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Retrospective analysis of patients with cutaneous lupus erythematosus: A single-center experience

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Abstract

Objective: Cutaneous lupus erythematosus (CLE) is a chronic inflammatory disease with different subtypes that exhibit variations in clinical, immunological, and prognostic features. This study aims to investigate the demographic and clinical characteristics of patients with CLE, the frequency of observed subtypes, antibody levels, the rate of co-occurrence with systemic lupus erythematosus (SLE), and the treatments administered.

Methods: The data of 56 patients diagnosed with CLE between November 2021 and December 2023 were retrospectively analyzed in this study. Demographic features, clinical findings, comorbidities, antinuclear antibody (ANA) and anti-dsDNA results, and treatments administered were recorded from patient files.

Results: The study included 38 females (67.9%) and 18 males (32.1%) with a mean age of 42.3±14.3 years. The most common clinical subtype was chronic CLE (CCLE) (85.7%). Within CCLE, discoid lupus erythematosus (DLE) constituted 76.8%. The most frequently affected anatomic region was the face. SLE was present in 16.1% of the patients. Among patients with acute CLE (ACLE), 100% had SLE, while this ratio was 66.7% for subacute CLE (SCLE) and 6.9% for DLE. ANA was positive in 42.9% of all patients and 32.6% of DLE patients.

Conclusion: In this study, it was observed that the most common clinical subtype was DLE, lesions most frequently occurred in the facial region, the highest risk of SLE was associated with ACLE, and the most commonly administered treatment was topical calcineurin inhibitors. Identifying the subtypes of CLE, initiating appropriate treatment, and regular monitoring of patients are crucial in the management of patients with CLE.

Keywords: Cutaneous Lupus Erythematosus, Discoid Lupus Erythematosus, Systemic Lupus Erythematosus, Antinuclear Antibody.

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Introduction

Lupus erythematosus (LE) is an autoimmune disease that can manifest across a broad clinical spectrum, ranging from limited skin involvement to systemic disease affecting vital organs. Cutaneous lupus erythematosus (CLE) can present as an isolated skin disease or as one of the various clinical manifestations of systemic lupus erythematosus (SLE). Skin lesions in LE are categorized into lupus-specific and lupus non-specific. Non-specific lupus lesions, such as Reynaud phenomenon, vasculitis, livedo reticularis, and alopecia, often accompany SLE and may also occur in other diseases unrelated to LE [1,2]. Lupus-specific skin lesions are referred to as CLE, and they are further classified into four groups based on clinical, histopathological, and laboratory features: acute, subacute, intermittent, and chronic [3]. Differentiating between these clinical types is crucial due to variations in their frequencies, clinical, histopathological, and laboratory characteristics, rates of progression or co-occurrence to SLE, and treatments. The prevalence of CLE varies according to geographic regions, ethnic backgrounds, age, and gender [1-3].

This study aims to investigate the demographic and clinical characteristics of patients diagnosed with CLE in our region, the frequency of observed subtypes, antibody levels, the rate of co-occurrence with SLE, and the treatments administered.

Methods

Study population

The files of patients diagnosed with CLE between November 1, 2021, and December 1, 2023, at the Dermatology outpatient clinics of Giresun Training and Research Hospital were retrospectively examined. The following data were recorded from patient files: age, gender, duration of the disease, dermatological examination findings, number of lesions, CLE type, biopsy diagnosis, presence of accompanying SLE, accompanying systemic diseases, antinuclear antibody (ANA), anti-dsDNA results, and treatments administered. CLE types were categorized into four main groups: acute CLE (ACLE), subacute CLE (SCLE), intermittent CLE (ICLE)/lupus tumidus, and chronic CLE (CCLE). CCLE was further classified as discoid lupus erythematosus (DLE), lupus erythematosus profundus (LEP), verrucous lupus erythematosus, and chilblain lupus erythematosus (3). Patients with incomplete data in their files were not included in the study.

Statistical analysis

Statistical analyses were conducted using SPSS version 23 software. The data were presented as mean ± standard deviation, percentage, and count. Descriptive statistical methods were employed in the evaluation of the data. For the comparison of numerical data between two groups, the independent samples t-test was used when the assumption of normality was met; otherwise, the Mann-Whitney U test from non-parametric tests was employed. Depending on the situation, either the Chi-square test or Fisher's exact tests were used for the comparison of categorical data between the two groups. The Spearman correlation test was used to evaluate the correlation between parameters that did not exhibit a normal distribution. A p-value less than 0.05 was considered statistically significant.

Ethics approval

The present study was conducted according to the Declaration of Helsinki and approved by the Clinical Research and Ethics Committee of Giresun Training and Research Hospital (Approval number: 24, date: 18.12.2023).

Results

A total of 56 patients diagnosed with CLE were followed at the dermatology clinic between the specified dates. While the age ranged from 18 to 74, the mean age was 42.3±14.3 years. Of the patients, 38 were female (67.9%), and 18 were male (32.1%). The mean age at diagnosis was 39.8±15.35 years. The diagnosis was confirmed by histopathological examination in 54 of the 56 patients (96.4%). Two patients without a biopsy diagnosis had the clinical subtype of ACLE.

The most common clinical subtype was CCLE (48 patients, 85.7%). Among CCLE patients, 43 patients (76.8%) had DLE, 4 patients (7.2%) had chilblain lupus, and 1 patient (1.8%) had LEP. 3 patients (5.4%) had SCLE, 3 patients (5.4%) had lupus tumidus, and 2 patients (3.6%) had ACLE. Associated systemic diseases were present in 21 patients (37.5%). Among these, 10 had hypertension, 5 had diabetes mellitus,

5 had malignancy, 5 had thyroid disease, 3 had a connective tissue disease other than SLE (1 with rheumatoid arthritis, 1 with Sjögren's syndrome, 1 with mixed connective tissue disease), 2 had coronary artery disease, 1 had morphea, and 1 had chronic obstructive pulmonary disease. SLE was present in 16.1% of patients (9 patients). In patients with ACLE and LEP, 100% had SLE, in patients with SCLE, 66.7% had SLE, in patients with chilblain lupus erythematosus, 25% had SLE, and in patients with DLE, 6.9% had SLE. Of the patients with CLE, 32 (57.1%) were ANA negative, and 24 (42.9%) were ANA positive (11 with 1/80, 5 with 1/160, 6 with 1/320, and 2 with >1/320 titers). ANA positivity was observed in 100% of patients with ACLE, LEP, and chilblain lupus, 66.7% of patients with SCLE, 33.3% of patients with lupus tumidus, and 32.5% of patients with DLE. Eight patients (14.3%) had positive anti-dsDNA. Anti-dsDNA positivity was observed in all patients with ACLE and LEP, 66.7% of patients with SCLE, 25% of patients with chilblain lupus, and 4.6% of patients with DLE. Treatment modalities included topical calcineurin inhibitors (TCI) in 18 patients, hydroxychloroquine (HQ) in 14 patients, HQ and systemic steroids in 9 patients, topical/intralesional corticosteroids in 6 patients, topical corticosteroids and calcineurin inhibitor combination in 6 patients, HQ and azathiopyrin in 2 patients, and systemic isotretinoin in 1 patient. The demographic, clinical, laboratory, and treatment characteristics of all patients are shown in Table 1.

In our study population, the most common clinical subtype was DLE (76.8%). The mean age of DLE patients, including 28 females (65.1%) and 15 males (34.9%), was 44.9±13.28 years. The mean age at diagnosis was 42.32±14.48 years. While 11 patients (25.6%) had a single lesion, 32 patients (74.4%) had multiple lesions. The most common location of the lesions was the face (55.8%), followed by the scalp (37.2%). The cheek was the most common facial area affected (27.9%). At least one systemic disease was present in 41.9% of patients. The most common accompanying systemic disease was hypertension (20.9%). SLE diagnosis was present in 3 patients (7%). ANA was positive in 14 patients (32.6%), with titers of 1/80 in 9 patients, 1/160 in 3 patients, and 1/320 in 2 patients. Anti-dsDNA was positive in 2 patients (4.7%). The most commonly prescribed treatment for patients with DLE was TCI (41.9%), followed by HQ (27.9%). The demographic, clinical, laboratory, and treatment characteristics of patients with DLE are shown in Table 2.

There was no significant difference between female and male patients with DLE in terms of age (p=0.387), age at diagnosis (p=0.264), lesion number (p=0.905), localization (p=0.062), frequency of accompanying systemic diseases (p=0.64), presence of accompanying SLE (p=0.541), ANA positivity (p=0.415), anti-dsDNA positivity (p=0.535), and treatments administered (p=0.991) (Table 2).

There was no significant difference between individuals with single or multiple DLE lesions in terms of age (p=0.535), age at diagnosis (p=0.89), presence of accompanying SLE (p=0.558), ANA positivity (p=0.311), anti-dsDNA positivity (p=0.985), and treatments administered (p=0.526).

Discussion

Lupus erythematosus encompasses a wide clinical spectrum, ranging from a serious systemic disease to localized disease confined to the skin, characterized by chronic inflammatory processes with relapses and remissions. The most commonly affected organs are the skin, joints, and kidneys. Skin lesions observed in LE are divided into lupus-specific and lupus non-specific categories [4]. Lupus-specific skin lesions, termed CLE, are further classified into four groups: acute, subacute, intermittent (lupus tumidus), and chronic. These groups, which differ clinically, histopathologically, and immunologically, also exhibit varying rates of association with SLE. While numerous studies have investigated the epidemiological, clinical, and laboratory characteristics of patients with SLE, there is limited research specifically focusing on CLE [1,2].

In our study, the majority of patients were diagnosed with CCLE (85.7%). Among the CCLE subtypes, the most commonly observed clinical type was DLE (76.8%). Other CCLE subtypes included LEP in 1 patient (1.8%), and chilblain LE in 4 patients (7.2%). The prevalence of DLE in our study is consistent with a retrospective evaluation of 186 LE patients, where DLE was the most frequent CLE type (72.5%). In that study, the frequencies of SCLE and ACLE were 8%

Table 1. The demographic, clinical, laboratory characteristics, and treatments of patients with cutaneous lupus erythematosus

	CLE (n=56)	CCLE (n=48)	SCLE (n=3)	Lupus tumidus (n=3)	ACLE (n=2)
Age, years (mean±SD)	42.3±14.3	42.6±14.3	40.3±22.2	46.3±10.9	32.5±10.6
Sex					
Female, n (%)	38 (67.9)	32 (66.7)	2 (66.7)	2 (66.7)	2 (100)
Male , n (%)	18 (32.1)	16 (33.3)	1 (33.3)	1 (33.3)	-
Age at diagnosis, years, (mean±SD)	39.8±15.35	40.25±15.03	39.67±23.12	46±11.27	19.5±7.78
Localisation of lesions, n (%)					
Face	28 (50)	24 (50)	-	2 (66.7)	2 (100)
Scalp	16 (28.6)	16 (33.3)	-	-	-
Trunk	2 (3.6)	-	1 (33.3)	-	-
Face, neck, upper limbs	2 (3.6)	1 (2.09)	2 (66.7)	-	-
Face, ears	1 (1.8)	1 (2.09)	-	-	-
Face, trunk, upper limbs	1 (1.8)	1 (2.09)	-	-	-
Face, neck	1 (1.8)	1 (2.09)	-	-	-
Upper and lower limbs	3 (5.4)	3 (6.25)	-	-	-
Upper lims	1 (1.8)	-	-	1 (33.3)	-
Lower limbs	1 (1.8)	1 (2.09)	-	-	-
Number of lesions, n (%)					
Single	12 (21.43)	12 (25)	-	-	-
Multiple	44 (78.57)	36 (75)	3 (100)	3 (100)	2 (100)
SLE					
Present	9 (16.1)	5 (10.42)	2 (66.7)	-	2 (100)
Absent	47 (83.9)	43 (89.58)	1 (33.3)	3 (100)	-
ANA					
Negative	32 (57.1)	29 (60.42)	1 (33.3)	2 (66.7)	-
1/80	11 (19.6)	11 (22.93)	-	-	-
1/160	5 (8.9)	4 (8.3)	1 (33.3)	-	-
1/320	6 (10.7)	3 (6.25)	1 (33.3)	1 (33.3)	1 (50)
>1/320	2 (3.6)	1 (2.1)	-	-	1 (50)

Anti-dsDNA					
Negative	48 (85.7)	44 (91.7)	1 (33.3)	3 (100)	-
Positive	8 (14.3)	4 (8.3)	2 (66.7)	-	2 (100)
Treatment					
TCI	18 (32.1)	18 (37.5)	-	-	-
TCS/ILCS	6 (10.7)	6 (12.5)	-	-	-
TCS+TCI	6 (10.7)	5 (10.42)	-	1 (33.3)	-
HQ	14 (25)	13 (27.08)	-	1 (33.3)	-
HQ + systemic steroid	9 (16.1)	4 (8.3)	3 (100)	1 (33.3)	1 (50)
HQ + AZA	2 (3.6)	1 (2.1)	-	-	1 (50)
Systemic isotretinoin	1 (1.8)	1 (2.1)	-	-	-

Abbreviations: CLE, cutaneous lupus erythematosus; CCLE, chronic cutaneous lupus erythematosus; SCLE, subacute cutaneous lupus erythematosus; ACLE, acute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus; ANA, antinuclear antibody; anti-dsDNA, anti-doublestrandedDNA; TCI, topical calcineurin inhibitors; TCS, topical corticosteroids; ILCS, intralesional corticosteroids; HQ, hydroxychloroquine; AZA, azathioprine; SD, standard deviation.

Table 2. The demographic, clinical, laboratory characteristics, and treatments of patients with discoid lupus erythematosus

	Female (n=28)	Male (n=15)	Total (n=43)	p
Age, years (mean±SD)	43.6±12.95	47.3±14	44.9±13.28	0.387†
Age at diagnosis, years, (mean±SD)	40.5±14.85	45.7±13.6	42.32±14.48	0.264†
Localisation of lesions, n (%)				0.062¶
Face	18 (64.28)	6 (40)	24 (55.8)	
Scalp	10 (35.72)	6 (40)	16 (37.2)	
Face, ears	-	1 (6.66)	1 (2.3)	
Face, trunk, upper limbs	-	1 (6.66)	1 (2.3)	
Face, neck	-	1 (6.66)	1 (2.3)	
Number of lesions, n (%)				0.905§
Single	7 (25)	4 (26.66)	11 (25.6)	
Multiple	21 (75)	11 (73.33)	32 (74.4)	
SLE				0.541¶
Present	3 (10.72)	-	3 (7)	
Absent	25 (89.28)	15 (100)	40 (93)	

ANA				0.415¶
Negative	18 (64.29)	11 (73.33)	29 (67.4)	
1/80	7 (25)	2 (13.33)	9 (20.9)	
1/160	1 (3.57)	2 (13.33)	3 (7)	
1/320	2 (7.14)	0	2 (4.7)	
AntidsDNA				0.535¶
Negative	26 (92.86)	15 (100)	41 (95.3)	
Positive	2 (7.14)	-	2 (4.7)	
Treatment				0.991¶
TCI	12 (42.86)	6 (40)	18 (41.9)	
TCS/ILCS	2 (7.14)	1 (6.66)	3 (7)	
TCS+TCI†	3 (10.72)	2 (13.33)	5 (11.6)	
HQ	7 (25)	5 (38.46)	12 (27.9)	
HQ + systemic steroid	2 (7.14)	1 (6.66)	3 (7)	
HQ + AZA	1 (3.57)	-	1 (2.3)	
Systemic isotretinoin	1 (3.57)	-	1 (2.3)	

Abbreviations: SLE, systemic lupus erythematosus; ANA, antinuclear antibody; anti-dsDNA, anti-doublestrandedDNA; TCI, topical calcineurin inhibitors; TCS, topical corticosteroids; ILCS, intralesional corticosteroids; HQ, hydroxychloroquine; AZA, azathioprine; SD, standard deviation. † Independent samples t test, ‡ Mann-Whitney U test, ¶ Fisher exact test, § Pearson chi-square test. P<0.05 is statistically significant. Bold values sign statistical significance.

and 15%, respectively [5]. Another series of 156 CLE patients reported DLE as the most common clinical type (82.7%), with 14.74% diagnosed with SCLE and 0.64% with ACLE [6]. In a multicenter study involving 1002 CLE patients, 39.62% had DLE, 30.34% had ACLE, 23.55% had SCLE, and 6.48% had lupus tumidus [7]. Our study aligns with these findings, highlighting DLE as the most prevalent CLE subtype, consistent with existing literature.

In our study, the female-to-male ratio for CLE was determined to be 2.1. Various studies have reported this ratio to range between 1.79 and 4.31 [4,6,7]. The mean age of disease onset in these studies was between 40 and 43 years, a range consistent with the mean onset age in our study. CLE lesions are more frequently observed on sun-exposed areas of the skin, particularly the head, neck, and arms [1]. In a study by Izquerdo et al., it was reported that CLE lesions most commonly occurred on the head and neck and it was observed that DLE and ACLE lesions were most commonly located on the head and neck, while SCLE lesions predominantly affected the trunk [4]. Similarly, our study revealed that CCLE lesions were most frequently located on the face, followed by the scalp.

In our study, SLE was present in 16.1% of the patients. In the literature, the rate of concurrent or subsequent SLE in CLE patients has been reported to be between 12.18% and 40.7% in different studies [6-8]. ACLE is the subtype of CLE with the highest risk of developing systemic disease [9]. Although the number of patients diagnosed with ACLE was quite small in our study, in line with the literature, all of these patients had a diagnosis of SLE, and they were positive for both ANA and anti-dsDNA.

In our study, 37.5% of the patients had concomitant systemic diseases. Among them, 10 patients had hypertension, 5 had diabetes mellitus, 5 had malignancy, 5 had thyroid disease, 3 had connective tissue diseases other than SLE, 2 had coronary artery disease, 1 had morphea, and 1 had chronic obstructive pulmonary disease. It has been shown that individuals with CLE are more likely to have autoimmune diseases (other than SLE) compared to the general population, with

Hashimoto's thyroiditis and Sjögren's syndrome being the most commonly associated autoimmune diseases [10]. While the increased risk of cancer is known in chronic autoimmune diseases, studies with isolated CLE patients, such as Singh et al.'s study involving 155 patients, did not find such a risk [11]. Conversely, in a larger series of CLE patients by Westermann et al., an increased risk of non-Hodgkin lymphoma, pancreas, lung, and ovarian cancer was demonstrated [12]. In our study, 1 patient had testis, 1 had breast, 1 had lung, 1 had thyroid, and 1 had colon and prostate cancer. The occurrence of associated malignancies may be coincidental, and these results need to be supported by more extensive studies involving a larger population of CLE patients. The most common concomitant systemic disease in our study was hypertension (17.8%). In a previous study, hypertension was reported to be the most common comorbidity with DLE at 18.2%, followed by diabetes mellitus at 6.8% [13]. Since diabetes mellitus and hypertension are common diseases in the middle-aged population, further extensive studies are needed to determine whether there is a significant association with DLE.

In our study, the majority of patients were DLE, while the number of patients in other clinical subtypes was quite low. Consistent with the literature, the average age at diagnosis for our patients was approximately 41, and females received about 2 times more DLE diagnoses than males [14]. It is rare for DLE lesions to involve the trunk without affecting the upper face and scalp, and when lesions are present below the neck, it is referred to as generalized DLE [15]. While localized DLE is more frequently observed (60-80%), generalized DLE is less common (20-40%) [15,16]. In our study, only one patient (2.32%) had generalized DLE. It is known that generalized DLE has a higher likelihood of progressing to SLE compared to localized DLE [15,17]. However, in our study, the patient with generalized DLE did not have SLE. Among the three DLE patients diagnosed with SLE, localized DLE in the head region was present in all cases.

The positivity of ANA has been shown to be significant in patients with DLE, serving as a potential indicator of progression to SLE in previous studies [13,17]. In various previous studies, ANA positivity in DLE patients has been reported at rates ranging from 16.1% to 67% [18,19]. In our study, ANA positivity was detected in 32.5% of patients with DLE, while all patients who developed SLE had a positive ANA (2 patients at 1/320, 1 patient at 1/160).

Treatment options for CCLE include topical corticosteroids, intralesional corticosteroids, TCI, and HQ as first-line therapies. In cases resistant to these treatments, a combination of HQ and systemic steroids, systemic isotretinoin, thalidomide, dapsone, methotrexate, mycophenolate mofetil, and other agents can be applied [3]. In our study, the most commonly used treatment was TCI, followed by HQ.

The main limitations of our study include its retrospective nature and being a single-center study, and a limited number of patients with clinical types other than DLE.

Conclusion

CLE is a rare skin disease with different clinical and immunological characteristics, exhibiting subtypes that vary in their association with or progression to SLE. As lesions often affect sun exposed areas of the skin, the most common subtype, DLE can lead to atrophy, scarring, and permanent hair loss, impacting the quality of life [14,17]. Therefore, determining the subtypes of the disease, initiating appropriate treatment, and regularly monitoring patients are of great importance. Our study revealed that DLE is the most frequently observed clinical type, with lesions predominantly affecting the facial region. The highest risk for SLE was associated with the ACLE, and the most commonly applied treatment was TCI. These findings reflect the demographic, clinical, and immunological features of CLE patients in our region, contributing to the literature in this regard.

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