A CLINICAL STUDY OF THE CUTANEOUS MANIFESTATIONS OF LUPUS ERYTHEMATOSUS

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ABSTRACT

BACKGROUND

Lupus Erythematosus (LE) is a group of heterogenous autoimmune diseases with an array of manifestations ranging from cutaneous lesions to life-threatening systemic manifestations. Cutaneous manifestations are the second most common feature and it serves as an important diagnostic aid. The nonspecific skin lesions are associated with more active disease.

The aim of the study is to study the pattern and prevalence of cutaneous manifestations in LE and to study the correlation between cutaneous manifestations and systemic involvement.

MATERIALS AND METHODS

Study comprised of 48 patients of lupus erythematosus who attended the Department of Dermatology and Venereology in a tertiary referral centre from a period of November 2010 to November 2012. Patients were subjected to detailed clinical examination, routine investigations, ANA, anti-dsDNA, ANA profile, non-lesional skin biopsy for lupus band test.

RESULTS

48 patients were taken for the study. The peak incidence was in the age group of 30-40 (33.33%) yrs. There was female predominance, the ratio being 5.86:1. Discoid Lupus Erythematosus (DLE) constitutes 37.5% and Systemic Lupus Erythematosus (SLE) 62.5%. Majority of DLE patients (38.89%) presented late in 5-9 yrs., whereas SLE patients presented early within 1-6 months (50%). Most frequent presenting features were arthralgia (54.17%), oral ulcers (45.83%). Renal system was the most common system affected (16.67%). Most common haematological abnormality was anaemia and raised ESR (40%). Most common immunological abnormality was raised ANA in 66.7% and raised anti-dsDNA (60%). Most frequent biochemical abnormality was albuminuria and raised 24-hours urine protein. Lupus band was positive in 58.33% and all had renal involvement. Mortality was 6.67%.

CONCLUSION

In this study, we got comparable results in epidemiological parameters like age and distribution with other studies. The incidence of ANA negative SLE was higher (33.33%) in our study. Though majority of patients with renal involvement had a positive lupus band test, a statistical significance could not be sought in this regard on account of low sample size.

KEYWORDS

Lupus Erythematosus, Cutaneous Lesions, System Involvement, Lupus Band Test.

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BACKGROUND

Lupus Erythematous (LE) is a group of heterogeneous autoimmune disease with a diverse array of clinical manifestation with antibodies directed against cell nuclei.[1] These manifestations encompass a spectrum ranging from a few discoid lesions of Cutaneous Lupus Erythematous (CLE) to the life-threatening manifestations such as nephritis, central nervous system disease and vasculitis of Systemic Lupus Erythematosus (SLE).[2] Skin is the second most commonly affected organ after joint involvement.[3] The Gilliam classification divides the cutaneous manifestation of lupus erythematosus into lupus specific and lupus nonspecific skin disease.[2,4] Lupus specific skin disease include Chronic Cutaneous Lupus Erythematosus (CCLE), Subacute Cutaneous Lupus Erythematosus (SCLE) and Acute Cutaneous Lupus Erythematous (ACLE).[2,4] Recognising the specific subsets of skin lesions in lupus erythematosus helps in prognosticating the likelihood of underlying systemic involvement.[2] Acute Cutaneous Lupus Erythematous (ACLE) is almost always associated with manifestations of systemic lupus erythematosus. Patients presenting with Subacute Cutaneous Lupus Erythematous (SCLE) lesions constitute 7-27% of patient with lupus erythematosus. Classic Discoid Lupus Erythematosus (DLE) lesions are present in 15-30% of patient with systemic lupus erythematosus.[2] Approximately, 5% of patients presenting with localised subsequently develop systemic lupus erythematosus.[2] Lupus

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nonspecific skin lesions are associated with more active disease and thus require more aggressive disease monitoring and therapy.[1] This study is undertaken to evaluate the pattern of cutaneous involvement, prevalence of cutaneous lesions and correlate cutaneous manifestations with systemic involvement.

MATERIALS AND METHODS

Forty eight patients with lupus erythematous who attended the Department of Dermatology and Venereology in a tertiary referral centre from November 2010 to November 2012 were included in the study. Ethical committee clearance is obtained initially. Detailed history was taken including age, onset of disease, duration, past history, any triggering factors and family history. A detailed clinical examination was carried out. The ACR criteria were used to diagnose the SLE patients. Investigations were done including routine blood with platelet count, urine examination, 24-hour urine protein, renal and liver function tests, serum electrolytes, random blood sugar, HIV, HbsAg, chest x-ray and ECG. Peripheral smear and LE cell demonstration were done in all patients. Immunological tests like ANA, ANA profile, VDRL, APLA, C3 and C4 were also done. Skin biopsy from the uninvolved covered area (buttock/inner aspect of thigh) was done in all patients who were willing and is sent in Michel's medium for Lupus Band Test (LBT).

Study Design- Descriptive study.
Analysis Method- Data entered in excel and statistical analysis performed using Microsoft Excel and Statistical Package for Social Sciences (SPSS).

RESULTS

The present study included forty eight patients of lupus erythematosus. The maximum number of patients were in fourth (33.33%) decade with a male-to-female ratio of 1:5.86. Out of 48 patients, 62.5% patients had SLE and 37.5% patients had DLE. No SCLE patients were there during the study period. Majority (50%) of SLE patients presented themselves within 6 months of disease duration. Most of the DLE patients presented in 5-9 years.

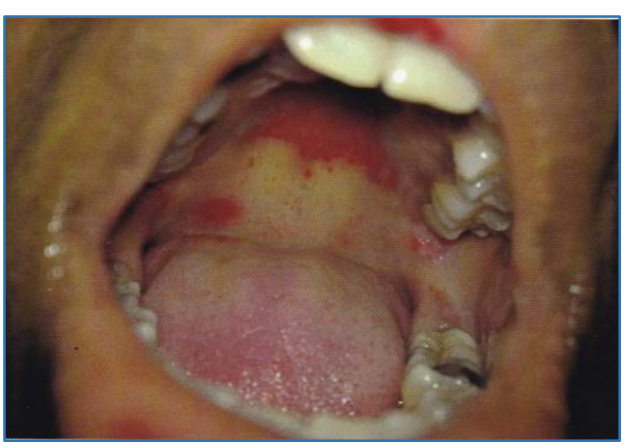

Figure 1. Oral Ulcer

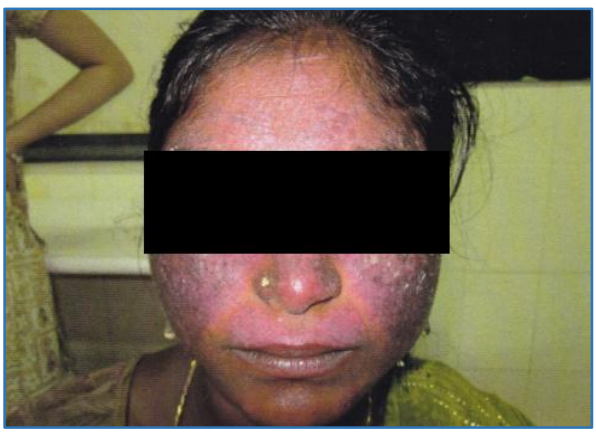

Figure 2. Malar Rash

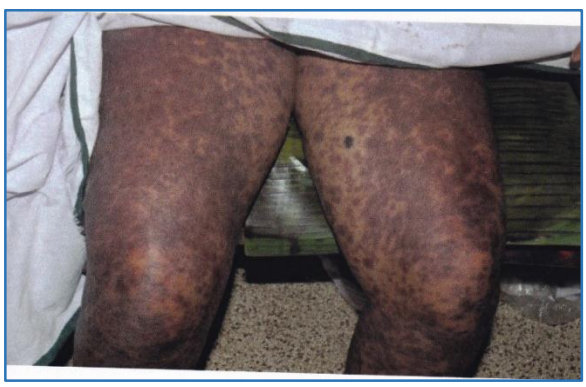

Figure 3. TEN like Rash

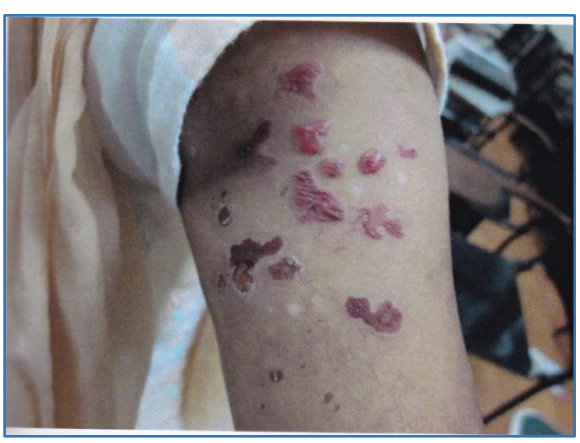

Figure 4. Bullous Lesion

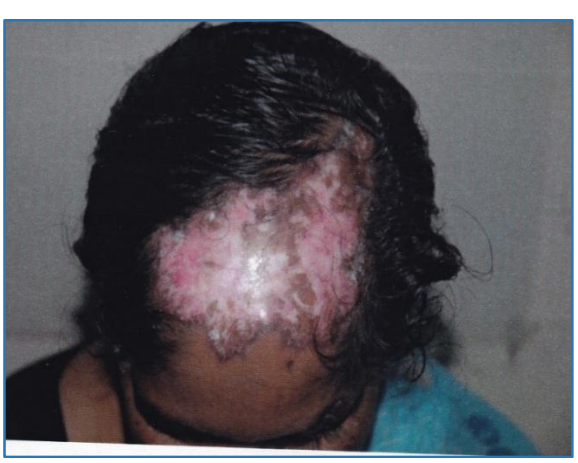

Figure 5. Scarring Alopecia

Of the 48 LE patients, the most frequent presenting feature was arthralgia in 26 (54.17%) closely followed by oral ulcer (Figure 1) in 22 (45.83%) and localised DLE plaques in 16 (33.33%). 13 (27.08%) patients had malar rash (Figure 2) and 11 (22.92%) patients had photosensitivity. 8 (16.67%) patients had pedal oedema. 6 (12.5%) patients each had generalised ACLE and generalised DLE rash. 5 (10.42%) patients had purpura and 4 (8.33%) patients each had diffuse alopecia and fever. 3 (6.25%) patients each had TEN-like rash (Figure 3), generalised bullous lesions (Figure 4), scarring alopecia (Figure 5), Raynaud's phenomenon, leg ulcers and urticated plaque lasting more than 24 hrs. Oral lichen planus was present in 2 (4.17%) patients. 1 (2.08%) patient each had chilblains, verrucous plaque, lichen planus plaque in other areas and fungating plaque on DLE lesion (Table 1).

Presentations	SLE	DLE
Malar rash	13 (43.33%)	0
Generalised rash	6 (20%)	0
TEN-like rash	3 (10%)	0
Bullous lesions-generalised	3 (10%)	0
DLE localised	3 (10%)	12 (66.67%)
DDLE	1 (3.33%)	5 (27.78%)
Arthralgia/arthritis	22 (73.33%)	4 (22.22%)
Oral ulcer	18 (60%)	4 (22.22%)
Photosensitivity	9 (32%)	2 (11.11%)
Alopecia-diffuse	4 (13.33%)	0
Alopecia-scarring	0	3 (16.67%)
Raynaud's phenomenon	3 (10%)	0
Fever	4 (13.33%)	0
Pedal oedema	8 (26.67%)	0
Purpura	5 (16.67%)	0
Lichen planus - oral	1 (3.33%)	0
Lichen planus - else where	1 (3.33%)	1 (5.56%)
Chilblains	1 (3.33%)	0
Verrucous plaque	0	1 (5.56%)
Sweet syndrome	0	1 (5.56%)
Urticarial vasculitis	3 (10%)	0
Leg ulcer	3 (10%)	0
Fungating plaque on DLE	1 (3.33%)	0

Table 1. Presenting Features in SLE and DLE

Type of Lesion	Number of Patients	Percentage (%)
1. ACLE		
A) Malar rash	13	27.08%
B) General rash	6	12.50
C) Ten-like rash	3	6.25%
2. SCLE	0	
3. CCLE		
Classic DLE-		
Localised	16	37.78%
Generalised (DDLE)	6	12.50%
Mucosal	2	4.17%
Chilblains	1	2.08%
LE/LP overlap	2	4.17%

Table 2. Type of LE Specific Lesions

Type of Nonspecific Lesions	Number of Patients	Percentage
1. Vascular		
A) Vasculitis		
I. Leukocytoclastic vasculitis		
a) Palpable purpura	5	10.42
b) Urticarial vasculitis	3	6.25
B) Periungual telangiectasia	1	2.08
C) Raynaud phenomenon	3	6.25
2. Non-scarring alopecia		
I. Lupus hair	4	8.33
2. Sclerodactyly	2	4.17
3. Le-nonspecific bullous lesion	3	6.25
4. Acanthosis nigricans	2	4.17
5. Leg ulcers	3	6.25
6. Lichen planus	3	6.25

Table 3. LE-Nonspecific Lesions

The most common general abnormality in SLE patients was pallor, which occurred in 21 (70%), followed by pedal oedema in 8 (26.67%) and fever in 5 (16.67%) patients. 3 (10%) patients had generalised lymphadenopathy and 2 (6.67%) patients had tachycardia. Most common specific lesion was localised DLE in 16 (37.78%) patients followed by malar rash in 13 (27.08%) patients. 6 (12.5%) patients each had generalised DLE and generalised ACLE rash. 3 (6.25%) patients presented with TEN like rash. 2 (4.17%) patients each had mucosal DLE lesion and LE/LP overlap and 1 (2.08%) patient had chilblains (Table 2). Table 3 shows nonspecific lesions.

SLE patients had erosions in the hard plate (29.17%), lips (12.5%) and under surface of tongue (4.17). In the DLE patients, 3 (6.25%) patients presented with erosions in the hard plate and 1 (2.08%) patient with white lacy plaque in the buccal mucosa.

Of the 48 patients, major involvement was noted in renal system. 8 (16.67%) of patients had albuminuria and elevated 24-hours urine protein. 2 (4.17%) patients each had altered renal function. In other systems, 2 (4.17%) patients each had seizures, CVA, retinal vasculitis, hepatomegaly and raised liver enzymes. 1 (2.08%) patient each had pulmonary artery hypertension. Patients with systemic involvement were all having SLE except one patient with retinal vasculitis having DDLE.

Most common haematological abnormalities among SLE patients were anaemia and raised ESR occurred in 12 (40%) patients. Leucopenia occurred in 9 (18.75%) patients and lymphopenia in 4 (8.33%) patients. 2 (6.67%) patients had thrombocytopenia. Most common immunological abnormality among SLE patients was raised ANA titre in 20 (66.67%) patients followed by raised anti-dsDNA titre in 18 (60%). Anti-Sm antibody was positive in 6 (20%) and SSA was positive in 5 (16.67%) patients. 4 (13.33%) patients each presented with AMA m2, nucleosome and

antiphospholipid antibody. 3 (10%) patients each had complement C3 deficiency and ribosomal P protein. 2 (6.67%) patients each had RNP and antihistone. 1 (3.33%) patients each had PCNA and complement C4 deficiency. Among DLE patients, 2 (11.11%) patients presented with positive ANA and 1 (5.56%) patients each presented with SSA and AMA M2. Out of 12 patients, 7 (58.33%) patients of SLE who were having positive lupus band had renal involvement and 4 (33.33%) patients with negative lupus band had no renal involvement. Lupus band was negative in 1 (3.33%) patient with renal involvement. Among SLE patients, 4 (13.33%) had hypothyroidism and 3 (10%) had hypertension. One patient had diabetes. One patient with DDLE had vitiligo. Among SLE patients, 2 (6.67%) patients each had cerebrovascular accidents, seizures, squamous cell carcinoma developing on DLE plaque and mortality. 1 (3.33%) patient each had fracture hip, retinal vasculitis, pulmonary embolism and pulmonary artery hypertension. 1 (5.56%) patient of DDLE developed retinal vasculitis.

DISCUSSION

The present study included forty eight patients of lupus erythematosus between 12 years to 60 years with majority of patients fourth decade (33.33%). Dubois and Tuffanelli reported an average age group of 27.7 yrs. in their study.[5] Studies from Norway and Sri Lanka reported average age of 36 years and 32 years, respectively.[6,7] In our study, majority were females (85.42%) with male-to-female ratio 1:5.86. Thumboo et al,[8] Moss et al[9] and Estes and Christian[10] reported 93%, 92% and 91% female sex, respectively. This explains the role of sex hormones in humoral autoreactivity.[2] Most studies have reported a male-to-female ratio of 1:8 to 1:15.[5,8,9,10,11] The occurrence of lupus erythematosus in manual labourers explains the role of sun exposure in the pathogenesis of lupus erythematosus.[12,13,14] None of them had any family history of similar illness.[15,16] There were no history of any precipitating drugs or infection in contrary to many studies, which purpose roles of infection,[2,17] stress and triggering drugs[18,19,20,21] in initiating autoreactivity. In our study, majority of patients had SLE (62.5%) compared to DLE (37.5%). We did not encounter any case of SCLE during the study period. Of the 48 patients, the most frequent presenting feature was arthralgia in 54.17% closely followed by oral ulcer, DLE plaques in 45.83% each and alopecia in 14.58%. Studies report arthralgia as the most frequent feature followed by cutaneous manifestations.[5,8,9,10,11] In this study, photosensitivity was present in 22.92% patients.

The incidence of arthralgia is lower compared to other studies. This maybe because other studies were mainly on SLE population, whereas in our study, we included all subtypes in the spectrum of LE. Thumboo et al[8] reported a lower incidence 62% similar to our study. The incidence of alopecia was lower (14.5%) compared to other studies. Moss et al reported 17% incidence of alopecia similar to our study. Our study had a lower incidence of photosensitivity (22.92%) compared with others.[9,11] We got a higher incidence of anaemia (70%) compared with other studies, 57% in Dubois' study. Most common specific lesion was localised DLE in 16 (37.78%) patients followed by malar rash in 13 (27.08%) patients. 6 (12.5%) patients had generalised ACLE rash. 3 (6.25%) patients presented with TEN like rash. Zeimer et al studied 17 cases of SLE presenting with TEN-like rash, which is a very rare form of acute LE.[22] We got only one case of chilblains. Around 20% cases of chilblains can develop SLE later.[2,23] Most frequent nonspecific lesion in this study is palpable purpura, which occurred in 5 (10.42%) of patients followed by lupus hair in 4 (8.33%). We got a similar incidence of leg ulcers in our study compared to 10% in the literature.[24] We got 3 cases of bullous LE in our study. This form of LE has a predilection to develop lupus nephritis or it occurs along with lupus nephritis. All 3 patients had lupus nephritis in our study.[2,25,26]

Most common haematological abnormalities among SLE patients were anaemia and raised ESR occurred in 12 (40%) patients, and in peripheral smear, all cases of anaemia showed a hypochromic microcytic picture. No cases of haemolytic anaemia were detected in our study. Leucopenia occurred in 9 (18.75%) patients and lymphopenia in 4 (8.33%) patients. 2 (6.67%) patients had thrombocytopenia. Tuffanelli reported 43% incidence of leucopenia and 7% incidence of thrombocytopenia. Most common immunological abnormality among SLE patients was raised ANA titre in 20 (66.67%) patients followed by raised anti-dsDNA titre in 18 (60%). Anti-Sm antibody was positive in 6 (20%) and SSA was positive in 5 (16.67%) patients, (10%) patients each had complement C3 deficiency and ribosomal P protein. Among DLE patients, 2 (11.11%) patients presented with positive ANA and 1 (5.56%) patient with SSA. Christian, Thumboo et al, Tan et al and Moss et al reported positive ANA titre in 87%, 93%, 99% and 94% patients, respectively. Thumboo et al, Tan et al and Moss et al reported anti-dsDNA in 86%, 67% and 60%, respectively. In our study, we got a lower incidence of antiphospholipid antibody (13.33%). A meta-analysis undertaken by Love and Santora estimated an average frequency of 34% for the lupus anticoagulant and 44% for anticardiolipin antibodies in studies representing over 1000 lupus patients.[27] ANA negative SLE is reported in 10% of SLE.[28,29] In our study, we got a higher incidence of ANA negative SLE (33.33%).

Only SLE patients had biochemical abnormalities with most common finding being albuminuria and raised 24-hour urine protein >500 mg in 8 (26.67%) patients each. 2 (6.67%) patients each presented with granular cast in the urine and altered LFT. 1 (3.33%) had altered renal function. Dubois, Tuffanelli and Moss et al reported renal involvement in 40% and 31%, respectively. Out of 12 patients, Lupus Band Test (LBT) was demonstrated in 58.33% and all these patients had renal involvement. The role of non-lesional lupus band in patients with renal involvement have been proposed in many studies. Burnham and Fine observed a 3 times more chance of renal involvement in covered skin LBT-positive patients. Studies by Dantzing et al[30] and Provost and Ahmed[31]also found a positive correlation between covered skin LBT and renal involvement in SLE. In our study, also a higher percentage of positivity of non-lesional lupus band

was obtained. However, its statistical significance could not be inferred on account of low sample size.

1 (3.33%) patient each had fractured hip, retinal vasculitis, squamous cell carcinoma on DLE plaque, pulmonary embolism and pulmonary artery hypertension. Pan et al reported pulmonary artery hypertension in 5.83% in their study.[32] Pulmonary thromboembolism in seen along with antiphospholipid antibody syndrome in 10%.[33] In our patient, however, antiphospholipids were negative. Grand mal seizures can occur as an initial manifestation in 5% of SLE and 20% of patients had developed it eventually in the course of the disease.[34] We could not correlate statistically between the cutaneous manifestations and systemic involvement on account of low sample size.

CONCLUSION

Age distribution showed a peak incidence in the fourth decade. Female-to-male ratio was 5:86:1. Among lupus erythematosus, majority were presented with SLE. Among lupus specific skin lesion, most common was DLE plaque. Nonspecific lesions were more encountered in SLE patients. We got a higher incidence of oral ulcers. Most common haematological abnormality was anaemia and raised ESR. Lupus band test was positive in all patients with renal involvement except in one patient.

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