Research article

Cutaneous manifestations in systemic lupus erythematosus patients attending a tertiary hospital in Nigeria

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Abstract

Background: Systemic Lupus Erythematosus (SLE) is a systemic autoimmune connective tissue disorder. The clinical presentation is protean and it affects the skin, joints and other internal organs. The American College of Rheumatology criteria for diagnosis has four cutaneous signs out of the eleven. SLE can be diagnosed in patients who present with only skin features, in the presence of a serological marker according to the Systemic Lupus International Collaborating Clinics (SLICC) criteria.
Objective: This study aimed to document the cutaneous findings in SLE patients who presented at the Lagos University Teaching Hospital (LUTH).
Methods: This was a retrospective study of SLE patients who presented to the Rheumatology/Dermatology clinics of LUTH. Data was obtained from the clinic register and patients' case record files.
Results: Systemic lupus erythematosus was diagnosed in 90 (23.9%) of the 377 patients with rheumatologic conditions. Fifty (55.6%) of these patients had cutaneous lesions. Twenty eight patients (48.9%) had acute cutaneous LE, 10 (21.3%) had sub-acute cutaneous LE; while 14 (29.8%) had chronic cutaneous LE. There was a female preponderance with the male to female ratio of 1: 14.7. The mean age of presentation was 33.5 + 14.3 (range was 9 - 68 years). The mean duration of symptoms was 28.4 ± 38.8 months. Other cutaneous lesions were alopecia, photosensitivity, oral ulcers and malar rash.
Conclusions: Skin lesions are common presentation of SLE, yielding valuable diagnostic information essential for early diagnosis, prompt management, and reduction in frequency of flares and complications.

Key words: Lupus, Connective tissue diseases, Cutaneous clues to systemic diseases

Introduction

Systemic Lupus Erythematosus (SLE) is a systemic autoimmune connective tissue disorder. The term was first coined by Sir William Osler in 1895 when he reported some cardiac, pulmonary, renal and cutaneous features of the condition. The modern concept of SLE was described in 1948 with discovery of LE cells by Hargraves and his colleagues[1,2]. It has a worldwide prevalence and is reported to be about four times more prevalent in blacks than whites, and a female preponderance. Until recently, it was thought to be rare in Africans as a result of paucity of data. The clinical presentation is protean ranging from cutaneous only to affectation of joints and other organs of the body[3].

The skin because of its visibility provides an early marker for SLE. While cutaneous lupus on its own does not cause severe morbidity or mortality, it is a pointer enabling early diagnosis of other life threatening features of SLE such as haematologic, renal and neurological manifestation. Cutaneous lupus has also been noted to severely impair the quality of life of individuals with lupus comparable to some common cutaneous and chronic systemic disorders[4]. The American College of Rheumatology (ACR) in 1997 developed a set of criteria for the diagnosis of SLE based on the specific findings of patients[5]. The importance of cutaneous manifestations in making a diagnosis of lupus is highlighted by the American College of Rheumatology criteria for diagnosis of SLE which includes 4 cutaneous criteria out of 11. The skin findings may be the initial presentation predating other systemic features; and SLE can be diagnosed in patients who present with only skin features, in the presence of a serological marker according to the more recent Systemic Lupus International Collaborating Clinics (SLICC) criteria[6].

Cutaneous changes of SLE are divided into two categories; lupus erythematosus specific (acute, subacute and chronic) and the lupus erythematosus non-specific skin lesions such as photosensitivity, Raynaud's phenomenon, vasculitis and hair changes[6,7]. These lupus specific cutaneous features are captured in the 2010 SLICC classification criteria of SLE, but not in the ACR criteria.

Treatment options depend on the severity of symptoms and specific organ involvement[7]. For mild diseases with predominantly skin and joint affectations, the disease modifying anti rheumatic drug hydroxychloroquine and low dose systemic steroids often control the symptoms while severe diseases are treated according to either the European League Against Rheumatologist (EULAR) or the ACR guidelines which involves the use of immune suppressants such as azathioprine, mycophenolate mofetil, dapsone, thalidomide and biologics that target specific cytokines[7,8].

Cutaneous manifestations of SLE have significant impact on the quality of lives of patients. On the background of the often documented late diagnoses of SLE, understanding the variability of the cutaneous findings of SLE creates an index of suspicion allowing early recognition and initiation of appropriate therapy. There are few reports on cutaneous manifestations of SLE amongst African blacks and Nigerians. This study will provide a baseline for further researches on SLE and cutaneous LE.

This study therefore aims to document the cutaneous findings in SLE patients who presented at the Lagos University Teaching Hospital (LUTH) Rheumatology/ Dermatology clinics between January 2012 and July 2016.

Materials and Methods

This is a retrospective study of SLE patients who presented at the Rheumatology clinic of Lagos University Teaching Hospital between January 2012 and July 2016. Rheumatology clinic of LUTH was started in January 2012 as part of the dermatology unit with the employment of the rheumatologist and training of specialist residents in rheumatology. All patients with SLE were seen by the rheumatologists; and individuals with cutaneous lesions were assessed and managed by the dermatologists. Diagnosis of skin lesions were confirmed by histology. Data of all patients presenting with SLE was obtained from the clinic records and patients' case record files.

Inclusion criteria were individuals who met the 1997 ACR criteria for diagnosis of SLE and or 2010 SLICC criteria. Individuals with inconclusive diagnosis; those who did not meet the ACR and or SLICC criteria; and those with purely cutaneous LE with no systemic findings and negative serology, were excluded. Approval from the Health Research and Ethics Committee was obtained. Information extracted from the case record files included age, sex, specific cutaneous LE (CLE) diagnoses and classification, other skin lesions, duration of disease and systemic findings. Investigation results such as Erythrocyte Sedimentation Rate (ESR), Antinuclear Antibody Titre (ANA), anti-Double Stranded Antibody (anti-dsDNA), medications used and management outcome were also included in the data.

Gilliam's classification of cutaneous LE lesions was used and these include: Acute CLE: localized (malar rash, butterfly rash), generalized (morbiliform eruption), and toxic epidermal necrolysis-like lesion. Subacute cutaneous LE includes annular lesion, papulosquamous/ psoriasiform eruptions, vesiculobulous eruption and toxic epidermal necrolysis-like lesion. Chronic cutaneous LE: Discoid LE, hypertrophic/verrucous LE, LE profundus/ panniculitis, LE tumidus/papulomucinous LE, mucosal LE (oral, nasal, conjunctival, genital), chilblain LE and lichenoid LE.

Data was captured on Microsoft excel spreadsheet and analyzed with IBM SPSS Statistics 21 (SPSS Inc., Chicago, IL., USA). Descriptive statistics were used; with tables and charts to summarize the data. Absolute and relative frequencies were calculated for qualitative variables; while quantitative data was documented with means and standard deviation. For comparison of variables, Pearson chi square was used and level of significance p value was put at <0.05.

Results

Ninety (23.9%) of the total number of patients with rheumatologic conditions (377) seen during the study period, were diagnosed as SLE. Fifty (55.6%) of the 90 patients with SLE had cutaneous lesions. Data extracted from records of forty seven patients were analyzed; data of 3 patients were excluded because they were incomplete. Twenty eight (48.9%) out of the 47 patients had acute cutaneous LE; 10 patients (21.3%) had subacute cutaneous LE; while 14 patients (29.8%) had Chronic Cutaneous Lupus Erythematosus (CCLE) (Table 1). There was a female preponderance with the male to female ratio of 1: 14.7. The mean age at presentation was 33.5 ± 14.3 years (range was 9 to 68). The peak age of presentation was in the 3rd decade of life (40.4%) followed by the 4th decade (Table 1).

Table 1: Demographics of SLE patients with cutaneous diseases

Parameters	Frequency	(%)
Total number of rheumatology patients seen	377	100
Total number of SLE patients	90	23.9
Number of SLE patients with skin findings	50	55.6
No of records included in analysis	47	
Sex distribution: n=47		
Males:	3	6.4
Females:	44	93.6
Male: female ratio	1:14.7	
Age range	9 -68 years	
Mean age + SD	33.51 + 14.3	
Age (years) of SLE patients with skin feature		
<20	7	14.9
20 – 29	19	40.4
30 – 39	10	21.3
40 – 49	3	6.4
50 – 59	5	10.6
>/= 60	3	6.4

Acute cutaneous LE was the most common LE specific cutaneous manifestation of SLE affecting 48.9% of patients. Figure 1 revealed Exanthematous eruption on the abdomen and extensor surface of the arm in acute cutaneous LE. Specific skin lesions include alopecia (scarring and non-scarring) in 48.8%, photosensitivity in 40.4%, oral ulcers in 40.4% and malar rash in 36.2%. Findings in other systems include anaemia in 59.6% of patients, fever in 57.4%, renal manifestation in 46.8%, and neuro psychiatric manifestation in 14.9% (Table 2). Figures 2 and 3 shows extensive scarring alopecia and depigmented atrophic patches which are features of chronic cutaneous LE. The mean duration of symptoms was 28.4 ± 38.8 (months). The mean duration of presentation at the rheumatology clinic was 28.4 (SD 38.8) months; and only 35.6% of patients presented within the first six months of onset (Table 3). Raised ESR was documented in 85.1% of patients; and the mean ± SD was 82.08 ± 48.3. Antinuclear antibodies and anti-dsDNA were raised in 68.1% and 72.4% of patients respectively.

Table 2: Clinical findings in SLE patients with cutaneous lesions

Clinical findings	Frequency	(%)
Classification of cutaneous LE: n=47		
Acute cutaneous lupus	23	48.9
Subacute cutaneous lupus	10	21.3
Chronic cutaneous lupus	14	29.8
Specific skin findings n=47		
Alopecia (non scarring-19; scarring 4)	23	48.8
Photosensitivity	19	40.4
Oral ulcers	19	40.4
Malar lesion	17	36.2
Discoid lesion	11	23.4
Bullous eruption	1	2.1
Systemic findings n=47		
Anaemia	33	70.2
Arthritis	28	59.6
Fever	27	57.4
Renal	22	46.8
Neuropsychiatric features	7	14.9
Leucopenia	4	8.5
Thrombocytopenia	4	8.5
Serositis	4	8.5
Lymphopenia	3	6.4
Raised ESR (n=47	40	85.1
Mean ESR + SD	82.08 + 48.3	
Positive ANA (n=47)	32	68.1
Positive dsDNA (n=29)	21	72.4
ENA (n=7)	6 positives	85.7

Table 3: Duration of symptoms in SLE patients with cutaneous disorders

Duration of symptoms (in months)	Frequency (%)
1-6	16 (35.6)
7-12	9 (20.0)
13-18	1 (2.2)
19-24	9 (20.0)
>24	10 (22.2)
Mean Duration (months) + Standard Deviation	28.4 + 38.8

Figure 1: Exanthematous eruption on the abdomen and extensor surface of the arm in acute cutaneous lupus erythematosus

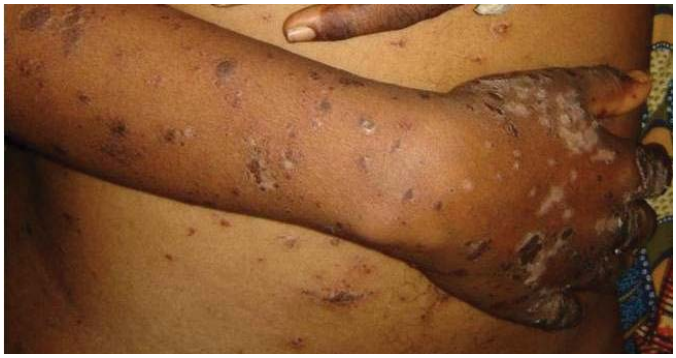


Figure 2: Extensive scarring alopecia on the scalp

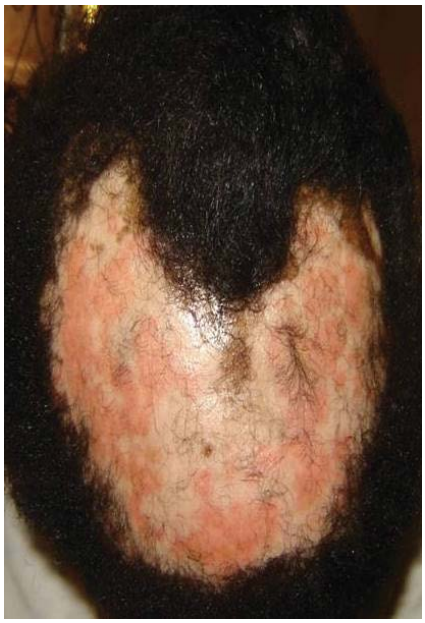
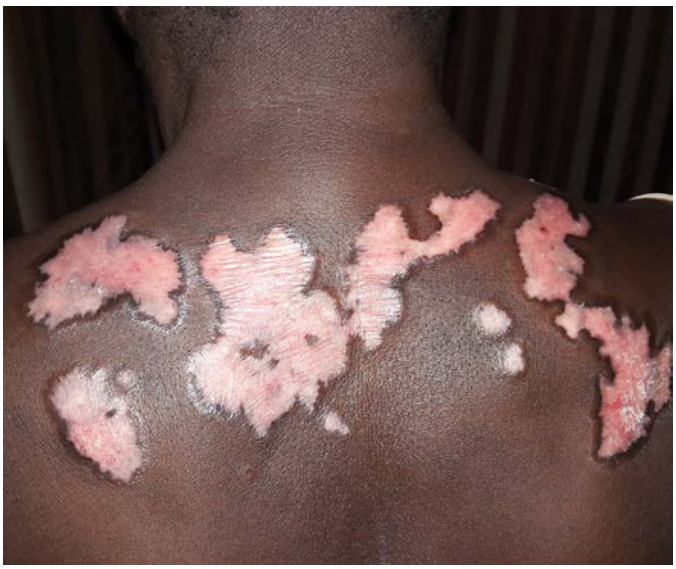


Figure 3: Depigmented atrophic patches with adherent scales on the back



The most commonly used medication was hydroxychloroquine in 45 patients (95.7%) followed by prednisolone in 42 (89.5%), azathioprine 18 (38.3%), steroid cream 17 (36.2%), non steroidal anti inflammatory drugs 6 (12.8%), cyclophosphamide 4 (8.5%), and methotrexate 3(6.7%) in descending order. Twenty patients (42.5%) had improvement in clinical findings; 14 (29.8%) had remission; 11 (23.4%) defaulted while 2 (4.3%) had worsening of symptoms. Part of the management of cutaneous LE included minimizing sun exposure and photoprotection with the use of sunscreen with SPF >50+ to prevent further UV induced skin lesions.

Discussion

The skin has been regarded as the window of the body and is the pointer to many systemic disorders including connective tissue disorders[9]. Systemic Lupus Erythematosus (SLE) may be diagnosed in the presence of cutaneous signs and positive serology[6]. The skin is one of the most common organ manifesting symptoms of SLE[7]. Cutaneous lesions were seen in 55.6% of all patients who presented with SLE during the study period. Adelowo *et al*[10] found a lower figure, in which 45% of their series presented with hair loss and 43.9 with discoid lesions[10]. Similar hospital based studies done in Malaysia, Pakistan and India revealed the frequencies of cutaneous lesions in the SLE patients to be 62%, 70% and 100% respectively[11-13]. A recent study in the US revealed the incidence of cutaneous LE to be 4.0/100,000 population similar to that done in Sweden[14,15]. There are few reports on cutaneous manifestation of SLE in African blacks and population studies are yet to be done on both SLE and cutaneous LE in Nigerians.

There is variable relationship between cutaneous LE and SLE. Individuals can present with cutaneous LE without systemic diseases; systemic diseases without skin manifestations; cutaneous flare independent of the internal organs; and the drugs used for cutaneous disorders may not be effective on systemic diseases[16]. All these suggest possibility that different pathophysiologic mechanisms may exist for the different presentations and courses of cutaneous LE. Trigger factors identified for cutaneous lupus erythematosus include Ultraviolet Light (UV), medications, hormones, stress, viruses and skin trauma[16].

Ultraviolet light has been found to induce release of pro-inflammatory cytokines, chemokines and adhesion molecules. Ultraviolet radiation also induce apoptotic bodies which bind with autoantibodies leading to the upregulation of the p53 protein expression, induction of cellular cytotoxicity, DNA damage and cytokine synthesis (such as IL1, IL6, IL8, IL10 and TNF)[16]. Subsequently there may be homing of inflammatory cells to the skin and upregulation of nitric oxide in the endothelial cells[16]. Specifically discoid LE has been associated with smoking, and subacute LE with medications and phototoxicity[16,17].

This study corroborates other studies that SLE is a disease found amongst females of childbearing age. The male to female ratio was 1:14.7; with 61.4% of the patients aged between 20 and 39 years; and a mean age of presentation of 33.51 ± 14.3, similar to work done by Adelowo *et al*[10]. The female predilection is thought to be due to both hormonal and genetic factors. The teen age to early forties, the age group most affected by SLE in females has been noted to correspond to the age of greatest hormonal instability[18]. The mean age found in this study is lower than that reported in other series where patients with cutaneous lupus are predominantly Caucasians. A multicenter study done in Europe reported the mean age of 43.0 + 15.7 (SD)[19]. The mean age for the cohort in Sweden was 54 years and Minnesota US 47.6 years[14,15]. Deligny *et al*[20] found lower age of presentation in their patients with African descent compared to the Caucasians counterpart in French Guiana in South America.

Cutaneous features of SLE in themselves, though sometimes painful, are not life threatening, but may impair the quality of life of the affected individuals. Facial lesions such as malar rash, discoid lesions; hair loss and hyperpigmentation from photosensitivity are of immense cosmetic significance. Studies show that cutaneous lupus erythematosus have severe effects on the quality of life, worse than skin conditions such as acne vulgaris, non melanoma skin cancers and alopecia; and comparable or worse mental health scores than systemic disorders such as hypertension, diabetes mellitus and congestive cardiac failure[4,21].

Systemic lupus erythematosus has been associated with late presentation in African Americans and Africans[7,10]. In this series, only about a third of the patients presented within 6 months of onset of symptoms; and the mean duration of symptoms was 28.4 months (2.3 years) which is comparable to an earlier study in Nigeria which reported 2.6 years[10]. One of the reasons suggested for this late diagnosis include low index of suspicion by the primary and the secondary health care givers, against the background of the previous belief that lupus is rare in Africans[3,22]. Good knowledge of the cutaneous features of SLE affords the patients and clinicians the benefit of early diagnosis and prompt management.

Our patients are managed using the American College of Rheumatology and the European League Against Rheumatologist (EULAR) recommendations[8,23]. One of the major constraints to management is paucity of funds as the health insurance scheme is not established in Nigeria and often does not include management of chronic illnesses like SLE, hence most patients pay out of pocket. This may be one of the factors implicated in the high rate of default and complications seen by African specialists[10,24,25]. Furthermore our patients also seek alternative therapy especially when there are no dramatic improvement. About a quarter of patients in this series defaulted treatment.

In accordance with the current understanding of lupus management, hydroxychloroquine was the most prescribed medication used in 95.7% of patients in this study. Ekwom[24] and Genga *et al*[25] reported the use of hydroxychloroquine in 77% and 92% of their patients respectively. Mucocutaneous and articular manifestations were the first indication for the use of hydroxychloroquine in lupus patients[26]. Hydroxychloroquine has been found to prevent flares, reduce damage to organs, reduce renal damage and improve survival rate, hence it is indicated in all lupus management[7,26,27]. Hydroxychloroquine use also improves lipid profile, prevents thrombotic events and reduces occurrence of congenital heart blocks in offspring of mothers who have lupus[7,26,27]. Apart from the medications, management of cutaneous LE includes minimizing sun exposure and photoprotection with the use of sunscreen with SPF >50+ to prevent further UV induced skin lesions.

Systemic lupus erythematosus is a multi organ disorder, although cutaneous disease may be the only presentation. Acute cutaneous LE is the most common presentation in this study. This is comparable to the findings from an English hospital which reported 51% acute cutaneous LE[28]. Cutaneous lesions are pointers and may help in the early diagnosis of the severe life threatening features of SLE such as renal, cardiopulmonary and neuropsychiatric symptoms[11]. In this series, anaemia was seen in 70.2%, arthritis in 59.6%, fever in 57% and renal disease in 46.8% of patients with cutaneous LE. It is advised that all patients with cutaneous lupus be screened for SLE.

The limitations of this study include the fact that this is a retrospective study and many less prominent cutaneous signs may not have been documented. Also in the setting of a severe flare which involves other organs, cutaneous lesions may not be documented. This is a hospital based study and patients seen will usually come with a flare; this study excludes cutaneous findings in patients who did not have a flare or significant/bothersome skin lesions or health challenges necessitating their visits to the clinic.

In conclusion, skin lesions in patients with SLE can yield valuable diagnostic as well as prognostic information essential for early diagnosis; prompt and efficient management; and in the long term reduction in the frequency of flares and complications. In view of this, educating primary care physicians, non-rheumatologists and non-dermatologists will aid early identification and referral, rather than administration of arbitrary topical therapies that will delay access to appropriate treatment.

Conflict of Interest: None to declare

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