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Original Research Article

Frequency of Systemic Lupus Erythematosus in Cutaneous Lupus Erythematosus

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Abstract
Background: *Lupus erythematosus (LE) is the root designation for a diverse array of illnesses that are linked together by distinctive clinical findings and characteristic patterns of polyclonal B-cell autoimmunity.*
Materials and Methods: *A clinical non-interventional descriptive study on 30 patients were conducted in a tertiary care centre over a period of 1 year.*
Aim of the study: *To find out the frequency of systemic lupus erythematosus in patients with cutaneous lupus erythematosus. General, dermatological, and systemic examination was done in all patients and documented in the proforma. Relevant investigations were done. Skin biopsies from representative lesions were done in all patients after obtaining their written consent. Detailed histopathological examination was done. 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.*
Results: *36.7% had systemic involvement. Polyarthritis was the most common systemic manifestation. Anti ds-DNA positive in 43.3% patients.83.3% patients with cutaneous LE were found to be ANA positive. Forty eight percent of patients with CCLE, 50% of patients with ACLE and 20% of SCLE patients had antids-DNA positivity. Fifty percent of patients satisfied revised ACR criteria to be classified as SLE.*
Conclusions: *CCLE is the most common type of cutaneous LE. Correlation between the clinical and histological diagnoses has been found to be quite good in CCLE and SCLE; but it has been poor in the case of ACLE.A significant proportion of patients with cutaneous LE is found fulfill the ACR criteria for systemic lupus erythematosus. Of the different types of cutaneous LE, ACLE shows the strongest association with SLE.*
Keywords: *systemic lupus erythematosus, cutaneous lupus erythematosus.*

Introduction

Lupus erythematosus (LE) is the root designation for a diverse array of illnesses that are linked together by distinctive clinical findings and characteristic patterns of polyclonal B-cell autoimmunity.[1]

Many physicians find it convenient to conceptualize LE as a clinical spectrum extending from limited cutaneous disease to life threatening systemic disease process(systemic lupus erythematosus).[1] Systemic lupus erythematosus (SLE) is a systemic disease characterized by multisystem organ inflammation most commonly skin, joints and vasculature, and associated immunologic abnormalities.[2]

Some patients present with serious systemic manifestations of SLE such as nephritis, central nervous system disease or vasculitis, whereas others express only cutaneous manifestations throughout their course of illness, though the basic underlying disease process is the same.[1]

The pattern of skin involvement expressed by an individual patient with LE can provide insight about the position on the spectrum where the patient's illness might best be placed.[1,3] The different types of skin lesions that may be encountered in patients with LE can be subdivided into two broad groups-those that have specific histopathologic features of LE (LE-specific skin disease) and those that are not histopathologically distinct for LE (LE-nonspecific skin disease).[4,5]

The term cutaneous often used synonymously with LE-specific skin disease. The three major categories of LE-specific skin disease are acute cutaneous lupus erythematosus (ACLE), subacute cutaneous lupus erythematosus (SCLE) and chronic cutaneous lupus erythematosus (CCLE).[1]

The types of skin lesions in each group are clinically distinct and recognizing the specific subsets helps in prognosticating the likelihood of underlying systemic lupus.[5] Over 80% of patients with systemic lupus have some form of cutaneous involvement during their course of illness.[6]

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 find out the frequency of systemic lupus erythematosus in patients with 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.

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 3patients, hepatitis in 1, pleuritis in 1 and CNS lupus in 1 patient.

Table - 1: Systemic involvement

Type of involvement	Frequency	Percentage
Polyarthritis	6	54.5
Systolic murmur	3	27.3
Hepatitis + Polyarthritis	1	9.1
Pleuritis + Polyarthritis + CNS lupus	1	9.1
TOTAL	**11**	**100**

Laboratory evaluation

Anaemia (Hb< 11gm% in females and <12gm% in males) was observed in 7 (23.3%) patients; it was of microcytic hypochromic type. Other findings noted were raised ESR (7), albuminuria (6), 24 hour urine protein > 500mg (2), raised urea and creatinine (1), ECG showing ST-elevation suggestive of myocardial infarction (1) and chest X-ray with bilateral lower zone haziness suggestive of pleural effusion (1).

Table - 2: Laboratory evaluation

Lab test	Frequency	Percentage
Anaemia	7	23.3
Raised ESR	7	23.3
Albuminuria	6	20.0
24hr urine protein > 500mg	2	6.7
Raised urea and creatinine	1	3.3
Raised liver enzymes	1	3.3
ECG ST-elevation	1	3.3
Chest X-ray bilateral lower zone haziness	1	3.3

Immunological parameters

Out of the 30 patients, ANA was positive in 25 (83.3%), antids-DNA positive in 13 patients (43.3%), LE cell positive in 3 (10%) patients and rheumatoid factor positive in 2 (6.7%) patients.

Table - 3: Autoantibodies

Autoantibodies	Frequency	Percentage
ANA alone	11	36.7
ANA + antids-DNA	10	33.3
ANA + antids-DNA + LE cell	2	6.7
ANA + antids-DNA + Rheumatoid factor	1	3.3
ANA + LE cell + Rheumatoid factor	1	3.3

LE specific skin lesions and ANA test

Twenty five (83.3%) patients with cutaneous LE were found to be ANA positive. Seventy two percent of patients with CCLE, 60% of SCLE patients and 100% of patients with ACLE, were found to be positive for ANA.

Table - 4: LE specific skin lesions vs. ANA positivity

LE specific types	Frequency	ANA	Percentage
CCLE	25	18	72
SCLE	5	3	60
ACLE	4	4	100

LE specific skin lesions and antids-DNA positivity

Forty eight percent of patients with CCLE, 50% of patients with ACLE and 20% of SCLE patients had antids-DNA positivity.

Table - 5: LE specific skin lesions and antids-DNA positivity

LE specific types	Frequency	Antids-DNA	Percentage
CCLE	25	12	48
SCLE	5	1	20
ACLE	4	2	50

SLE

Fifty percent of patients satisfied revised ACR criteria to be classified as SLE.

SLE patients included 9 (60%) cases of classic discoid LE localised, 5 (55.5%) cases of classic discoid LE generalized, 1 (20%) of SCLE and 3 (75%) of ACLE.

Table - 6: LE specific skin lesions and SLE

Types	SLE			
	Yes	Percentage	No	Percentage
CCLE classic discoid (localised)	9	60	6	40
CCLE classic discoid (generalised)	5	55.5	4	45.5
SCLE	1	20	4	80
ACLE	3	75	1	25

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.

In this study, half of the patients with cutaneous LE were found to have SLE. They included 9 (60%) cases of CCLE classic discoid localised type, 5 (55.5%) cases of CCLE classic discoid generalised type, 1 (20%) of SCLE, and 3 (75%) cases of ACLE. Thus, a total of 14 patients (58.3%) with CCLE classic discoid type were found to have SLE. Data from the literature has shown that the risk of development of SLE in a patient presenting with CCLE classic discoid localised alone, is less than 5% and in the case of CCLE classic discoid generalised it is 22%.The findings in our study was in contrast to this. The high value obtained in the present study might be due to the patient selection. The inclusion of patients who had CCLE classic discoid as a manifestation of SLE might account for the high incidence of SLE in these patients.

Among the 5 SCLE patients, only 1 (20%) satisfied the ACR criteria to be classified as SLE. Out of the four patients with ACLE, 3 (75%) patients were found to have SLE of which two patients had malar rash and one had maculopapular rash. Though 56.6% of patients complained of various systemic symptoms, only 36.7% patients had evidence of systemic involvement in this study. Musculoskeletal involvement in the form of polyarthritis (72.5%) was the most common systemic involvement noted. This was in accordance with data from literature.[7,8] Hepatitis, pleuritis, CNS lupus, and ischemic heart disease were the other manifestations of systemic involvement.

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.[9] Other nonspecific findings noted in this study were Raynaud's phenomenon, sclerodactyly and leg ulcers.

Various investigations were done to evaluate these patients for systemic involvement. Though 11 (36.6%) patients had pallor, only seven patients showed laboratory evidence of anaemia which was of microcytic hypochromic type. This was in contrast to the normochromic normocytic anaemia probably associated with systemic lupus erythematosus. Microcytic hypochromic anaemia noted in this study may be part of the disease itself, or more commonly due to iron deficiency which is quite common in our population. In this study, six patients showed evidence of nephritis on investigation. Immunological parameters found to be positive in this study were ANA in 83.3% patients, antids-DNA in 43.3%, LE cell test in 10%, and rheumatoid factor in 6.7% of patients. Seventy two percent of CCLE patients were found to be ANA positive. This was in contrast to a study by Beck.[10] This high value of ANA observed in CCLE discoid type in this study might be due to patient selection. If serum samples from patients with classic discoid LE with extracutaneous disease were to be excluded, only a small percentage of patients with classic discoid LE would have had ANA positivity. Sixty percent of SCLE and all the ACLE patients were found to be positive for ANA.

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 peri-appendageal 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.

Conclusion

The most common clinically diagnosed LE-specific skin disease in this study was CCLE (83.3%) and the classic discoid type (localized 62.5%, generalized 37.5%) was the commonest type of CCLE noted. Papulosquamous type of skin lesions was noted in all SCLE patients and malar rash (75%) was the most common finding in patients with ACLE.

The most common LE nonspecific finding was alopecia seen in 87.5% of patients. Twenty percent of patients with cutaneous LE had nail changes and nail fold erythema was the most common nail involvement observed. Oral mucosal involvement was seen in 33.3% of patients and oral ulcers were the most common oral lesion noted. Musculoskeletal involvement in the form of polyarthritis was the most common systemic manifestation seen in 72.7% of patients.

Seventy two percent of CCLE, 60% percent of SCLE, and 100% percent of ACLE patients were ANA positive. Forty eight percent of CCLE, 20% percent of SCLE and 50% percent of ACLE patients were antids-DNA positive.

CCLE (classic discoid type) was the commonest histologic type of LE specific skin disease (83.3%) noted in this study. Clinical and histopathological correlation was seen in 100% of CCLE patients, 80% of SCLE, and in only 20% of ACLE patients.

Fifty percent of patients with cutaneous LE satisfied the ACR criteria to be classified as systemic lupus erythematosus. They included 60% of CCLE classic discoid (localised), 55.5 % of CCLE classic discoid (generalized), 20% of SCLE and 75% of ACLE.

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Bibliography

1. Costner MI, Sontheimer RD. Lupus erythematosus. In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, editors. Fitzpatrick's Dermatology in General Medicine. 6th ed. New York : McGraw Hill; 2003. 1677-93.
2. Goodfield MJD, Jones SK, Veale DJ. The connective tissue diseases. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Text Book of Dermatology. 7th ed. Massachusets: Black well Science; 2004. 56.1-56.147.
3. Petty RE, Laxer RM. Systemic lupus erythematosus. In: Cassidy JT, Petty RE, Laxer RM, Linsley CB, editors. Textbook of Paediatric Rheumatology. 5th ed. Philadelphia: Elsevier Saunders; 2005. 342-83.
4. Sontheimer RD. The lexicon of cutaneous lupus erythematosus. A review and personal perspective on nomenclature and classification of cutaneous manifestation of LE. Lupus. 1997; 6: 84-95.
5. Callen JP. Update on the management of cutaneous lupus erythematosus. Br J Dermatol. 2004; 151: 731-36.
6. Kotzin BL, West SG. Systemic lupus erythematosus. In: Rich RR, Fleisher TA, Shearer WT, Schroeder Jr HW, editors. Clinical Immunology Principles and Practice. 2nd ed. New York: Mosby; 2001. 60.1- 60.24.
7. Hahn BH. Systemic lupus erythematosus. In : Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. Harrison's principles of Internal Medicine. 16th ed. New York: Mc Graw Hill; 2005. 1960-67.
8. Hahn BH, Karpouzas GA, Tsao BP. Pathogenesis of systemic lupus erythematosus. In: Harris ED, Budd RC, Pirestein GS ,Genovese MC, Sergent JS, Ruddy S et al, editors. Kelley's textbook of Rheumatology. 7th ed. Philadelphia: Elsevier Saunders; 2004. 1174-1200.
9. Tebbe B. Clinical course and prognosis of cutaneous lupus erythematosus. Clin Dermatol. 2004; 22: 121-4
10. Beck JS, Rowell NR. Discoid lupus erythematosus. A study of the clinical features and Biochemical and Serological abnormalities in 120 patients with observations on the Relationship of this disease to systemic lupus erythematosus. Q J Med. 1966; 35: 119-136.