A Clinico-Pathological Study of Cutaneous Lupus Erythematosus

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Abstract

Background: Lupus erythematosus (LE) is a heterogenous autoimmune disease marked by diverse patterns of autoantibody production that can affect one or more vital internal organs as well as skin. Skin is the second most commonly affected organ in patients with lupus erythematosus. Skin involvement may occur alone or as a part of serious systemic disease.

Materials and Methods: A clinical non-interventional descriptive study was conducted in a tertiary care centre over a period of 1 year.

Aim:
1. To study the clinical patterns and histopathology of these clinical patterns of cutaneous lupus erythematosus.
2. To study the risk factors, all the required data were collected by clinical examination of patients.

Results: Thirty patients with clinical features of cutaneous lupus erythematosus were studied and the following observations were made. Patients with cutaneous LE ranged in age from 20-62 years. the male to female ratio was 1:5. Seventy percent of the patients were unemployed. Scaly rash was the most frequent complaint. Seventeen (56.7%) patients with cutaneous LE had systemic complaints. Majority of patients (26) had short duration illness of less than 1 year. Seventeen (56.7%) patients attributed sunlight as an exacerbating factor Chronic CLE (CCLE) was the most common form of cutaneous LE observed in this study. LE nonspecific lesions were observed in 53.3% patients with cutaneous LE. Among the 25 histopathologically diagnosed cases of classic CCLE, hyperkeratosis, follicular plugging and atrophy were present in 76%, keratotic plugging in 32%, acanthosis in 24% and hypergranulosis with parakeratosis in 4%.

Keywords: cutaneous lupus erythematosus, CCLE, SCLE, ACLE, histopathology.

Introduction
Lupus erythematosus (LE) is a heterogenous autoimmune disease marked by diverse patterns of autoantibody production that can affect one or more vital internal organs as well as skin. Though the exact aetiology is unknown, it is thought to
result from interaction of many factors, genetic and acquired with an end result of grossly disordered immunity and immunologic injury. Skin is the second most commonly affected organ in patients with lupus erythematosus. Skin involvement may occur alone or as a part of serious systemic disease (Systemic lupus erythematosus). The cutaneous manifestations of LE have been divided into LE-specific and LE-nonspecific. The LE-specific skin lesions have the characteristic histologic hallmark-interface dermatitis along with other diagnostic features specific for LE. The term “cutaneous LE” is used synonymously with LE-specific skin disease. It includes three major categories-acute cutaneous lupus erythematosus (ACLE), subacute cutaneous lupus erythematosus (SCLE), and chronic cutaneous lupus erythematosus (CCLE). ACLE is characterized by malar rash or generalized maculopapular rash, SCLE by papulo-squamous or annular lesions and CCLE by classic discoid type and variants. The early recognition of cutaneous LE patients and differentiation between the LE-subtypes based upon the constellation of clinical, histological and immunofluorescence findings is very important because the type of skin involvement can predict the risk to develop systemic lupus erythematosus. Therefore a thorough systemic and dermatological examination, a careful diagnostic evaluation including skin biopsy is required to screen for underlying systemic lupus erythematosus (SLE). A lesional skin biopsy may help to confirm or rule out other causes of disease. There are many reports based on the clinical studies from the western literature about the different morphological patterns of cutaneous LE and their histopathology, but such studies are lacking in Indian literature. Thus this study was undertaken with the objective of describing the different clinical patterns of cutaneous LE and to study the histopathology of the LE-specific skin lesions of patients attending our department. Another aim was to correlate the clinical patterns with the histologic features and to find out the frequency of systemic lupus erythematosus in these patients. It was also borne in mind that early recognition of cutaneous LE may help not only the patients to take preventive measures against disease triggering factors but also the physicians to deliver prompt and appropriate treatment.

Materials and Methods
This is a Descriptive study done on 30 consecutive patients with clinical features of cutaneous lupus erythematosus (cutaneous LE) attending the outpatient wing of the Department of Dermatology and Venereology, Medical College Hospital, Thiruvananthapuram, during a period of 1 year. Patients with clinical diagnosis of cutaneous LE and patients willing were included in the study. Pregnant women, children of age less than 5 years and patients with bleeding diathesis were excluded from the study.

Aim of the Study
To study the clinical patterns and histopathology of these clinical patterns of cutaneous lupus erythematosus.

Method of study
A proforma was constructed in consultation with an expert. Based on the proforma, detailed clinical history with particular reference to predisposing factors, onset, distribution of lesions and symptomatology of systemic involvement were obtained from all the patients. General, dermatological, and systemic examination was done in all patients and documented in the proforma. A complete haemogram, peripheral smear, urine routine examination, 24 hour urine protein estimation, renal function tests, liver function tests, LE cell test, ECG, chest X-ray, VDRL test, tests for rheumatoid factor, ANA test and antids-DNA test were done in all cases. Skin biopsies from representative lesions were done in all patients after obtaining their written consent. Detailed histopathological examination was done and findings noted. Correlation of the clinical and
Histological features was done in all the patients in this study. The results were tabulated and analyzed in consultation with the clinical epidemiologist.

**Statistical analysis**
Data were entered into a personal computer using statistical software after preparing a master chart. Frequencies were found out and their percentages were also calculated and represented in tables and charts.

**Observations**
Thirty patients with clinical features of cutaneous lupus erythematosus attending the outpatient wing of the Department of Dermatology and Venereology, Medical College Hospital, Thiruvananthapuram during the period 2004-2007 were subjected to the study and the following observations were made.

**Age**
Patients with cutaneous LE ranged in age from 20-62 years. The most common age group, in which the maximum number of patients (33.3%) was found, was 30-39 years. Disease onset over 60 years was noted in two patients.

**Table - 1: Age distribution**

| Age   | Number | Percentage |
|-------|--------|------------|
| 20-29 | 8      | 26.7       |
| 30-39 | 10     | 33.3       |
| 40-49 | 6      | 20.0       |
| 50-59 | 4      | 13.3       |
| ≥ 60  | 2      | 6.7        |
| TOTAL | 30     | 100        |

**Sex**
There were 25 females and 5 males, and the male to female ratio was 1:5.

**Occupation**
Seventy percent (21) of the patients were unemployed. Of these, 19 were females and 2 were males. Fifteen out of the nineteen females were housewives and 4 were students. Self employed included skilled labourers like cook (1), home nurse (1), tailor (2) and manual labourer (3). The employed were two teachers.

**Figure 1: Sex distribution**

**Figure 2: Occupation**

**Marital status**
Among the 30 patients, 25 were married and 5 were unmarried.

**Figure 3: Marital status**

**Presenting complaints**
Scaly rash was the most frequent complaint, present in 96.7% of patients followed by photosensitivity in 50%, hair loss in 46.7% and oral ulcers in 23.3%. Three (10%) patients complained of malar rash, and one (3.3%) had widespread skin rash.

**Figure 1: Sex distribution**
Table - 2: Presenting complaints

| Type of complaint               | Number | Percentage |
|---------------------------------|--------|------------|
| Scaly papules and plaques       | 29     | 96.7       |
| Photosensitivity                | 15     | 50.0       |
| Hair loss                       | 14     | 46.7       |
| Oral ulcers                     | 7      | 23.3       |
| Malar rash                      | 3      | 10.0       |
| Raynaud’s Phenomenon            | 3      | 10.0       |
| Pruritus                        | 3      | 10.0       |
| Facial edema                    | 3      | 10.0       |
| Lip ulcers                      | 2      | 6.7        |
| Generalised skin rash           | 1      | 3.3        |
| Conjunctival congestion         | 1      | 3.3        |
| Hyperpigmentation               | 1      | 3.3        |
| Leg ulcers                      | 1      | 3.3        |

Constitutional Symptoms

Nine (30%) patients with cutaneous LE had constitutional symptoms. Weakness and easy fatiguability was the most common, followed by fever and weight loss.

Table - 3: Constitutional Symptoms

| Symptoms                          | Frequency | Percentage |
|-----------------------------------|-----------|------------|
| Weakness and easy fatiguability   | 6         | 20         |
| Fever                             | 3         | 10         |
| Weight loss                       | 3         | 10         |

Systemic complaints

Seventeen (56.7%) patients with cutaneous LE had systemic complaints.

The most common systemic complaint was arthralgia found in 13 (76.5%) patients, followed by myalgia in 4 (23.5%), palpitations in 4 (23.5%) and dyspnoea in 3 (17.6%); two (11.8%) patients had headache. Other systemic complaints noted were orthopnoea (1), recurrent sore throat (1), dysphagia (1) and abdominal pain (1).

Table - 4: Systemic Complaints

| Type of systemic complaint         | Frequency | Percentage |
|------------------------------------|-----------|------------|
| Arthralgia                         | 13        | 76.5       |
| Myalgia                            | 4         | 23.5       |
| Palpitations                       | 4         | 23.5       |
| Dyspnoea                           | 3         | 17.6       |
| Headache                           | 2         | 11.8       |
| Orthopnoea                         | 1         | 5.9        |
| Dysphagia                          | 1         | 5.9        |
| Recurrent sore throat               | 1         | 5.9        |
| Abdominal pain                      | 1         | 5.9        |

Duration of illness

Duration of illness ranged from less than 1 year to more than 7 years. Majority of patients (26) had short duration illness of less than 1 year.

Table - 5: Duration of illness

| Period          | Frequency | Percentage |
|-----------------|-----------|------------|
| Less than 1 year| 26        | 86.7       |
| 1-3 years       | 2         | 6.7        |
| 4-7 years       | 1         | 3.3        |
| More than 7 years| 1       | 3.3        |
| TOTAL           | 30        | 100        |

Triggering factors

Seventeen (56.7%) patients attributed sunlight as an exacerbating factor of their skin lesions and three (10%) patients attributed exposure to cold as a precipitating factor.

Abortions

Five (16.7%) of the 30 patients had a history of abortions.

Family history of SLE

Two (6.7%) out of the 30 patients, had a family history of the disease.

General examination

Pallor was a significant finding in 11 patients with cutaneous LE. Other findings noted were cyanosis (1), clubbing (1) and pedal edema (1).

LE specific skin lesions

Of the 30 patients studied, 26 patients had monomorphic lesions and 4 patients had bimorphic lesions. Chronic CLE (CCLE) was the most common form of cutaneous LE observed in this study (83.3%). Subacute CLE (SCLE) represented only 16.7% of cutaneous LE and acute CLE (ACLE) was detected in 13.3% of patients.

Table - 6: LE Specific skin lesions

| Types   | Frequency | Percentage |
|---------|-----------|------------|
| CCLE    | 25        | 83.3       |
| SCLE    | 5         | 16.7       |
| ACLE    | 4         | 13.3       |

CCLE

Classic discoid type represented 96% (24) of patients with CCLE and verrucous type represented 4% (1). Classic discoid LE localised was the most common type representing 62.5%
(15) of cases while the generalised form represented only 37.5% (9).

**SCLE**
All the 5 patients with subacute LE presented with papulo-squamous type of lesions. Four patients had monomorphic lesions of SCLE while 1 (20%) patient had a combination of SCLE (papulo-squamous) with CCLE (classic discoid).

**ACLE**
Three (75%) out of 4 patients had malar rash, while 1 patient showed widespread maculo-papular eruption.

**LE nonspecific skin lesions**
LE nonspecific lesions were observed in 16 (53.3%) patients with cutaneous LE. Alopecia was the most common LE nonspecific cutaneous finding observed in 14 (87.5%) patients. Other findings were facial edema (18.8%), Raynaud’s phenomenon (12.5%), leg ulcer (6.3%) and sclerodactyly (6.3%).

**Table - 7: LE nonspecific skin lesions**

| Skin lesions        | Frequency | Percentage |
|---------------------|-----------|------------|
| Alopecia            | 14        | 87.5       |
| Facial edema        | 3         | 18.8       |
| Raynaud’s phenomenon| 2         | 12.5       |
| Sclerodactyly       | 1         | 6.3        |
| Leg ulcer           | 1         | 6.3        |

**Nail involvement**
Twenty percent of patients with cutaneous LE were found to have nail changes. Nailfold erythema was the most common nail involvement observed (50%).

**Table - 8: Nail involvement**

| Nail involvement        | Frequency | Percentage |
|-------------------------|-----------|------------|
| Nailfold erythema       | 3         | 50.0       |
| Nailfold telangiectasia | 2         | 33.3       |
| Leuconychia             | 1         | 16.7       |
| **TOTAL**               | **6**     | **100**    |

**Oral mucosa**
Ten (33.3%) patients had mucosal changes like oral ulcers (5) erosions of the lips (4), whitish plaques on the buccal mucosa (1) and fissuring of the tongue (1). Oral ulcer was the most common mucosal lesion observed (50%).

**Table - 9: Oral mucosal findings**

| Oral findings                   | Frequency | Percentage |
|---------------------------------|-----------|------------|
| Oral ulcers                     | 5         | 50         |
| Lip erosions and crusting       | 3         | 30         |
| Tongue fissuring                | 1         | 10         |
| Lip erosions and crusting + white plaques | 1    | 10         |
| **TOTAL**                       | **10**    | **100**    |

**Systemic involvement**
Out of the 30 patients, 11 (36.7%) had systemic involvement. Polyarthritis was the most common systemic manifestation found in 8 patients (72.7%) followed by ejection systolic murmur in 3 patients, hepatitis in 1, pleuritis in 1 and CNS lupus in 1 patient.

**Table - 16: Histopathologic diagnosis**

| Types                   | No. of Patients | Percentage |
|-------------------------|-----------------|------------|
| CCLE classic discoid    | 25              | 83.3       |
| CCLE verrucous          | 1               | 3.3        |
| SCLE                    | 7               | 23.3       |
| ACLE                    | 1               | 3.3        |

**Histopathological findings**

**Classic CCLE**
Among the 25 histopathologically diagnosed cases of classic CCLE, hyperkeratosis, follicular plugging and atrophy were present in 76%, keratotic plugging in 32%, acanthosis in 24% and hypergranulosis with parakeratosis in 4%. Basal cell degeneration was present in all the cases. Pigment incontinence was present in 36%, dermal edema in 40%, collagen degeneration in 8% and lymphocytic vasculitis in 8%. The dermal infiltrate was patchy in distribution, predominantly perivascular and periappendageal with the infiltrate mainly composed of lymphocytes.
Table - 17: Histopathological findings

|                      | Classic CCLE (25) | SCLE (7) | ACLE (1) | Verrucous CCLE (1) |
|----------------------|-------------------|----------|----------|-------------------|
|                      | No.   | %     | No.   | %     | No.   | No.   | %     |
| 1 Hyperkeratosis     | 19    | 76%   | 6     | 85.7% | 0     | 0     | 1     | 100%  |
| 2 Hypergranulosis    | 1     | 4%    | 0     | 0%    | 0     | 0     | 0     |       |
| 3 Parakeratosis      | 1     | 4%    | 0     | 0%    | 0     | 0     | 0     |       |
| 4 Follicular plugging| 19    | 76%   | 4     | 57.1% | 0     | 0     | 1     | 100%  |
| 5 Keratotic plugging | 8     | 32%   | 0     | 0%    | 0     | 0     | 0     |       |
| 6 Atrophy            | 19    | 76%   | 2     | 28.6% | 0     | 0     | 0     |       |
| 7 Acanthosis         | 6     | 24%   | 3     | 42.9% | 0     | 0     | 1     | 100%  |
| 8 Basal cell degeneration | 25  | 100%  | 7    | 100%  | 1     | 100%  | 1     | 100%  |
| 9 Pigment incontinence| 9    | 36%   | 2     | 28.6% | 0     | 0     | 1     | 100%  |
| 10 Dermal edema      | 10    | 40%   | 3     | 42.9% | 1     | 100%  | 0     |       |
| 11 Dermal infiltrate- |        |        |       |        |       |       |       |       |
| Patchy               | 25    | 100%  | 0     | 0%    | 0     | 0     | 0     |       |
| Diffuse              | 0     | 0%    | 0     | 0%    | 0     | 0     | 1     | 100%  |
| Upper dermal only    | 0     | 0%    | 7     | 100%  | 1     | 100%  | 0     |       |
| 12 Type of Dermal infiltrate (lymphocyte) | 25 | 100% | 7 | 100% | 1 | 100% | 1 | 100% |
| 13 Collagen degeneration | 2   | 8%    | 1     | 14.3% | 0     | 0     | 0     |       |
| 14 Vasculitis        | 2     | 8%    | 0     | 0%    | 0     | 0     | 0     |       |

SCLE
In 7 histopathologically proven cases of SCLE, hyperkeratosis was found in 85.7%, follicular plugging in 57.1%, acanthosis in 42.9%, dermal edema in 42.9%, atrophy in 28.6% and pigment incontinence in 28.6%. Basal cell degeneration was found in all the patients. In all these patients the infiltrate was mainly in the upper dermis and was predominantly composed of lymphocytes. Collagen degeneration was found in 14.3%.

ACLE
There was only a single patient with histopathological diagnosis of ACLE. The findings noted were focal basal cell degeneration with marked upper dermal edema and sparse lymphocytic infiltrate in the upper dermis. Proliferated blood vessels with prominent endothelial cells were noted in the upper dermis.

Verrucous CCLE
The histopathological findings were marked hyperkeratosis, follicular plugging, acanthosis, and basal cell degeneration with pigment incontinence. There was a dense diffuse lymphocytic infiltrate along with a few plasma cells extending to the deep dermis.

Clinical and histopathological correlation
Clinically 24 patients were diagnosed as classic CCLE, 5 patients were diagnosed as SCLE, 4 patients were diagnosed as ACLE, and 1 patient as verrucous CCLE.

Histopathologically 25 patients were found to have classic CCLE, 7 patients were found to have SCLE, 1 patient with ACLE, and 1 patient with verrucous CCLE.

Table - 18: Clinical and histopathological correlation

| Clinical diagnosis | Histopathological diagnosis |
|-------------------|-----------------------------|
|                   | CCLE | SCLE | ACLE |
| CCLE              | 25   |      |      |
| SCLE              | 1    | 4    |      |
| ACLE              |      | 3    | 1    |

All the 24 patients with the clinical diagnosis of classic CCLE were histopathologically proven to be the same. Out of the 5 patients diagnosed as SCLE clinically, 4 patients showed histopathological findings consistent with SCLE, but 1 patient was diagnosed histopathologically as classic CCLE. Clinically 4 cases were diagnosed as ACLE. One patient with ACLE was histopathologically diagnosed as the same. Three patients with clinical diagnosis of ACLE, showed histopathological features of SCLE.

Discussion
LE is a chronic autoimmune inflammatory disease characterized by a multifactorial aetiology and by
a spectrum of cutaneous manifestations. The specific cutaneous lesions are represented by CCLE, SCLE and ACLE.

Thirty patients with clinical features of cutaneous lupus erythematosus attending the department of Dermatology and Venereology, Medical College Hospital, Thiruvananthapuram were studied. On the basis of a careful morphological evaluation, they were separated into three groups: CCLE, SCLE and ACLE. In every patient, clinically diagnosed to have LE specific skin disease, a lesional skin biopsy was taken for histological confirmation. The aims were to study the different clinical patterns and histopathologic features of cutaneous LE, to correlate them and to find out the frequency of systemic lupus erythematosus in patients with cutaneous lupus erythematosus.

In the present study, there were 10 patients belonging to the age group 30-39 years, followed by 8 patients to 20-29 years and 6 patients to 40-49 years. The commonest age group, in which maximum number of patients was found, was 30-39 years. According to the data from literature, cutaneous LE is more commonly seen in the age group of 20-40 years\(^1\),\(^2\) and in this study, 18 (60%) patients belonged to this group. In the present study, majority of patients were females (83%) whereas only 17% were males. The male to female ratio was 1:5 and this female preponderance is well documented in the literature\(^3\). Majority of patients (70%) were unemployed and this high proportion of unemployment may be due to higher proportion of females in this study.

Presenting complaints included scaly rash in 96.6% of patients, followed by photosensitivity in 50%, oral ulcers in 23.3% and Raynaud’s phenomenon in 10% in addition to pruritus, facial oedema, malar rash, lip ulcers, conjunctival congestion, generalised hyperpigmentation, leg ulcers and generalised rash. Systemic complaints were present in seventeen patients and arthralgia was the most common (76.5%). The duration of LE at the time of study ranged from 1 month to 8 years. Majority (86.7%) of patients had short duration illness of less than one year. Among the precipitating factors for cutaneous LE, sunlight was found to be the main culprit. More than half the patients (56.6%) complained that new skin eruptions appeared or the existing lesions flared on exposure to sunlight.

Two (6.7%) out of 30 patients with cutaneous LE had a family history of the disease and classic discoid LE was the LE specific skin manifestation noted in these 2 patients. This was in contrast with the data from various studies regarding the familial occurrence of LE which showed frequencies varying between 12% and 18\(^4\). Pallor was a significant finding noted in 11 (36.6%) patients.

LE-specific skin lesions of different morphological patterns were noted in this study. Majority (86.7%) had monomorphic lesions and the rest had bimorphicles. CCLE (83.3%) was the most common form of cutaneous LE observed. Classic discoid type represented 96% (62.5% localised, 37.5% generalised) of patients with CCLE whereas verrucous type of CCLE was observed in one patient (4%). The localized form of CCLE classic discoid was the most common type representing 62.5% of cases while generalised form represented only 37.5%. This was in conformity with the study by Cardinali\(^5\),\(^6\). The next common type of LE-specific skin lesion observed in this study was SCLE in 5 patients. Analysis of literature has showed that SCLE is usually characterized by papulosquamous and/or annular polycyclic lesions; but in this study, all the 5 (100%) patients had papulo-squamous type of skin lesions. This was in contrast to the study by Cardinali which showed predominantly the annular polycyclic type\(^6\).

Four patients were diagnosed clinically as ACLE and malar rash (75%) was the most common form of ACLE observed in this study, which was in accordance with a previous study\(^6\). Widespread maculopapular rash characteristic of ACLE was seen only in one patient.

LE-nonspecific skin lesions were observed in 16 (53.3%) patients with cutaneous LE. Alopecia was the most common LE nonspecific cutaneous
finding observed (87.5%) and this was in accordance with a study by Tebbe.\(^7\) Other non-specific findings noted in this study were Raynaud’s phenomenon, sclerodactyly and leg ulcers.

Skin biopsy was performed in all the cases, haematoxylin and eosin stained serial sections were studied. Twenty six patients were diagnosed histologically to have CCLE (classic discoid type 25, verrucous type 1), 7 SCLE, and 1 ACLE. CCLE (classic discoid) was found to be the most common histological type noted in 25 (83.3%) patients, followed by SCLE in (23.3%) patients, ACLE in one (3.3%) patient and CCLE verrucous type in a single patient. The histological hallmark of these LE-specific skin lesions was interface dermatitis-basal cell layer vacuolar degeneration with an inflammatory infiltrate at dermo-epidermal junction. Most of the CCLE patients showed characteristic histopathological features like hyperkeratosis (76%), follicular plugging (76%) and keratotic plugging. Epidermis showed variable atrophy (76%) and acanthosis (24%) which is a characteristic finding in CCLE (classic discoid). Pronounced acanthosis reflects greater lesional age. Dermal edema (40%) was a prominent finding in these patients. Superficial as well as deep dermal involvement was noted in almost all patients with a lymphocytic infiltrate predominantly around blood vessels and appendages. Lymphocytic vasculitis was an additional finding observed in 2 patients. Certain discrepancies were observed in the histopathology like hypergranulosis (4%) and parakeratosis (4%). All the 25 patients with CCLE were correlated clinically and histopathologically.

Of the 5 patients diagnosed as SCLE clinically, 4 of them showed histological findings consistent with SCLE. The distinguishing characteristic features of cutaneous LE were found in these patients but the striking feature was an upper dermal lymphocytic infiltrate predominantly around the upper dermal vessels, and in some showing a lichenoid pattern. Thus in 80% of SCLE patients a clinico-histopathological correlation was seen. In a single patient, the clinical diagnosis of SCLE could not be correlated histologically. The dense inflammatory infiltrate, its patchy distribution perivascularly and periappendageal along with significant epidermal atrophy and follicular plugging with diffuse basal cell degeneration favoured the diagnosis of CCLE (classic discoid).

Of the 4 patients diagnosed as ACLE, only one patient had the histopathology consistent with this diagnosis. All the 3 patients with the clinical diagnosis of malar rash were histopathologically proven to be SCLE. Thus a clinico-histological correlation was found only in 25% of patients with ACLE.

Thus a clinical and histopathological correlation was found in 100% of CCLE patients, 80% of SCLE, and 25% of ACLE patients.

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