Original article

Clinical Presentation, Treatment and Outcome of Patients with SLE at a Rheumatology Clinic in Douala, Cameroon.

Aspects cliniques et thérapeutiques du lupus érythémateux systémique dans une consultation rhumatologique à Douala, Cameroun

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ABSTRACT

Background:
Systemic lupus erythematosus (SLE) was reported to be rare in sub-Saharan Africa. We aimed to present our experience on SLE clinical and biological characteristics

Patients and methods:
We reviewed all the clinical records of patients suspected SLE in the General Hospital, Douala- Cameroon from 1999 to 2009. Patients fulfilling the 1987 ACR criteria for SLE were included

Results:
83 patients were diagnosed SLE, 39 fulfilling ACR criteria were analyzed: 36 female; mean age 39.2 ± 10.2 (19 – 59) years at the time of diagnosis. Dermatological (n= 25), musculoskeletal (n=23) and renal involvements (n = 7) were the main presenting complains. Clinical features in the course of disease included: musculoskeletal (n=39); hematologic (n=25); skin (n=22); renal (n=12); cardiac (n=16); neuropsychiatric (n=8); Constitutional symptoms included fever (n =20), fatigue (n = 20), weight loss (n = 12), and anorexia (n = 11). Raised erythrocyte sedimentation rate (n=35); positive anti nuclear antibodies (n= 31) urinalysis abnormalities (n=16)
All patients received corticosteroids at some stage of the disease. Antimalarial were administered to 27 patients. 12 patients with lupus nephritis received Intravenous cyclophosphamide. Improvement was noted in 27 patients. Severe complications included chronic kidney disease (n=3); encephalitis (n=3); infection (n=2). There were 2 deaths, from neurologic involvement and from dialysis-related sepsis

Conclusion:
Clinical presentation of SLE in Cameroon is similar to data available from other sub-Saharan Africa countries, but complications and mortality rates appear to be lower than previously described. Multicentric prospective studies are needed to better appreciate epidemiology and severity of SLE in sub-Saharan Africa

Key words:
Systemic lupus erythematosus; epidemiology; complications; Africa

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RÉSUMÉ :

Background :
Le Lupus érythémateux systémique (LES) est décrit comme rare en Afrique subsaharienne

But :
Décrire le mode de présentation, les caractéristiques cliniques et biologiques du LES à l'Hôpital Général de Douala, Cameroun

Patients et méthodes :
Une étude rétrospective a été menée sur les dossiers de patients suivis pour LES de 1999 à 2009. Étaient inclus ceux remplissant les critères de l'American College of Rheumatology (ACR) du LES. Les données démographiques, cliniques, biologiques et les traitements utilisés ont été analysés

Résultats :
83 patients portaient le diagnostic de LES, 39 remplissaient les critères ACR ; 36 étaient des femmes. L'âge moyen au moment du diagnostic était de 39.2 ± 10.2 (19 – 59) ans. Le mode de présentation était dermatologique (n= 25), musculosquelettique (n=23) et rénal (n=7). Les manifestations cliniques relevées au cours de l'évolution étaient : fièvre (n =20), fatigue (n = 20), amaigrissement (n = 12), anorexie (n = 11) ; arthralgies (n=25) ; dermatologiques (n=22) ; sérites (n=21) ; neuropsychiatriques (n=8). Parmi les anomalies biologiques : une vitesse de sédimentation élevée (n=35) ; anémie (n= 18) ; leucopénie (n= 14 ; protéinurie (n= 11), facteur antinucléaire positif (n= 31) anomalies du sédiment urinaire (n=16)
Les traitements reçus comportaient : corticothérapie chez tous les patients, antimalariques (n= 27) ; Cyclophosphamide (n=12) chez patients avec néphropathie lupique. Les complications sévères recensées : maladie rénale chronique (n=3) ; encéphalite (n=3) et infection (n=2). Deux décès étaient enregistrés (septicémie chez patient hémodialysé et état de mal convulsif)

Conclusion :
La présentation clinique du LES est similaire aux données de la littérature, cependant les complications sévères et la mortalité semblent moins fréquentes

Mots-clés :
Lupus érythémateux disséminé ; Complications. Afrique

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem, autoimmune, connective-tissue disorder with a broad spectrum of clinical presentations (1) .Despite the high prevalence of SLE reported in populations of African descent, it seems to be rare in sub-Saharan Africa, particularly West Africa (2,3). Both genetic and environmental factors have been proposed as explanations for this discrepancy (1,3,4). Recent studies however show similar SLE prevalence rates in recent migrants from sub-Saharan Africa and Afro-Caribbean women (1,3) .Furthermore, the number of reports and patients with SLE in sub-Saharan Africa appears to be on the rise (5–17) . The only report on features of SLE in the Cameroonian population is now over 15 years old; and was a study based on observations in a nephrology unit, which revealed frequent severe renal involvement at diagnosis. It was therefore necessary to review the clinical features, treatment and outcome of patients with SLE seen within the last decade from a multidisciplinary recruitment of SLE patients. This study therefore aimed to describe the frequent clinical and laboratory features associated with SLE in Cameroon, as well as the various therapeutic combinations commonly used.

PATIENTS AND METHODS

After prior ethical clearance from the National Ethical Review Board, we reviewed the case records of 6485 patients who were followed between January 1999 and December 2009 in the Internal Medicine Department of the Douala General Hospital (DGH), Cameroon. DGH is a tertiary referral centre for the Littoral, West and South West regions of Cameroon, which harbor a population of about eight million inhabitants. A diagnosis of SLE was established if the patient fulfilled at least four of the ACR 1982 revised criteria for the classification of SLE (18). Medical records (one patient=one file) of patients with SLE were identified and analyzed.

Relevant parameters retrieved from patient records included clinical data (age, sex, duration of symptoms, symptoms and clinical signs at diagnosis and during follow-up) and laboratory data (Full blood count, erythrocyte sedimentation rate, C-reactive protein level, human immunodeficiency virus serology, hepatitis B and C virus serology, urinalysis), immunological markers (rheumatoid factors, anti-nuclear antibodies – ANA, anti-double-stranded DNA – anti-dsDNA – antibodies). Treatment received as well as patient outcome were also noted. Outcome indicators evaluated were improvement in the presenting clinical features, occurrence of complications (organ involvement not present at diagnosis), and death.

Statistical methods: Categorical variables were presented as number (%) and continuous variables presented as mean and standard deviation. Statistical significance was considered at *p values < 0.05*. Data were analyzed using the Stata® software (College Station, Texas, USA)

RESULTS

A total of 39 (36 females) patients fulfilled the criteria for SLE. They were recruited from the Dermatology, Rheumatology and Nephrology units of the Internal medicine Department. The mean age was 39.2 ± 10.2 [range, 19 – 59] at the time of diagnosis, with 4 patients above 50 years old.

A. Clinical features

Musculoskeletal involvement was the main presenting feature present in 23 patients (58.9%), followed by renal involvements (n = 7, 17.9%), serositis (n = 4, 10.3%), neurologic involvements (n = 4, 10.3%), and dermatological involvements (n = 1, 2.6%). The main organ system involvements are summarized in Table 1. All patients developed musculoskeletal involvement at some point in the course of the illness. Lupus nephritis was found in 12 (30.8%) patients in the course of the disease of which 3 cases evolve into end stage kidney disease. Constitutional symptoms found included fever (n =20, 51.3%), fatigue (n = 20, 51.3%), weight loss (n = 12, 30.8%), and anorexia (n = 11, 28.2%).

TABLE 1: THE MAIN CLINICAL FEATURES OF SLE AT PRESENTATION (N=39)

Clinical features	Number (%)
Malar rash	6 (15.4)
Discoid lesions	2 (5.1)
Photosensitivity	3 (7.7)
Oral ulcer	4 (10.3)
Hair loss	8 (20.5)
Vitiligo	5 (12.8)
Arthralgia	25 (64.1)
Oligoarthritis	7 (17.9)
Jaccoud's hand	7 (17.9)
Pericarditis	12 (30.8)
Pleurisy	9 (23)
Psychosis	6 (15.4)
Seizures	5 (12.8)
Hypertension	4 (10.3)
Abortion at 2nd trimester	12 (42.9)

B. Laboratory findings (Table2)

ESR was raised in 35 tested patients; ANA was positive in ()86.1% of cases, with 72% speckled. Anemia, leucopenia, and proteinuria were present in

72%, 56% and 28.2% respectively. None of the patients underwent a renal biopsy.

TABLE 2: BIOLOGICAL ABNORMALITIES OF SLE PATIENTS

Biological features	Number tested	Frequency (%)
Proteinuria (> 0.5 g/24h)	39	11 (28.2)
Cellular casts	39	3 (7.7)
Elevated serum creatinine (>14 mg/L)	13	5 (38.5)
Anemia	25	18 (72)
Leucopenia	25	14 (56)
Lymphopenia	25	11 (44)
Thrombocytopenia	25	4 (16)
Elevated ESR	35	35 (100)
C reactive protein, positive	19	17 (89.5)
Positive HIV serology	19	1 (5.3)
Positive HBV and HCV serology	21	0
Positive ANA	36	31 (86.1)
ANA pattern: Speckled / Homogeneous	25	18 (72) / 7 (28)
Positive Anti-dsDNA antibodies	34	25 (73.5)
Positive Anticardiolipin antibodies	8	4 (50)
Positive Rheumatoid factor	17	3 (17.6)

C. Treatment

All patients received corticosteroids at some stage of the disease. In addition, at diagnosis, disease modifying agents included antimalarial drugs alone in 27 (69.2%) patients, and combined with methotrexate in 4 (10.3%) patients who had resistant arthritis. Methotrexate was used alone in one patient (2.6%) with known hydroxychloroquine allergy. A sequential immunosuppressive regimen consisting of six doses of once -monthly pulse cyclophosphamide in combination with steroids for induction of remission, followed by maintenance therapy with azathioprine and steroids was prescribed for all 12 patients (30.8%) with lupus nephritis.

D. Outcome

Improvement was noted in 27 patients (69.2%). Five patients (12.8%) were lost to follow-up.

Complications occurred in 11 patients (28,2%); SLE complications included end stage kidney disease (ESKD) in 3 of the 12 patients with lupus nephritis, cerebrovascular disease in 2 patients and seizures in one patient. Treatment linked complication were mainly infections and diabetes mellitus (Table 3). There were 2 deaths (5.1%), one from neurologic involvement and the other from dialysis-related sepsis.

TABLE 3: COMPLICATIONS PRESENTED BY SLE PATIENTS

Type	Complications	Number (%)
SLE complications	End stage kidney disease	3 (7.7)
	Cerebrovascular disease	2 (5.1)
	Seizures	1 (2.6)
Iatrogenic complications	Tuberculosis	1 (2.6)
	Facial cellulitis	1 (2.6)
	Diabetes	2 (5.1)
	Aseptic necrosis of hip	1 (2.6)

DISCUSSION

Systemic lupus erythematous is essentially a disease of the young female with musculoskeletal and renal involvement being the main clinical features in this indigenous Cameroonian population. Anemia, leucopenia and raised acute phase proteins are common laboratory abnormalities. The frequency of raised acute phase reactants, positive ANA and antibodies against double-stranded DNA was high. Treatment was by immunosuppressive drugs depending on organ involvement. Outcome was acceptable with improvement of symptoms in the majority and mortality of 5.1% of cases.

In this study, 83 patients had a clinical suspicion of the disease but did not meet the ACR criteria in the absence of immunological markers. It is however likely that the number of cases is increasing in our setting. The reported cases SLE in blacks equally saw an increase from 17 patients in 1977(11) to 111 black South Africans in 1996(12). In Senegal, the first case was published in 1960 (7), but subsequently, 30 patients in 1988(8), and 142 patients were published in 2011 (9,10).

Clinical features of SLE seen were similar to reports from other black populations with musculoskeletal, dermatological, hematological and renal involvement common (8,9,11,12); dermatological manifestations were found more frequently as presenting complain followed by musculoskeletal complains as in other sub Saharan studies. Constitutional symptoms like fever as seen in over half of our study population have been described in other studies and may in our context be mistaken for endemic malaria, thus delaying the patient SLE diagnosis and early adequate medical care (13,14,15). Renal involvement has been reported as more severe and the main predictor of death in SLE among black populations (3,19,20). Lupus nephritis (LN) found in 30% of our study population was described in 57%, 56%, 43.8% in Senegal, Tunisia, and South Africa respectively (10,17,21). LN lead to ESKD in 3 (7%) patients, lower than what was reported in previous studies in Senegal and Cameroon, 25 and 26% respectively (10,13). The early use of Hydroxychloroquine has been shown to provide a beneficial role in organ involvement such as lupus nephritis. Also, early SLE

diagnosis and adequate treatment reduce risk of mortality due to complications and this can be achieve through the referral systems to specialized health care providers in developing countries.
Biological findings are similar to data obtained from other sub-Saharan African studies (6–17) with the high frequency of positive ANA and anti-dsDNA antibodies in our study confirming previous data which are suggestive of a higher frequency of immunologic markers of SLE in native Africans and African-descendants compared to Caucasians (5,12,19,20).

Corticosteroids, methotrexate, cyclophosphamide and azathioprine were the immunosuppressive agents often used. Hydroxychloroquine was the most used as recommended in International guidelines because of its affordability in our area and its known positive effect in preventing end organ involvement (2,19). The absence of renal histology did not allow for a histology-based therapy for lupus nephritis as recommended by several guidelines. Early renal biopsy in lupus nephritis has been shown to adequately evaluate and classify lesions thus allowing corresponding immunosuppressive therapies, reversing the evolution to ESKD. All patients with an active urinary sediment and renal impairment were considered to have class III or IV lupus nephritis with active lesions and therefore treated with a short course NIH protocol for inductions. Newer drugs such as mycophenolate mofetil and rituximab currently in use in developed countries are unaffordable in our context (22).
The overall mortality rate was 5.1%, different from 25, 27 and 29% previously reported in Cameroon, Senegal and South Africa (8,13,17). It is known that SLE patients with African ancestry have a poorer outcome with a higher risk of mortality when compared with their Caucasian counterparts (2,19,20). This differential risk by ethnicity was not seen in several of the studies that adjusted for socioeconomic status like income, insurance status, housing or education level (2,19). The mortality rate could be high in those early 1990 studies in Africa because African patients generally tend to seek healthcare only when the disease had reached and advanced stage (8,16) and also because of the few available health care centers able to provide adequate SLE diagnosis and treatment (8,9,13,17). However, this high mortality rate was not encountered in more recent studies in sub-Saharan Africa (9,14,16), with a 5-year survival rate up to 96%. Also the major cause of death have progressively been shifted from SLE complications mainly ESKD in the past, to complications of immunosuppression and other SLE treatments today (8,15,16). Improving the availability of adequately trained medical personnel and raising the awareness on SLE in our population may reduce the burden of the disease and its evolution to ESKD in a setting where hemodialysis and kidney transplant are not readily available (21).
Like most all studies published in sub-Saharan Africa (8–17), the retrospective and hospital based design is the main limitation of this study. Thirty-nine cases of SLE may seem small over a period of 10 years. The limited access to immunological testing in our and other sub-Saharan African settings does not permit the diagnosis confirmation in suspected cases. It is therefore likely that the number of cases reported here underestimates the reality. However, the aim of this study was to describe our experience with SLE despite the numbers.
In conclusion, the characteristics of SLE in Cameroon seem comparable to data available from other recent sub-Saharan Africa countries and from African-descendants population. Even though disease frequency is on the rise, its complications and mortality rates are lower than what was previously described. Multicentric prospective studies are needed to better appreciate the epidemiologic aspects of SLE in sub-Saharan Africa and evaluated the severity of the disease as well as the response to available treatment. .

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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