

Pain and pruritus in cutaneous lupus: their association with dermatologic quality of life and disease activity

S. Méndez-Flores¹
R. Orozco-Topete¹
P. Bermúdez-Bermejo²
G. Hernández-Molina²

¹Department of Dermatology, and

²Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico.

Silvia Méndez-Flores, MD

Rocío Orozco-Topete, MD

Paola Bermúdez-Bermejo, MD

Gabriela Hernández-Molina, MD, MS

Please address correspondence and reprint requests to:

Gabriela Hernández-Molina, MD, MS.

Department of Immunology and Rheumatology,

Instituto Nacional de Ciencias

Médicas y Nutrición Salvador Zubirán, Vasco de Quiroga 15, Col. Sección XVI, 14000, México City, México.

E-mail: gabyhm@yahoo.com

Received on May 20, 2013; accepted in revised form on July 19, 2013.

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Key words: pruritus, pain, cutaneous lupus

ABSTRACT

Objective. To evaluate the association of pain and pruritus with Dermato-logic Quality of Life (QoL) and cutaneous disease activity in patients with 1) specific cutaneous lupus erythematosus (CLE) lesions, 2) non-specific CLE lesions and 3) both types of CLE lesions. **Methods.** We evaluated 42 consecutive SLE patients with at least one active lesion attributed to lupus. Pain and pruritus were evaluated using a visual analogue scale, dermatologic QoL with the DLQI, clinical activity with the CLASI score and systemic activity with the SLEDAI-2K.

Results. The patients were predominantly females, mean age 34.2 ± 11.2 years and median SLE duration of 7 years. Sixteen patients (38%) had specific lesions, 12 (28.5%) non-specific lesions and 14 patients (33%) both lesions. Patients with both lesions had the highest CLASI activity scores (median 17) ($p < 0.0001$), all the cases of severe activity ($p = 0.002$) and higher (worst) DLQI scores (median 11.5, $p = 0.04$). The overall median pain score was 5 (0-9). Patients with non-specific or the combination of both CLE lesions had more pain ($p < 0.008$). Pain correlated with the DLQI ($\tau = 0.38$, $p = 0.001$) and the CLASI activity score ($\tau = 0.47$, $p = 0.002$). Pain was more intense in vasculitis and bullous lesions followed by oral ulcers. Pruritus score did not differ among groups (median 6) and did not correlate with the DLQI or the CLASI activity score.

Conclusion. We identified pain as a factor that correlated with dermatologic QoL and cutaneous activity. In this sense, this feature needs to be considered as part of the treatment targets in lupus.

Introduction

Cutaneous lupus erythematosus (CLE) is a complex disease (1). Traditionally it is classified according to morphologic and histopathologic parameters, in specific and non-specific lesions (2) being the non-specific lesions the most prevalent ones (3). CLE-specific lesions are further divided in acute (ACLE), subacute (SCLE) and chronic (CCLE) varieties (3). On the other

hand, non-specific lesions include skin manifestations not entirely exclusive to lupus such as non-scarring alopecia, ulcers, vasculitis, Raynaud's phenomenon, livedo, bullous lesions, periungual telangiectasias, calcinosis cutis, etc. (2-3). According to Zecević, CLE specific lesions are associated with milder systemic disease (4).

Skin disease is recognised as having an adverse psychosocial impact; for instance patients with discoid lesions have reported a poor dermatologic quality of life (QoL) (5). Risk factors associated with poor dermatologic QoL are female gender, generalised discoid lesions or SCLE (6), severe disease (7), at least one facial lesion, alopecia (8) and low income and education level (7). Although self-reporting of symptoms such as pain and itch are common in rheumatic disorders, their associations with CLE activity and dermatologic QoL have not been assessed so far. The aim of our study was to evaluate the association of pain and pruritus with dermatologic QoL and cutaneous disease activity in patients with 1) specific CLE lesions, 2) non-specific CLE lesions and 3) both types of CLE lesions.

Methods

We evaluated consecutively patients with SLE who attended the Instituto Nacional de Ciencias Médicas y Nutrición, a tertiary referral centre (2011-2012). In order to be included, patients should have at least one active cutaneous manifestation attributed to lupus in consensus by a specialist in rheumatology and a specialist in dermatology. Patients with concomitantly skin lesions secondary to other causes were excluded. All patients underwent a physical examination and laboratory assessment that included urinalysis, complete blood count, anti-double stranded DNA antibodies and complement. Based on a careful clinical morphological evaluation and according to a biopsy when available, the patients were divided into three groups: a) only with CLE specific lesions, b) only with CLE non-specific lesions and c) with both types of lesions.

Pain and pruritus were evaluated by means of a 10-point visual analogue

Competing interests: none declared.

Table I. Demographic and clinical features.

Variable	Specific Lesions n=16	Non-specific Lesions n=12	Both specific and non-specific lesions n=14	p-value
Females, n (%)	14 (87.5)	11 (91.7)	13 (92.9)	0.87
Age in years	36.6 ± 11.7	31.2 ± 7.8	33.3 ± 13	0.37
SLE duration in years	8.2 (1.5-31.2)	5.5 (0-16.1)	4.5 (0-20)	0.08
Lesion subtype, n (%)				
ACLE	2 (12.5)	NA	9 (64.3)	0.004
SCLE	6 (37.5)		0	
CCLE	8 (50)		5 (35.7)	
Median pain score	0 (0-8)	5.5 (0-8)	6 (2-9)	0.008
Median pruritus score	6 (1-9)	4 (0-7)	6.5 (0-8)	0.18
Median DLQI score	7 (2-13)	7.5 (2-19)	11.5 (5-28)	0.04
Median CLASI activity score	10 (3-14)	7 (3-13)	17 (8-48)	<0.0001
Mild activity, n (%)	7 (43.8)	8 (66.7)	1 (7.7)	
Moderate activity, n (%)	9 (56.3)	4 (33.3)	8 (57.1)	0.002
Severe activity, n (%)	0	0	5 (35.7)	
Immunosuppressors, n (%)	10 (62.5)	6 (50)	8 (57.1)	0.80
Antimalarial, n (%)	10 (62.5)	4 (33.2)	6 (42.9)	0.28
Oral steroid, n (%)	10 (62.5)	7 (58.3)	8 (57.1)	0.95

scale (VAS). Systemic disease activity was measured with the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K) (9), and cutaneous activity and damage with the CLASI score (10). According to the latter score, activity may be mild 0–9, moderate 10–20 or severe 21–70. Dermatology QoL was assessed using the validated Spanish version of the DLQI (11). This instrument covers six domains including symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. The final maximum score is 30, indicating a poor dermatological QoL. The study was approved by our Institutional Review Board and all subjects provided written informed consent according to the Helsinki Declaration.

Statistical analysis

We used parametric and non-parametric statistics as appropriate. We reported non-parametric correlations using Kendall's tau coefficients and considered significant a two-tailed $p < 0.05$. We used SPSS for Windows 20.0® (SPSS Inc).

Results

We included 42 patients, 90% females, mean age of 34.2±11.2 years and median SLE duration of 7 years [0-31]. Sixteen patients (38%) had only CLE spe-

cific lesions, 12 (28.5%) only CLE non-specific lesions and 14 patients (33%) both lesions. Among the CLE specific lesion group, the CCLE subtype predominated and all patients in this subtype had discoid lesions. Conversely, in the group with both lesions, the majority of patients had ACLE, none of them had SCLE and again all the cases of CCLE were discoid lupus (Table I). CLE non-specific lesions included non-scarring alopecia (n=11), vasculitis (n=10), bullous lesions (n=3), livedo (n=1) and mucosal ulcers (n= 14).

The overall median score of pain was 5 (0–9). Patients with non-specific CLE or both lesions had more pain ($p < 0.008$) (Table I), being more intense among those with vasculitis (median 6 [0–9]), bullous lesions (median 6 [6–8]) and oral ulcers (median 5.5 [0–9]). The overall median score for pruritus was 6 [0–9] and we did not find differences between the groups (Table I).

The median DLQI score was 8 points (2–28) and patients were more concerned about symptoms and feelings, daily activities and leisure. Patients with both CLE lesions had statistically higher DLQI scores than the other groups ($p = 0.04$) (Table I).

Among all the study population, the median CLASI score was 11 (3–48) for the activity component (38.1% mild activity, 50% moderate activity, 11.9% se-

vere activity). The group with both CLE lesions had the highest CLASI activity score, all the severe cases and more mucous membrane involvement (Table I). Overall, the median CLASI damage score was 0 (0–11) and chronic mucous membrane involvement was more prevalent in patients with both CLE lesions (0% specific, 33.3% non-specific, 71.4% both lesions, $p < 0.0001$). The overall median SLEDAI score was 4 (0–20) and there was no difference between groups (Table I). Systemic activity was similar among groups with the exception of haematologic activity that was absent in patients with specific lesions versus 33% in the non-specific group and 35% in both lesion groups ($p = 0.03$). There was no difference in the use of oral prednisone and immunosuppressors (Table I).

Correlations

Overall, the pain score correlated with the DLQI ($\tau = 0.38$, $p = 0.001$) and the CLASI activity score ($\tau = 0.47$, $p = 0.002$). However, when analysing by lesion type, the correlation of pain and DLQI was only significant at the non-specific lesion ($\tau = 0.47$, $p = 0.04$) and both lesion ($\tau = 0.40$, $p = 0.05$) groups. Overall, we did not find any correlation with pruritus and the DLQI ($\tau = 0.11$, $p = 0.32$) or with the CLASI activity score ($\tau = 0.14$, $p = 0.30$). However in the group with specific lesions, the pruritus and activity CLASI scores were correlated ($\tau = 0.57$, $p = 0.01$).

Discussion

Although originally recognised as important features at the CLASI design, associated symptoms such as pain and pruritus were not integrated into the score (13). Moreover, there is scarce information about these symptoms. Herein, we found that pain correlated with the DLQI and the CLASI activity score, whereas pruritus did not.

Traditionally, CLE skin lesions are classified into specific and non-specific (2-3), but they may coexist in the same patient (6). Here we found a higher CLASI activity score among patients with both specific and non-specific lesions, whereas patients with only CLE non-specific lesions had the lowest

score. However, it is important to highlight that the CLASI was not designed to score CLE non-specific lesions.

We did not demonstrate an association between the type of lesion (specific, non-specific, both) and systemic activity as measured with the SLEDAI index. Conversely, Zeclevic reported higher SLEDAI scores in patients with non-specific lesions (4). In a previous study, patients with SCLE and CLE had higher SLEDAI scores when compared with the ACLE variety (6), but due to our sample size we were not able to compare the CLE specific lesion subgroups. Recently, discoid lupus was associated with accrual integument damage, leukopenia, vasculitis, chronic seizures and with a lower frequency of arthritis and ESRD in a multi-ethnic cohort (12). We did not find an association of any cutaneous lesion with organ involvement, however haematologic activity was absent among patients with specific lesions.

Regarding the dermatologic QoL, a previous study reported similar Skin-dex-29 scores among ACLE, SCLE and CLE subsets (13); while another found higher scores among CLE subjects (6). Herein we found a worse dermatologic QoL among patients with both specific and non-specific lesions. Finally, the main finding of our study was the assessment of self-reported symptoms such as pain and pruritus. We found that pain correlated with the DLQI and the CLASI activity score. Currently, only one study was carried out regarding these symptoms (14). Goreshi *et al.* compared CLE and Dermatomyositis (DM) patients, and found that DM patients had a higher pruritus score but similar pain score (14). Now, we explored these symptoms in different types of CLE lesions and found that pain was present in non-specific CLE

lesions, and vasculitis the most associated one. In addition, pain correlated with dermatologic QoL and cutaneous activity. Pruritus was similar among all groups, and contrary to Goreshi *et al.*'s study, did not correlate with dermatologic QoL (14).

There are some limitations of this study. First, a small sample size that limited a subgroup analysis. Second, as the evaluation of dermatologic QoL was done in acute lesions, the results may not be extrapolated to scarring disease. Finally, the cross-sectional nature of the study made it difficult to ascertain the relationship between symptoms, cutaneous activity and dermatologic QoL over time.

Despite this, we identified a correlation between pain, dermatologic QoL and cutaneous activity. Thus, if pain has an impact in dermatologic QoL, it may be modified with treatment. In this vein, during a consensus of treat-to-target SLE strategies, patients' reported outcomes were recognised as important targets to be taken into consideration in clinical trials and in clinical practice (15-16).

In conclusion, pain is a self-reported outcome associated with poor dermatologic quality of life and cutaneous activity. Treatment strategies regarding patients' reported symptoms will be a matter of interest in the coming years.

References

1. AGMON-LEVIN N, MOSCA M, PETRI M, SHOENFELD Y: Systemic lupus erythematosus one disease or many? *Autoimmunity Rev* 2012; 11: 593-95.
2. GILLIAM J, SONTHEIMER R: Distinctive cutaneous subsets in the spectrum of lupus erythematosus. *J Am Acad Dermatol* 1981; 4: 471-75.
3. GRÖNHAGEN C, GUNNARSSON J, SVENUNGSSON E, NYBERG F: Cutaneous manifestations and serological findings in 260 patients with systemic lupus erythematosus.

Lupus 2010; 19: 1187-94.

4. ZECEVIĆ R, VOJVODIĆ D, RISTIĆ B, PAVLOVIĆ MD, STEFANOVIĆ D, KARADAGLIĆ D: Skin lesions - an indicator of disease activity in systemic lupus erythematosus? *Lupus* 2001; 10: 364-67.
5. MARTINS PR, SKARE T, FERRARI TA, SILVA AP, ALESSIO BF: Comparative analysis of the quality of life of patients with discoid lupus erythematosus and systemic lupus erythematosus with skin injuries. *Ann Bras Dermatol* 2012; 87: 326-8.
6. MOGHADAMA-KIA S, CHILEK K, GAINES E *et al.*: Cross-sectional analysis of a collaborative web-based database for lupus erythematosus associated skin lesions: 114 prospectively enrolled patients. *Arch Dermatol* 2009; 145: 255-60.
7. VASQUEZ R, WANG D, TRAN Q *et al.*: A multicenter, cross-sectional study on quality of life in patients with cutaneous lupus erythematosus. *Br J Dermatol* 2013; 168: 145-53.
8. KLEIN R, MOGHADAM-KIA S, TAYLOR L *et al.*: Quality of life in cutaneous lupus erythematosus. *J Am Acad Dermatol* 2011; 64: 849-58.
9. GLADMAN D, IBAÑEZ D, UROWITZ M: Systemic lupus erythematosus disease activity index 2000. *J Rheumatol* 2002; 29: 288-91.
10. ALBRECHT J, TAYLOR L, BERLIN J *et al.*: The CLASI (Cutaneous Lupus Erythematosus Disease Area and Severity index): an outcome instrument for cutaneous lupus erythematosus. *J Invest Dermatol* 2005; 125: 889-94.
11. TIEDRA A, MERCADAL J, BADÍA X, MASCARU J, HERDMAN M, LOZANO R: Adaptación transcultural del español del cuestionario Dermatology Life Quality (DLQI): el Índice de Calidad de Vida Dermatológica. *Acta Dermo-Sifilogr* 1998; 89: 692-700.
12. SANTIAGO-CASAS Y, VILA L, MCGWIN G *et al.*: Association of discoid lupus erythematosus with clinical manifestations and damage accrual in a multiethnic lupus cohort. *Arthritis Care Res* 2012; 64: 704-12.
13. GAINES E, BONILLA-MARTINEZ Z, ALBRECHT J *et al.*: Quality of life and disease severity in a cutaneous lupus erythematosus pilot study. *Arch Dermatol* 2008; 144: 1061-2.
14. GORESHI R, CHOCK M, FOERING K *et al.*: Quality of life in dermatomyositis. *J Am Acad Dermatol* 2011; 65: 1107-16.
15. MOSCA M, BOUMPAS D, BRUCE I *et al.*: Treat-to-target in systemic lupus erythematosus: where are we today? *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S112-115.