

Original Article

Cutaneous manifestations of systemic lupus erythematosus

系統性紅斑狼瘡的皮膚病學表現

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Cutaneous manifestations are important aspects of systemic lupus erythematosus (SLE) disease. This study intended to study the cutaneous manifestations of SLE patients from the Chinese population in Hong Kong. This is a cross-sectional study based on Gilliam's Classification of Lupus Erythematosus (LE)-Associated Skin Lesions. Telogen effluvium (27.8%), Raynaud's phenomenon (14.8%), periungual telangiectasia (13.0%) and urticaria (9.6%) were the most common LE-non-specific skin diseases at interview. Localised acute cutaneous lupus erythematosus (ACLE, 38.3%), discoid lupus erythematosus (DLE, 9.6%) and subacute cutaneous lupus erythematosus (SCLE, 9.6%) were the most common LE-specific skin diseases.

皮膚病學表現是系統性紅斑狼瘡的重要方面。是項研究著眼於本港華人系統性紅斑狼瘡患者的皮膚病學表現。是項研究為按Gilliam氏紅斑狼瘡皮損分類法的橫斷性研究。休止期落髮(27.8%)，雷諾氏現象(14.8%)，指甲週毛細血管擴張(13.0%)及蕁麻疹(9.6%)為最常見的非紅斑狼瘡特異性皮損。局限性急性皮膚型紅斑狼瘡(ACLE, 38.3%)，盤狀紅斑狼瘡(DLE, 9.6%)，亞急性皮膚型紅斑狼瘡(SCLE, 9.6%)為最常見的紅斑狼瘡特異性皮損。

Keywords: Chinese, cutaneous manifestations, Systemic lupus erythematosus

關鍵詞：華人、皮膚病學表現、系統性紅斑狼瘡

Introduction

Systemic lupus erythematosus in Chinese

Systemic lupus erythematosus (SLE) is the most diversifying autoimmune disease affect any organ of the body. The diversity of expression of the

disease is determined by genetic, demographic and environmental factors.^{1,2} Study had shown that the Chinese had higher prevalence of SLE^{3,4} compared with other ethnic groups with an estimated point prevalence of 0.06% in Southern Chinese.⁵

Gilliam's classification of cutaneous manifestations

Lupus erythematosus (LE) patients are at risk of developing an extremely diverse array of clinically distinctive types of skin lesions. The overall percentage of all types of skin lesions in SLE patients ranged from 55% to 100%.⁶ Skin

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involvement has long been central to the conceptual framework that physicians have used to deal with this disease.⁷

Gilliam initially proposed the nomenclature and classification system for cutaneous manifestations in LE patients in 1977.^{8,9} The classification attempted to clarify the confusion from the use of ambiguous and competing terms for the plethora of skin lesions that can be encountered in LE patients. Gilliam classified the cutaneous manifestations of LE according to: 1) those which show the characteristic histopathology of lupus erythematosus (LE-specific) and 2) those that are associated phenomena without any characteristic histopathologic changes of LE (LE-nonspecific). The LE-specific lesions can be further subdivided into acute, subacute and chronic forms (Table 1).

The aim of this study is to study the cutaneous manifestations in SLE patients in our locality using the Gilliam's classification system.

Materials and methods

Subjects and setting

SLE patients were recruited from three large rheumatological centres in Hong Kong: Queen Elizabeth Hospital (QEH), Tai Po Hospital (TPH) and Queen Mary Hospital (QMH).

Inclusion criteria

All patients who were ethnic Chinese with the diagnosis of SLE in the medical notes were recruited. An informed consent was obtained from each patient for study participation.

Exclusion criteria

Patients who were unable to give accurate data or consent due to cognitive impairment or psychiatric illness were excluded. Those with skin lesions only (that is, cutaneous lupus erythematosus without systemic involvement) as well as drug-induced LE were excluded.

Duration

These study centres were visited on a weekly basis for six months from March 2005 to August 2005.

Analysis

Continuous variables were expressed as mean \pm standard deviation (SD) unless otherwise specified. The cutaneous lesions were categorised into LE-specific and non LE-specific.

Statistical analyses were performed using SPSS software, version 11.0 (Chicago, Illinois).

Results

Demographic data

During the study period, a total number of 115 patients were recruited (Table 1). All consecutive patients joined the study. Nine patients (7.8%) were male, constituting a male to female ratio of 1 to 12. The mean age at the time of interview was 38.8 (± 11.9) years old while the median was 39.0 (25th and 75th percentile were 30 and 46 respectively). The median duration of illness was 6 years (first and third quartile were 3 and 11 years respectively). The majority needed systemic steroid for disease control ($n=82$, 71.3%). For those who were on steroid, the mean dose of prednisolone was 8.7 mg (± 6.4 mg) per day while the median dose was 5 mg (first and third quartile were 0.0 and 10 mg respectively). Nearly half of them were on anti-malarials ($n=57$, 49.6%). Systemic immunosuppressives were prescribed in 55 patients (47.8%).

American College of Rheumatology (ACR) criteria (Table 2)

The mean number of clinical and laboratory features that fulfilled the ACR classification criteria (ACR criteria) for the study population was 5.4 (± 1.4) (Table 3). The five most frequent positive criteria were: (1) positive ANA (titre ≥ 160)-92.2%,

Table 1. Gilliam's Classification of Lupus Erythematosus (LE)-Associated Skin Lesions⁹**I. LE-non-specific rheumatological skin diseases**

- A. Cutaneous vascular disease
 - 1. Vasculitis
 - 1.1 Leukocytoclastic
 - 1.1.1 Palpable purpura
 - 1.1.2 Urticarial vasculitis
 - 1.1.2 Periarthritis nodosa like cutaneous lesions
 - 2. Vasculopathy
 - 2.1 Degos' disease-like lesions
 - 2.2 Secondary atrophie blanche (livedoid vasculitis, livedo vasculitis)
 - 2.3 Periungual telangiectasia
 - 2.4 Livedo reticularis
 - 2.5 Thrombophlebitis
 - 2.6 Raynaud's phenomenon
 - 2.7 Erythromelalgia (erythermalgia)
- B. Nonscarring alopecia
 - 1. Lupus hair
 - 2. Telogen effluvium
 - 3. Alopecia areata
- C. Sclerodactyly
- D. Rheumatoid nodules
- E. Calcinosis cutis
- F. LE-nonspecific bullous lesions
- G. Urticaria
- H. Papulonodular mucinosis
- I. Cutis laxa/aneuroderma
- J. Acanthosis nigricans

II. LE-specific skin diseases

- A. Acute cutaneous LE [ACLE]
 - 1. Localised ACLE
 - 2. Generalised ACLE
- B. Subacute cutaneous LE [SCLE]
 - 1. Annular SCLE
 - 2. Papulosquamous SCLE
- C. Chronic cutaneous LE (CCLE)
 - 1. Classic discoid LE [DLE]
 - 1.1 Localised DLE
 - 1.2 Generalised DLE
 - 2. Hypertrophic/verrucous DLE
 - 3. Lupus profundus/lupus panniculitis
 - 4. Mucosal
 - 4.1 Oral
 - 4.2 Conjunctival
 - 5. Lupus tumidus (urticarial plaque of LE)
 - 6. Chilblains LE (chilblains lupus)
 - 7. Lichenoid DLE (LE/lichen planus overlap)

Table 2. The 1982 revised criteria for classification of SLE¹⁰

Criterion	Definition
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging, atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
5. Arthritis	Nonerosive arthritis involving 2 or more peripheral joints, characterised by tenderness, swelling or effusion
6. Serositis	a) Pleuritis-convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion OR b) Pericarditis-documented by ECG or rub or evidence of pericardial effusion
7. Renal disorder	a) Persistent proteinuria greater than 0.5 gms per day or greater than 3+ if quantification not performed OR b) Cellular casts-may be red cell, haemoglobin, granular, tubular, or mixed
8. Neurologic disorder	a) Seizures-in the absence of offending drugs or known metabolic derangements, e.g., uraemia, ketoacidosis, or electrolyte imbalance b) Psychosis-in the absence of offending drugs or known metabolic derangement; e.g., uraemia, ketoacidosis, or electrolyte imbalance
9. Haematologic disorder	a) Haemolytic anaemia-with reticulocytosis OR b) Leukopenia-less than 4,000/mm ³ total on 2 or more occasions OR c) Lymphopenia-less than 1,500/mm ³ on 2 or more occasions OR d) Thrombocytopenia-less than 100,000/mm ³ in the absence of offending drugs
10. Immunologic disorder#	a) Positive LE cell preparation OR b) Anti-DNA: antibody to native DNA in abnormal titre OR c) Anti-SM: presence of antibody to SM nuclear antigen OR d) False positive serologic test for syphilis known to be positive for at least 6 months and confirmed by <i>Treponema pallidum</i> immobilisation or fluorescent treponemal antibody absorption test
11. Antinuclear antibody	An abnormal titre of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome

A person shall be said to have SLE if any 4 or more of the 11 criteria are present, serially or simultaneously, during any interval of observation. (Adopted from Tan EM. Special antibodies for the study of systemic lupus erythematosus: an analysis. Arthritis Rheum 1982;25:753-6.)

Update from the Diagnostic and Therapeutic Criteria Committee of the ACR in 1997: Delete 10 a), change 10 d) to positive finding of antiphospholipid antibodies based on 1) an abnormal serum level of IgG or IgM anticardiolipin antibodies, 2) a lupus anticoagulant using a standard method, 3) false positive serologic test for syphilis known to be positive for at least 6 months and confirmed by *Treponema pallidum* immobilisation or fluorescent treponemal antibody absorption test.

(2) arthritis-83.5%, (3) immunologic disorder-81.7%, (4) malar rash-76.5%, (5) photosensitivity-64.3%.

Skin manifestations at presentation and interview

The skin manifestations at interview were shown in Figures 1, 2 and 3. The data on presentation were included for comparison.

LE-specific skin diseases at interview

Forty-four patients (38.3%) had localised ACLE while nine patients (7.8%) had generalised ACLE. Eleven patients had SCLÉ lesions (9.6%); six belonged to the annular subtype (5.2%) and five belonged to the papulosquamous subtype (4.3%). Eleven (9.6%) patients had classic DLE. Eight of them had localised form and presented

Table 3. ACR criteria in the study cases

Criteria	Frequency (N=115)	Percentage
Malar rash	88	76.5
Discoid rash	12	10.4
Photosensitivity	74	64.3
Oral ulcers	17	14.8
Arthritis	96	83.5
Serositis	14	12.2
Renal disorder	36	31.3
Neurologic disorder	16	13.9
Haematologic disorder	64	55.7
Immunologic disorder	94	81.7
Antinuclear antibody	106	92.2
ACR criteria (mean, SD)	5.37 (1.38)	
Range (min - max)	1 - 8	
Median (1st & 3rd quartile)	5 (5, 6)	

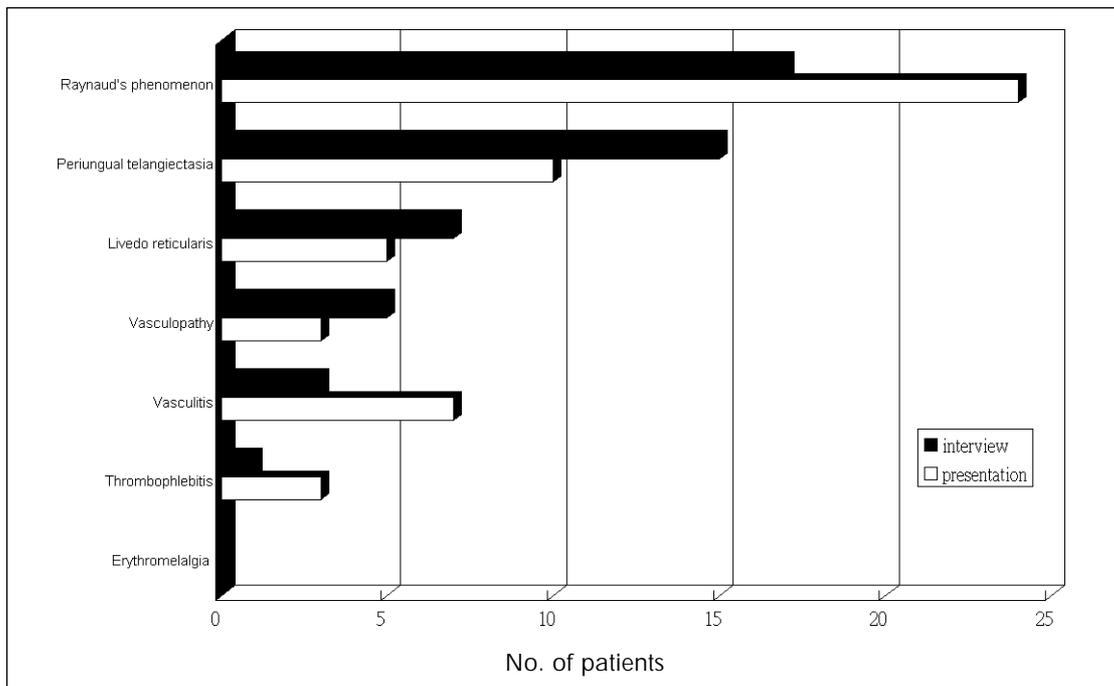


Figure 1. Cutaneous vascular diseases at presentation and interview.

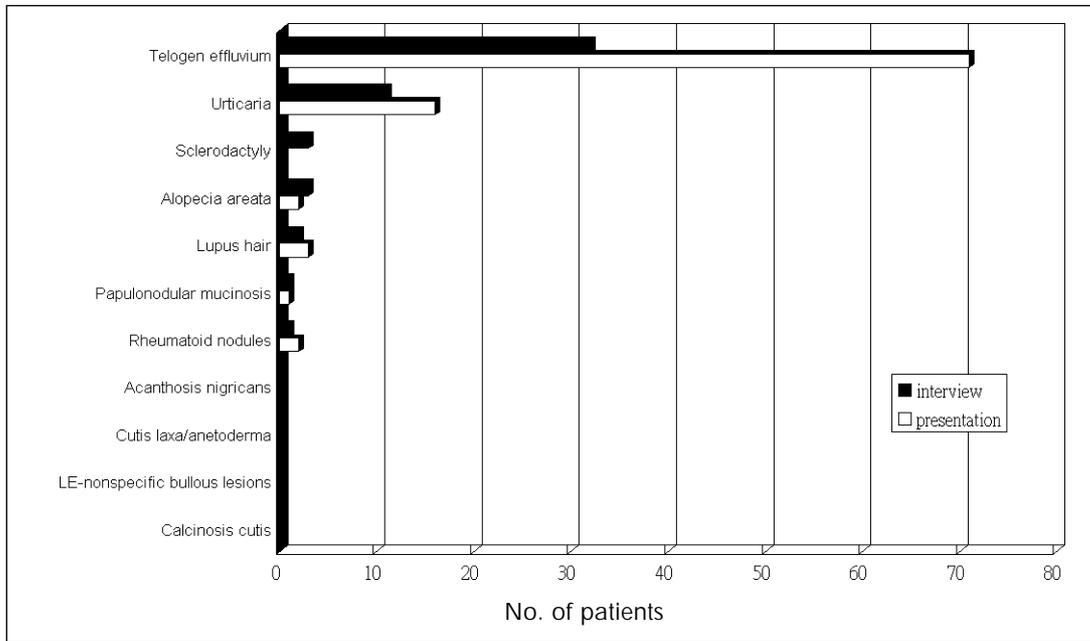


Figure 2. Other LE-nonspecific lesions at presentation and interview.

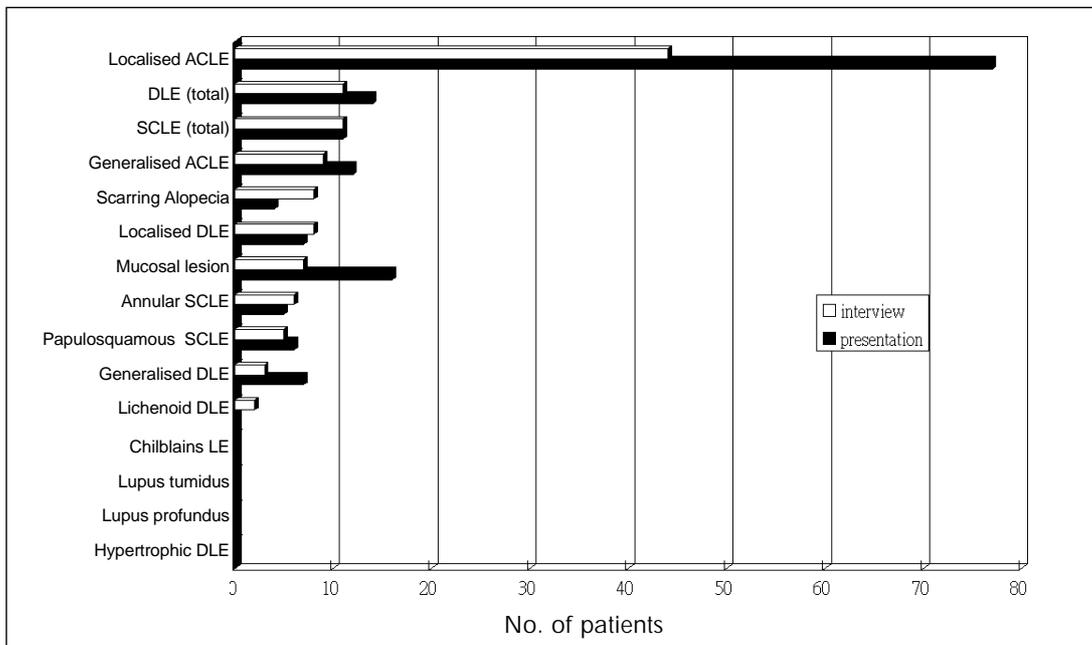


Figure 3. LE-specific lesions at presentation and interview.

with scarring alopecia as solitary lesion or accompanied by other localised DLE features. The remaining three had generalised DLE. Seven patients (5.1%) had oral mucosal lesions. Two patients (1.7%) had lichenoid DLE.

LE-nonspecific skin diseases at interview

The commonest finding in this category was telogen effluvium (n=32, 27.8%). This was followed by Raynaud's phenomenon (n=17, 14.8%), periungual telangiectasia (n=15, 13%) and urticaria (n=11, 9.6%).

Non-rheumatological skin diseases at interview

The commonest skin manifestation in this category was xerosis and ichthyosis (n=57). This was followed by steroid-induced changes (n=29). Fungal infection was noted in 16 patients. Among which, four had more than one site of fungal infection and one had three sites. The commonest infection was tinea pedis (n=15). Nail abnormalities were noted in eight patients. These consisted of onycholysis, ridging and thickening of the nails. Other dermatosis noted during the interview included eczema (n=21), acne (n=5), seborrheic dermatitis (n=5), psoriasis (n=2) and drug eruption (n=2). Ten patients had skin pigmentation after taken anti-malarial drugs.

Discussion

ACLE

The commonest cutaneous manifestation related to SLE in our patients was localised acute cutaneous LE or malar rash. Two third of our patients presented with ACLE while other overseas studies showed that ACLE were present in 21-58% of their patients.^{1,6,11} A tendency of higher prevalence of localised acute cutaneous LE (56-70%) was reported by other local studies.^{5,8,12,13} It frequently coincides with exacerbations of systemic disease.⁸ Generalised ACLE is a less common variety which presents as a more widespread morbilliform or exanthematous eruption. ACLE is very photosensitive and can be transient, lasting only several days or weeks. A comparison was made for cutaneous manifestations between our patients and the cutaneous aspects from previous local and overseas studies (Table 4).

Telogen effluvium

The prevalence of telogen effluvium was also higher in our patients. Gilliam as well as other workers had used this term to describe the diffuse, non-scarring hair loss in LE patients.^{14,15}

However, in usual dermatological practice, telogen effluvium may have slight different

implications. Telogen effluvium refers to an acute, diffuse hair loss occurring 3-4 months after a medical event. Surgical shock, haemorrhage, high fever, crash dieting, drugs, childbirth and psychological illness are common causes. Anagen hairs are prematurely precipitated into catagen phase during the illness. As the hairs reach the telogen phase, new anagen hairs develop and displace the telogen hairs resulting in abrupt hair loss. Recovery is expected in about 3 to 4 months spontaneously.

In LE patients, the diffuse nonscarring alopecia is the result of the severe catabolic effects of the lupus disease activity. It can be acute or occurring 2 to 3 months after a flare of the lupus disease activity and can also be chronically associated with a 'silent' continuing lupus disease activity. As a result, the hair loss may be long-lasting in some patients even though they are clinically quiescent otherwise.

Photosensitivity

The percentage of photosensitivity was 64%, which was higher than that in the Euro-lupus cohort.¹ In fact, a wide range of photosensitivity prevalence was reported in the literature in SLE patients, ranging from 24% to 83%.^{1,4,6,7,9,11,14,15} There is a clear relationship between ultraviolet radiation (UVR) and the clinical manifestations.¹⁶ Moreover, UVR not only induces cutaneous eruptions, but also it will cause systemic reactions like weakness, fatigue, fever, hair loss and joint pain.^{9,14,15} There can be a delay of several months after the UV exposure in the summer months for the disease flare.

Urticaria

There were some suggestions that urticaria was associated with more aggressive clinical activity as reported previously.⁶ However, these studies were deficient in the sense that a distinction was not made between urticaria and urticarial vasculitis. A clear distinction of urticaria from urticarial vasculitis would require not only detailed clinical history, but also skin biopsy to confirm the clinical suspicion. Patients with typical urticarial

Table 4. Skin lesions (LE and LE-nonspecific) at both presentation and interview, comparison between different studies

	Presentation	Interview	Yell ⁶	Weinstein ¹¹	Cervera ¹ Presentation	Cervera ¹ Interview	Mok ⁵	Wong ¹³
No. of cases	115	115	73	84	1000	1000	709	156
Year of study	2005	2005	1996	1990	2003	2003	2003	1991
	N (%)	N (%)	%	%	%	%	%	%
I. LE-nonspecific skin diseases								
A. Cutaneous vascular disease								
1. Vasculitis	7 (6.1)	3 (2.6)	11	18				26
2. Vasculopathy	3 (2.6)	5 (4.3)						
3. Periungual telangiectasia	10 (8.7)	15 (13.0)		16				
4. Livedo reticularis	5 (4.3)	7 (6.1)		18	5	14		
5. Thrombophlebitis	3 (2.6)	1 (0.9)						
6. Raynaud's phenomenon	24 (20.9)	17 (14.8)	60		18	34	24	19
7. Erythromelalgia	0 (0)	0 (0)						
B. Nonscarring alopecia								
1. Lupus hair	3 (2.6)	2 (1.7)	40					
2. Telogen effluvium	71 (61.7)	32 (27.8)					41	20
3. Alopecia areata	2 (1.7)	3 (2.6)						
C. Sclerodactyly								
D. Rheumatoid nodules	0 (0)	3 (2.6)						
E. Calcinosis cutis	2 (1.7)	1 (0.9)						
F. LE-nonspecific bullous lesions	0 (0)	0 (0)						
G. Urticaria	0 (0)	0 (0)						
H. Papulonodular mucinosis	16 (13.9)	11 (9.6)	44					
	1 (0.9)	1 (0.9)						
II. LE-specific skin diseases								
A. Acute cutaneous LE								
1. Localised ACLE	77 (67.0)	44 (38.3)	45	21	40	58	56	56
2. Generalised ACLE	12 (10.4)	9 (7.8)						
B. Subacute cutaneous LE								
1. Annular SCLE	5 (4.3)	6 (7.8)		21	3	6		
2. Papulosquamous SCLE	6 (5.2)	5 (4.3)	7					
C. Chronic cutaneous LE								
1. Classic discoid LE	14 (12.2)	11 (9.6)	25	11	6	10	12	3
1.1 Localised DLE	7 (6.1)	8 (7.0)						
Scarring Alopecia	4 (3.5)	8 (7.0)	14					
1.2 Generalised DLE	7 (6.1)	3 (2.6)						
2. Hypertrophic DLE	0 (0)	0 (0)						
3. Lupus profundus	0 (0)	0 (0)						
4. Mucosal involvement	16 (13.9)	7 (5.1)	55		11	24	11	4
5. Lupus tumidus	0 (0)	0 (0)						
6. Chilblains LE	0 (0)	0 (0)	21					
7. Lichenoid DLE	0 (0)	2 (1.7)						

Note (Table 2):

- LE-nonspecific skin diseases: our patients had lower frequency of cutaneous vasculitis compared with other oversea studies. The ranges of prevalence of livedo reticularis and Raynaud's phenomenon in other studies were 18-60% and 5-18% respectively. The prevalence in our patients for both conditions was at the lower end of the range. Similarly, the prevalence of periungual telangiectasia was also in the lower end of the range. In other words, our SLE patients tended to have less cutaneous vascular disease. The prevalence of telogen effluvium was higher while the prevalence of urticaria was lower than other studies.
- LE-specific skin diseases: two third of our patients had localised ACLE at presentation. The prevalences of SCLE as well as DLE were comparable with other studies.

vasculitis may present with pain, pyrexia (systemic upset), purpura, post-inflammatory hyperpigmentation and pruritus in addition to the cutaneous lesions lasting for more than 24 hours.

Limitations of the study

The patients were recruited from three centres. There could be observer bias due to different management approach and interpretation. Different treatment regimens among patients may affect the cutaneous presentation. The skin lesions at presentation were retrospectively retrieved from the medical records and thus could contribute to errors. The patient numbers in some of lesion categories were too small to produce statistical significant results. Clinically unstable patients requiring hospital admission and patients having cutaneous lupus without systemic involvement were not included.

Conclusion

In summary, this study has demonstrated the protean cutaneous manifestations of SLE patients in our local population. The impacts of skin morbidities on patients' quality of life deserve further evaluation in the future.

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