<th>PGA(^c)</th>
<th>CLASI(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>directCLE</td>
<td>.438</td>
<td>.971</td>
<td>.542</td>
<td>.094</td>
</tr>
<tr>
<td>genCLE</td>
<td>.077</td>
<td>.831</td>
<td>.398</td>
<td>.949</td>
</tr>
<tr>
<td>genSkin</td>
<td>.843</td>
<td>.356</td>
<td>.017</td>
<td>.488</td>
</tr>
<tr>
<td>genRxn</td>
<td>.098</td>
<td>.003</td>
<td>.051</td>
<td>.712</td>
</tr>
<tr>
<td>genSys</td>
<td>.359</td>
<td>.135</td>
<td>.021</td>
<td>.754</td>
</tr>
</tbody>
</table>

**CLASI**, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLE, cutaneous lupus erythematosus; directCLE, direct sun-induced cutaneous lupus erythematosus flare; genCLE, general exacerbation of cutaneous lupus erythematosus; genRxn, general pruritus/paresthesias; genSys, sun-induced systemic symptoms; PGA, Physicians Global Assessment; PS, photosensitivity; SLE, systemic lupus erythematosus.

*Discoid lupus erythematosus, subacute CLE, acute CLE, tumid lupus erythematosus, chronic CLE other, \(>1\) CLE subtype.

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<tbody>
<tr>
<td>directCLE</td>
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<td>.695</td>
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<tr>
<td>genCLE</td>
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<td>genSys</td>
<td>.511</td>
<td>.619</td>
<td>.064</td>
<td>.419</td>
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Clinical interviews using the PS survey allowed us to carefully characterize self-reported PS among a primarily CLE population. There was tremendous variability in how patients with LE experience PS. Overall, we found that 81% of subjects report PS. Unlike previous reports suggesting that PS occurs more commonly in whites compared with other racial groups, we found no associations between any PS phenotype and race.1,26,27 Not surprisingly, most PS reactions fell in the CLE-specific category. The most common PS phenotype was directCLE with 62% of PS subjects reporting specific examples of sun-induced CLE flare. In contrast to reports describing a delay between sun exposure and CLE induction, the majority of subjects reported sun-induced CLE flares occurring early after sun exposure.1 Exacerbations were commonly described as transient as opposed to lasting (for weeks to months). Interestingly, there was a trend for subjects with higher CLASI activity scores to report directCLE phenotype. We have shown previously
that higher CLASI activity scores were correlated with PS in LE.²⁰ It would be interesting to investigate whether patients with more active CLE disease have a greater degree of PS or whether sun-induced reactions lead to more active CLE disease.

CLE-nonspecific PS reactions were related to systemic disease activity and SLE diagnosis. More active systemic disease (as measured by PGA) but not SLE diagnosis predicted PMLE-like reactions and systemic reactions, whereas SLE diagnosis and PGA predicted the genRx phenotype of pruritus/paresthesia. Although these reactions nearly always occurred in association with a CLE-specific phenotype (ie, directCLE or genCLE), experiencing a non-specific cutaneous reaction to sunlight may suggest more active systemic disease.

A PMLE-like reaction was reported by 43% of patients, which is consistent with prior reports that suggest an increased prevalence of this form of eruption in patients with LE, compared with the general population.¹³,¹⁴ These reactions, however, often occurred immediately after sun exposure, resolved within 1 day, and rarely occurred in the absence of CLE-specific PS reactions. Because these reactions differ from PMLE in timing and setting, these findings suggest that PMLE-like reactions may occur as part of a PS spectrum in LE¹⁶ rather than PMLE as a co-occurring disorder.²⁶,²⁰

Over one third of patients reported systemic reactions to sunlight; only 50% met criteria for SLE and analysis indicated that higher PGA scores were predictive of the genSys phenotype. Furthermore, immunohistochemical analysis of sun-exposed skin of a subset of patients with genSys was associated with an increased number of mDC and a trend toward more T cells compared with patients who had PS without genSys. Skin resident T-cell and mDC populations have been described recently,³⁰,³¹ and greater prevalence of immunologically active cells was found resident in the skin of patients with CLE and SLE features. These results highlight the complexity of ultraviolet radiation effects in LE and suggest that resident inflammatory cells in the skin may play a role in systemic reactions of PS in LE.

This study had several limitations. First, study participants were treated at the autoimmune skin disease clinic of the University of Pennsylvania, which is a referral-only center. Second, PS reactions were inferred and were not directly observed. Third, study staff made every effort to use open-ended questions in the clinical interview pertaining to PS to minimize patient recall bias, however, some element of recall bias is likely present, which could artificially inflate the prevalence of PS phenotypes in the sample. Further, data collection occurred across seasons, which may contribute to recall bias. Finally, investigation of the pathomechanism of self-reported PS was hypothesis-generating in nature. With only a small number of subject biopsy specimens for immunohistochemistry, our analyses were not powered to detect differences that might truly exist in resident cell populations among the various cutaneous PS phenotypes or specific CLE diagnoses.

CONCLUSION

Characterization of self-reported PS in LE reveals that patients experience combinations of CLE-specific, CLE-nonspecific, and systemic reactions to sunlight. Sun-induced CLE flares are associated with more active CLE disease. PMLE-like, generalized pruritus/paresthesia, and systemic reactions are associated with more active systemic disease regardless of SLE diagnosis. Although the pathomechanism of these varied PS phenotypes is far from understood, these data suggest that resident immune cells in the skin might contribute to both SLE and CLE activity. Future studies, examining immunologically active cells in nonlesional skin both before and after ultraviolet radiation exposure, could help elucidate the contribution of resident skin cells on various PS phenotypes and explain how PS contributes to both CLE-specific and systemic disease activity.

REFERENCES