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STUDY OF CLINICAL PROFILE IN PATIENTS WITH CUTANEOUS LUPUS ERYTHEMATOSUS & THEIR CORRELATION BETWEEN TYPES OF LESION.

Medicine

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ABSTRACT

Background: This study was done to find out incidences of various types of cutaneous lupus erythematosus lesions & presence or abscence of clinical findings pertaining to various organ systems of the body among them. We also studied correlation between those clinical findings with types of cutaneous lupus erythematosus.

Methods: 79 pts of Clinically diagnosed cases of cutaneous LE having LE specific skin lesions as classified by Gilliam's criteria & indeterminate cases diagnosis was done by histopathology of skin lesions were included in this study after considering exclusion criteria over a period of one year. Detailed history,physical examinations, routine blood,urine investigations & histopathology of skin lesions were done as per proforma & data were analyzed with appropriate statistical tests to determine the significance and power of the study.

Results: We studied 79 CLE patients (satisfying the inclusion criteria) over the entire study period of 12 months. The study population had male:female ratio of 4:75. Mean age of study population was 27.58yr. Among the 79 patients 32 patients had pure ACLE i.e.40.51%, 19 patients had SCLE i.e. 24.05%, 15 patients had pure CCLE i.e. 18.99%, 11 patients had both ACLE and CCLE i.e. 13.92% ,1 patient had Bullous LE i.e. 1.27% and 1patients had both ACLE and Bullous LE i.e. 1.27%. In our study, systemic features correlated with types of CLE. While correlating ACLE with different systemic features we found significant association with fever($p=0.022$), history of seizure and psychosis($p<0.0001$), palpable lymphnode and hepatosplenomegaly($p=0.0002$), serositis($p=0.003$) but no association was found with pallor, oral ulcer, pedal oedema and periorbital puffiness.In case of SCLE significant association was found with fever($p=0.022$), pallor($p=0.022$), history of psychosis($p=0.022$) and palpable lymphnode($p=0.022$) but no association was found with other systemic parameters.In case of CCLE significant association was found with fever($p=0.002$), pallor($p=0.01$) and periorbital puffiness($p=0.039$) and in case of ACLE-CCLE overlap significant association was found with fever($p=0.016$) and periorbital puffiness($P=0.016$).

Conclusion: Our study indicates that presence of fever, psychosis, history of seizure , hepatosplenomegly, lymphadenopathy in patients presenting with cutaneous lupus erythematosus should alert the physician regarding systemic involvement and thus in those situation relevant investigation should be conducted to evaluate the presence of systemic involvement.

KEYWORDS

CLE-Cutaneous Lupus Erythematosus,ACLE-Acute Cutaneous Lupus Erythematosus,SCLE-Subacute Cutaneous Lupus Erythematosus,CCLE-Chronic Cutaneous Lupus Erythematosus.

Introduction:

The autoimmune disease lupus erythematosus is associated with a broad range of cutaneous pathology. Cutaneous manifestations are frequently the presenting sign of lupus erythematosus (LE), and in the case of certain cutaneous lupus erythematosus (CLE) subtypes, they can occur in the absence of systemic disease. CLE is two to three times more frequent than SLE. [1]A Swedish population based study found that 25% of CLE patients previously held an SLE diagnosis, and that 20% of newly diagnosed CLE patients received a diagnosis of SLE within three years.Gilliam proposed a classification system that separated LE-specific lesions from LE-nonspecific lesions, based on histopathology. The various morphologies of CLE fall under the umbrella of LE-specific lesions, including acute cutaneous LE (ACLE), subacute cutaneous LE (SCLE), and chronic cutaneous LE (CCLE). Acute cutaneous LE typically presents in the third decade of life and is frequently associated with active SLE. [2] There are localized and generalized forms of ACLE. The localized form is the frequently described malar, or "butterfly" rash, which refers to erythema that occurs over both cheeks, extends over the nasal bridge, and spares the nasolabial folds. [3]These lesions are classically transient, sun-induced, and non-scarring, although dyspigmentation can occur. [4] Patients may initially mistake this rash for a sunburn, and only seek medical attention when it persists for several days. A fine surface scale and/or edema may be associated with the erythema. Malar rashes have been reported to be present in up to 52% of SLE patients at the time of diagnosis, with clinical activity of the rash paralleling that of the systemic disease. This rash can be confused with acne rosacea and seborrheic dermatitis, however the former is associated with the formation of papules and pustules, and the latter occurs within the nasolabial folds. [5]

As with SLE, Subacute Cutaneous Lupus Erythematosus (SCLE) occurs primarily in young to middle aged women. [6] SCLE is highly photosensitive, with 70-90% of patients meeting the ACR definition of abnormal photosensitivity.[7]There are two morphologic variants of SCLE: annular and papulosquamous. The annular type is characterized by scaly annular erythematous plaques, which tend to coalesce and produce a polycyclic array. [8]The papulosquamous variant can resemble eczema or psoriasis, as well as pityriasis in some instances.[9][10]SCLE lesions occur in sun-exposed areas, including the upper thorax ('V' distribution), upper back, and the extensor surfaces of arms and forearms. The central face and scalp are usually spared, and lesions typically do not occur below the waist. [3].The cutaneous lesions are not indurated and heal without scarring, although vitiligo-like hypopigmentation may occur. [11] An estimated 50% of SCLE patients meet criteria for SLE. [12] Patients with SCLE usually have only mild systemic symptoms, most commonly arthritis and myalgias, while severe systemic symptoms, such as lupus vasculitis, CNS lupus, and nephritis occur in less than 10%. [13] CCLE encompasses discoid LE (DLE), LE profundus (LEP), chilblain LE (CHLE), and LE tumidus (LET). [14] Discoid lesions are the most common lesions of CCLE. DLE occurs more frequently in women in their fourth and fifth decade of life. [3] Patients with DLE generally have a more benign disease course as compared to patients with other CLE subtypes, with only a reported 5-10% developing SLE throughout their disease course. [14,15]Studies have shown that patients with generalized DLE are more likely to progress to systemic disease, compared to patients with localized DLE. [9] Localized DLE commonly involves the head and neck, and particularly the scalp and ears. Generalized DLE, which occurs both above and below the neck, is less common and typically involves the extensor forearms and hands.[3] Occasionally, DLE can occur on mucosal surfaces, including lips, and oral, nasal, and genital mucosa. DLE lesions appear as a well-demarcated, scaly, erythematous macule or papule, which gradually develops into an indurated discoid (coin-shaped) plaque with an adherent scale that is painful to remove. Plaques tend to extend into the hair follicle, resulting in scarring alopecia. Through time, these lesions typically become atrophic, with hyperpigmentation peripherally and depigmentation centrally. Sun exposure or trauma (Koebner phenomenon) can exacerbate disease. Squamous cell carcinoma can occur within a DLE lesion. [16] LE-nonspecific lesions, on the other hand, include findings that are not characteristic of, but are frequently seen in SLE. Such lesions include Raynaud's phenomenon, periungual telangiectasias, livedo reticularis, and leukocytoclastic vasculitis. CLE diagnosis should be based on the findings of patient history, clinical exam, laboratory studies, serology, as well as histology and direct immunofluorescence (DIF) exam of skin biopsies if the histology is not diagnostic.

Material & Methods:

79 pts of Clinically diagnosed cases of cutaneous LE having LE

specific skin lesions as classified by Gilliam's criteria & in indeterminate cases diagnosis were done by histopathology of skin lesions,were included in this study after considering exclusion criteria over a period of one year. Detailed history, physical examinations, routine blood, urine investigations & ANA titre-pattern ,histopathology of skin lesions were done as per proforma & data were analyzed with appropriate statistical tests to determine the significance and power of the study.

Results & Analysis:

We studied 79 CLE patients (satisfying the inclusion criteria) over the entire study period of 12 months. The study population had male:female ratio of 4:75. Mean age of study population was 27.58yr.

The study population 11.39% were from urban area and 88.61% were from rural area. The study population 55.70% were working at home and 44.30% were working outside home.

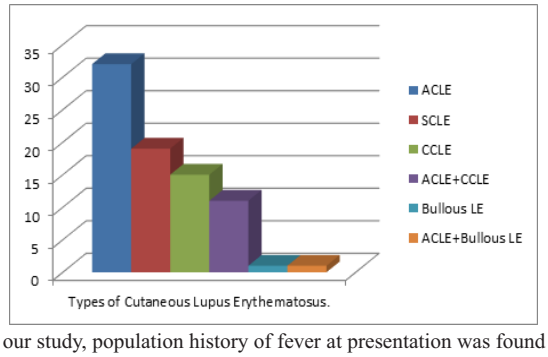
Table 1: Distribution of study population acc. to types of CLE

	Cutaneous Lupus without systemic involvement (n=6)	Cutaneous Lupus with systemic involvement (n=73)	Total=79	P value
Types of Cutaneous Lupus				
ACLE	2	30	32	p< 0.0001*
SCLE	2	17	19	0.0098*
CCLE	2	13	15	0.0013*
ACLE+CCLE	0	11	11	
Bullous LE	0	1	1	
ACLE+ Bullous LE	0	1	1	

Test for significance of difference performed by * Unpaired T-test and ** Fisher's Exact Test

Among the 79 patients 32 patients had pure ACLE i.e.40.51%, 19 patients had SCLE i.e. 24.05%, 15 patients had pure CCLE i.e. 18.99%, 11 patients had both ACLE and CCLE i.e. 13.92% ,1 patient had Bullous LE i.e. 1.27% and 1patients had both ACLE and Bullous LE i.e. 1.27%[Table1,Figure1].

Figure1: Distribution of study population according to type of CLE (n=79)



In our study, population history of fever at presentation was found in 56.96% patients. Thus it can be proposed that fever could be strong predictor of systemic involvement in patients with CLE (Table2). Fever had similar incidence as compared to the large scale studies on presentations of SLE[17-19].While correlating fever with types of CLE significant association was found with ACLE(p=0.002), SCLE(p=0.022), CCLE(p=0.002) and ACLE-CCLE overlap(p=0.016). (Table 3a,3b,3c,3d)Thus irrespective of types of CLE fever is a strong predictor and necessitate exploring systemic involvement. Thus importance of fever is highlighted in definition of lupus flare where flares were frequently characterized by constitutional symptoms like fever, weight loss, musculoskeletal involvement, cutaneous involvement, and decreasing levels of C3 and C4 in prospective cohort study of Petri M, Genovese M et al[20].Photosensitivity was present 70.89% study population.

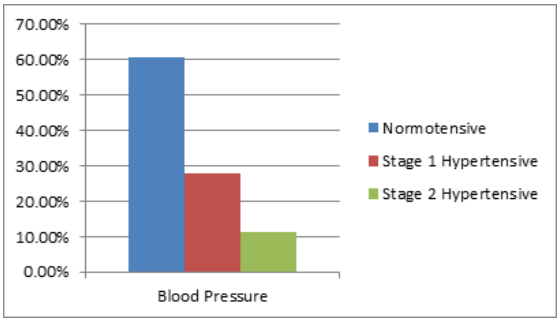
Table 2: Clinical profile of Study population

Clinical Profile	Present	Absent	P value
Fever (Present: Absent)	45	34	0.0048**
Photosensitivity (Present:Absent)	56	23	0.3496**
Pallor (Present: Absent)	52	27	0.0162**
Periorbital puffiness (PresentAbsent)	20	59	1.0000**
Oral ulcer (Present: Absent)	43	36	1.0000**
Alopecia (Present: Absent)	32	47	0.0373**
Pedal edema (Present: Absent)	33	46	0.3921**
Joint Pain (Present: Absent)	47	32	0.2158**
History of Seizure (Present: Absent)	5	74	1.0000**
Psychosis (Present: Absent)	8	71	1.0000**
Bleeding manifestation (Present: Absent)	11	68	0.5875**
Digital gangrene (Present: Absent)	3	76	1.000**
Tachycardia (Present: Absent)	28	51	0.0842**
Blood pressure			0.1341*
Normotensive	6	42	
Stage 1 Hypertensive	0	22	
Stage 2 Hypertensive	0	9	
Lymphnode (Present: Absent)	8	71	1.0000**
Hepatosplenomegaly (Present: Absent)	13	66	0.5820**
Serositis (Present: Absent)	16	36	0.3383**

Test for significance of difference performed by * Unpaired T-test and ** Fisher's Exact Test

In the study population, tachycardia was present 35.44% of study population and 38.36% patients of CLE with systemic involvement. During presentation 60.76% patient had normal blood pressure, 27.85% patient had stage 1 hypertension and 11.39% patient had stage 2 hypertension according to JNC-7 classification of hypertension.(Figure2) In South-eastern United States inception cohort studied at Johns Hopkins Medical centre in 140 patients of Lupus nephritis 64% were hypertensive[18].

Figure2: Distribution of study population according to Blood Pressure. (n=79)



Pallor was present 65.82% of study population. Pallor is strong predictor of systemic involvement and chance of haematological involvement is very high. In our study pallor shows significant association with SCLE (p=0.022) and CCLE(p=0.01).Oral ulcer was present in 54.43% of study population. Majority of patients with different systemic involvement had oral ulcer. Alopecia was present 40.51% patients of study population and 83.33% patients of CLE without systemic involvement had alopecia. Pedal oedema, a common clinical marker of renal involvement, was present in 41.77% cases, and periorbital puffiness was there in 25.32% cases in our study. In our study periorbital puffiness had significant association with SCLE(p=0.039) but no association found between pedal oedema and types of CLE.(Table3b,3c)

Table3a: Correlation between Clinical profile and ACLE.

Types of CLE	Systemic features (yes/no)	Chi-square	Significance level
ACLE (n=32)	Fever (23/9)	5.281	P = 0.022
	Pallor(22/10)	3.781	P = 0.052
	Oral ulcer(13/19)	0.781	P = 0.377
	Pedal oedema(15/17)	0.031	P = 0.860
	Periorbital puffiness(13/19)	0.781	P = 0.377
	History of seizure(1/31)	26.281	P < 0.0001
	History of psychosis(4/28)	16.531	P < 0.0001

	Lymph node(5/27)	13.781	P = 0.0002
	Hepatosplenomegaly(5/27)	13.781	P = 0.0002
	Serositis(7/25)	9.031	P = 0.003

Table3b: Correlation between Clinical profile and SCLE.

Types of CLE	Systemic features (yes/no)	Chi-square	Significance level
SCLE(n=19)	Fever(15/4)	5.263	P = 0.022
	Pallor(15/4)	5.263	P = 0.022
	Oral ulcer(10/9)	0.000	P = 1.000
	Pedal oedema(10/9)	0.000	P = 1.0000
	Periorbital puffiness(12/7)	0.842	P = 0.039
	History of psychosis(4/15)	5.263	P = 0.022
	Lymph node(4/15)	5.263	P = 0.022
	Hepatosplenomegaly(5/14)	3.368	P = 0.067
	Serositis(5/14)	3.368	P = 0.039

Table3c: Correlation between Clinical profile and CCLE.

Types of CLE	Systemic features (yes/no)	Chi-square	Significance level
CCLE (n=15)	Fever (14/1)	9.600	P =0.002
	Pallor(13/2)	6.67	P = 0.010
	Oral ulcer(9/6)	0.267	P = 0.606
	Pedal oedema(9/6)	0.267	P = 0.606
	Periorbital puffiness(12/3)	4.267	P = 0.039
	History of psychosis(4/11)	2.400	P = 0.121
	Lymph node(4/11)	2.400	P = 0.121
	Hepatosplenomegaly(5/10)	1.067	P = 0.302
	Serositis(5/10)	1.067	P = 0.302

Table3d: Correlation between Clinical profile and ACLE+CCLE.

Types of CLE	Systemic features (yes/no)	Chi-square	Significance level
ACLE+CCLE	Fever (10/1)	5.818	P = 0.016
	Pallor(9/2)	3.273	P = 0.070
	Oral ulcer(7/4)	0.364	P = 0.547
	Pedal oedema(7/4)	0.364	P = 0.547
	Periorbital puffiness(10/1)	5.818	P = 0.016
	History of psychosis(4/7)	0.364	P = 0.547
	Lymph node(3/8)	1.455	P = 0.228
	Hepatosplenomegaly(4/7)	0.364	P = 0.547
	Serositis(5/6)	0.000	P = 1.000

Joint pain was present 59.49% of study population and 61.64% patients of CLE with systemic involvement. Joint pain is strong predictor of systemic involvement and this finding was similar to large scale studies from Europe [21-24].

History of seizure and psychosis was present 6.33% and 12.12% of study population respectively and 6.85% and 10.96% patients of CLE with systemic involvement had history of seizure and psychosis respectively (Table2). In our study history of seizure had significant association with ACLE($p<0.0001$) and significant association also found between history of psychosis and ACLE($p<0.0001$) and SCLE($p=0.022$). Thus presence of ACLE lesions in patients with history of seizure and psychosis necessitates the exploration for neurological involvement. In our study, 13.92% had bleeding manifestation and 3.8% had digital gangrene(Table 2).Vocks E et al reported that digital gangrene is a rare manifestation of SLE without APLA syndrome[24].

During presentation 16.46% of our patients had hepatosplenomegaly and 10.12% patient had significantly palpable lymph nodes. In the multiethnic Grupo Latino Americano de Estudio de Lupus (GLADEL) cohort, it was present in 5% of subjects at disease onset, and in 15% during evolution[13]. In our study, significant association was found between hepatoslenomegaly and ACLE($p=0.0002$). Significant association was found between lymphadenopathy and ACLE($p=0.0002$) and SCLE($p=0.022$).In our study, Serositis was present 20.25% of study population. As only clinical examination was performed to detect serositis, presence of parietal oedema could have masked the diagnosis. In our study, serositis had significant association with SCLE with p value 0.039(Table3b). Thus presence of SCLE necessitates the exploration for serositis.

Conclusion:

Our study indicates that presence of fever, psychosis, history of seizure , hepatosplenomegly, lymphadenopathy in patients presenting with cutaneous lupus erythematosus should alert the physician regarding systemic involvement and thus in those situation relevant investigation should be conducted to evaluate the presence of systemic involvement.

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