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Profiles of systemic lupus erythematosus patients with co-existing sickle cell disease: a coincidence or true association?

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Abstract

Introduction: Systemic lupus erythematosus (SLE) and sickle cell disease (SCD) are distinct multisystemic diseases that commonly affect blacks. There are few reports of their co-existence in Western literature and a paucity of reports in Sub-Saharan Africa. Their co-existence is associated with diagnostic delay and treatment dilemmas. The aim is to describe the clinical, laboratory, and treatment profile of Nigerian lupus with sickle cell disease

Material and methods: A 7-year retrospective descriptive study of lupus patients with sickle cell disease was performed. Medical records of eligible patients were extracted into a proforma, transferred into SPSS, and analyzed with descriptive statistics. Sociodemographic, clinical, laboratory, and treatment data were presented as frequency and percentages.

Results: Twelve SLE-SCD cases (female 11, male 1) were identified. The mean age was 28.5 years and the mean duration of illness prior to diagnosis was 9.5 years. The median follow-up period was 3.1 years and the common presentations were mucocutaneous (66%), renal, (50%) serositis (33%), and neurological (16%) in decreasing order. All had anemia and positive antinuclear antibody, 33% had pancytopenia and 75% had positive anti-dsDNA and anti-Smith. Two are on maintenance hemodialysis, one with interstitial lung disease, and one on long-term anticoagulation due to deep vein thrombosis.

Conclusions: Sickle cell disease and SLE should be considered in SCD with atypical clinical and laboratory features. We hope this report will raise diagnostic suspicion and prompt early diagnosis and treatment to prevent multiorgan damage that may ensue from such an association.

Key words: lupus, sickle cell diseases, profile, clinical, laboratory.

Introduction

Sickle cell disease (SCD) and systemic lupus erythematosus (SLE) share certain characteristics. They are chronic multisystemic diseases with a preferential increase in prevalence, morbidity, and mortality among young blacks [1, 2]. Their difference lies in etiology and pathophysiology, resulting in the same outcome: chronic inflammation and multi-organ damage.

Sickle cell disease is a monogenic autosomal recessive disorder due to a missense mutation in the *HBB* gene encoding the β-globin subunit of hemoglobin [3]. Individuals with a single sickle mutation develop sickle cell traits, while those with a double mutation with at least one sickle mutation develop sickle cell disease. The consequence is abnormally shaped red blood cells, causing hemolysis, microvascular occlusion, ischemia, and organ damage [3].

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Although monogenic lupus exists in children [4], lupus is predominantly a polygenic systemic autoimmune disease with an interplay of multiple genes, environmental factors, hormones, and epigenetics factors [5]. Thus, both disorders are associated with organ damage and microangiopathy through different mechanisms.

According to the 2021 Global Burden of Disease (GBD) report, cases of other musculoskeletal disorders, including lupus and other connective tissue diseases, are estimated to increase by 115% to 1,060 million in 2050 from the current 495 million [2]. They are also the sixth-largest cause of years lost to disability and the 19th-largest cause of disability-adjusted life years [2].

The 2021 GBD report for SCD showed that the high-income super region of the world had a 33.3% drop in the prevalence of SCD in contrast with a 27% increase observed in Sub-Saharan Africa and a 5.6% rise in the Caribbean and Latin America [1]. The upsurge in prevalence has been attributed to population growth in the region mentioned above. Similarly, the 2021 GBD also reported a 30.1% increase in specific mortality and 65.1% in all-cause mortality from SCD in Sub-Saharan Africa, the region with the highest SCD mortality burden worldwide [1]. This is likely due to a dysfunctional health system and failure of advocacy and awareness aimed at preventing sickle cell disease.

In contrast to SCD, the prevalence of lupus is lower in low-income countries than in high-income countries. However, recent reports from a systematic review and meta-analysis showed that lupus is common in low- and medium-income countries (LMIC) with significant variation in prevalence across regions [6]. In Sub-Saharan Africa, the pooled prevalence of SLE was 1.7% in a meta-analysis of 15 hospital-based studies [7]. A Nigerian multicenter descriptive retrospective study reported 913 cases of lupus over four years [8].

Generally, there is a considerable gender difference in lupus, unlike in SCD, where the female-to-male proportion is comparable [1]. Estrogen-mediated lymphocyte stimulation, the role of the microbiome, microchimerism, and X chromosome immunogenic potential have been suggested as the reasons for the female preponderance [9].

There are a few reports of SCD coexisting with lupus, all case reports and case series [10–15]. The mechanism underlying this association is still sketchy. Sickle cells adhere, damage, and stimulate the vascular endothelium and surrounding cells, leading to a chronic inflammatory state [16–18]. The repeated cycles of endothelial activation, damage, and heightened inflammation lead to tissue damage and gradual loss of immunological tolerance [16–18]. Recent reports have shown a qualitative and quantitative reduction in anti-inflammatory interleukin (IL)-10-producing B-reg cells in lupus patients with SCD compared with those without SCD [19].

Repeated blood transfusion, functional asplenia, and recurrent infection have also been implicated in triggering autoimmune conditions in SCD. Furthermore, the faulty innate immune systems are evidenced by failure of alternate complement pathways, defective opsonization, and phagocytosis, leading to impaired clearance of the immune complex [16–18].

Nigeria, the most populous black nation on Earth, remains the global capital of SCD, as its population accounts for 2 to 3% of SCD cases worldwide [20]. Additionally, both conditions frequently affect individuals of African descent, and their coexistence is rarely reported in Sub-Saharan Africa. Furthermore, they represent distinct diseases with overlapping clinical and laboratory features, posing potential challenges in diagnosis and management. The dual burden of both conditions is expected to increase morbidity and mortality, reduce quality of life, and cause functional impairment. In light of these factors, the study aimed to describe the clinical, laboratory, and treatment profile of Nigerian lupus with sickle cell disease.

Material and methods

Study design

This study was a retrospective descriptive study conducted over 7 years from September 2017 to December 2023. The study was carried out at the Rheumatology Unit of Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria. The unit is one of the few accredited Rheumatology training centers in Nigeria and provides outpatient and inpatient rheumatology services to residents of Lagos and neighboring states. The LASUTH is a leading tertiary hospital in the densely populated and cosmopolitan city of Lagos.

Inclusion and exclusion criteria

All patients who met the inclusion and exclusion criteria were recruited. The inclusion criteria were all known SLE or lupus overlap patients with co-existing SCD. All other systemic autoimmune conditions and lupus patients with normal hemoglobin and sickle cell traits were excluded.

Study procedure

The medical records of all patients who met the inclusion criteria were identified. Data from the records were captured using a proforma to document the sociodemographic, clinical, and laboratory profiles as well as treatment outcomes of the recruited patients. The pa-

tients were classified as having lupus based on one of the three criteria, as appropriate: the 1997 American College of Rheumatology (ACR), 2012 Systemic Lupus International Collaborating Clinics (SLICC), or 2019 ACR/European Alliance of Associations for Rheumatology (EULAR) criteria [21–23]. The diagnosis of sickle cell disease was confirmed via the performance of hemoglobin electrophoresis after obtaining the information from the patient's medical history. The autoantibodies and laboratory tests were analyzed using standard and validated methods. Three patients had renal biopsies. Two patients declined renal biopsy and one had a contraindication to renal biopsy.

Statistical analysis

Data were analyzed by descriptive statistics and presented as tables of comparison of case summaries. The categorical variables were presented as frequency and percentages while continuous normally distributed variables were presented as mean and standard deviation.

Bioethical standards

The ethical approval was issued by the National Health Research Ethics and Committee of Nigeria (NHREC) as the data and study center was part of the Nigeria Multicenter Retrospective Lupus Cohorts and Registry. The ethical approval number was NHREC/01/01/-2007/26/01/2022.

Results

Sociodemographic and clinical profiles of sickle cell disease with lupus

Data from 12 SLE-SCD patients (11 female and 1 male) from a total of 256 SLE patients (4.7%) were analyzed. The mean age at diagnosis and mean duration of illness before presentation were 28.5 years and 9.5 years, respectively. All were diagnosed with SCD before lupus confirmation. There were three with SC genotypes and 2 with lupus overlap syndrome (lupus myositis and lupus-rheumatoid arthritis overlap). The majority were from the Yoruba tribe (58.3%), unmarried (91.7%), and had tertiary education (75%). Three were inpatients, and 9 were seen at the outpatient clinic. Nine patients were referred by hematologists.

All presented with a variable combination of constitutional and musculoskeletal manifestations. Recurrent fever and fatigue were recorded in all patients, as were progressive weight loss and night sweats in 75% and 50%, respectively. The inflammatory pattern of chronic persistent polyarthralgia was seen in all patients with myalgia and joint stiffness in 75% and 83.3% of patients, respectively. Definite clinical synovitis was documented in 41.7% of the patients. Mucocutaneous, renal, serositis, and neurological manifestations were recorded in 66.7%, 50%, 33.3%, and 16%, respectively. Photosensitive rash, non-scarring hair loss, and mouth ulcers were seen in 8 patients each, while malar rash, discoid rash, subacute lupus rash, sore throats, nasal ulcers, and scarring alopecia were recorded in 6, 4, 1, 5, 1, and 3 patients, respectively.

Nephrotic syndrome was documented in 3 patients, and 4 had cardiopulmonary effusion. Two class IV and one class V nephritis were seen in the biopsy report of 3 patients who had biopsies, with none showing renal thromboembolic diseases.

Transverse myelitis was diagnosed in 1 patient, and another had a multiple sclerosis-like demyelinating disorder. The median follow-up period was 3.1 (2.8) years, and all are still being followed up, with 2 patients on maintenance hemodialysis, another on lifelong anticoagulation due to chronic recurrent deep vein thrombosis (DVT), and one with interstitial lung disease, while eight had significant clinical improvement based on the resolution of inflammatory features. Table I shows the sociodemographic and clinical profile of sickle cell disease with lupus.

Laboratory profile and treatment of systemic lupus erythematosus patients with sickle cell disease

The mean hematocrit level was 18.8 ±4.6%, with all patients being anemic. The average leucocyte count and the platelet count were approximately 6,000/ml and 180,000/ml, respectively. About 5 (41.6%) and 4 (33.3%) patients had leucopenia and thrombocytopenia, respectively. The mean lymphocyte count was 1425.3/ml.

The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were elevated in all patients, with average values of 90.3 ±26.2 mm/h and 53.9 ±37.7 mg/dl, respectively. Of the 12 patients, only 10 did a Coombs test, with only 3 of them having a positive result. Pancytopenia was present in only 33.3% of patients.

The median urine protein-creatinine ratio (UPCR) was 1.1 (2.4 IQR), with approximately 7 patients (58.3%) showing proteinuria on a dipstick test and 5 patients (41.6%) having active urine sediments. The median serum creatinine level was 1.5 (6.3 IQR), and about 4 (33.3%) had a reduced estimated glomerular filtration rate (eGFR).

All patients had positive antinuclear antibodies (ANA), with the most common ANA titers being 1 : 5,120 (33.3% of cases) and 1 : 1,280 (25% of cases), respectively. Only 1 patient had a homogeneous ANA pattern. The fraction of patients with positive anti-dsDNA and anti-Smith results was three-fourths of the total. About 5 (45%)

Table I. Sociodemographic and clinical profile of sickle cell disease with lupus

Sociodemographic characteristics											
Case	Age at diagnosis [years]	Gender	Duration of disease [years]	Median follow-up [years]	Ethnicity	Marital status	Educational level	Occupation	Lupus overlap	Type of sickle cell disease	Hospital setting
Mean (SD)	28.5 (8.2)		5.1 (3.2)	3.3 (2.0)*							
1	23	Female	5	3	Yoruba	Single	Tertiary	Student	No	SS	Clinic
2	18	Female	2	5	Yoruba	Single	Tertiary	Student	No	SS	Clinic
3	32	Female	8	1	Igbo	Single	Tertiary	Nurse	No	SS	Ward
4	24	Female	1	2	Yoruba	Single	Tertiary	Dentist	No	SS	Clinic
5	20	Female	2	6	Yoruba	Single	Tertiary	Student	No	SC	Ward
6	45	Female	10	1.5	Yoruba	Married	Tertiary	Lecturer	Yes	SC	Clinic
7	37	Female	8	4	Ijaw	Single	Primary	Trader	No	SC	Clinic
8	26	Female	2	3.2	Igbo	Single	Tertiary	ICT	No	SS	Clinic
9	29	Female	5	1	Igbo	Single	Tertiary	Banker	Yes	SS	Clinic
10	21	Male	3	4	Yoruba	Single	Tertiary	Student	No	SS	Clinic
11	38	Female	5	7	Yoruba	Single	Tertiary	Student	No	SS	Clinic
12	30	Female	10	2	Efik	Single	Secondary	Trader	No	SS	ICU

Clinical presentation						
Case	Constitutional symptoms	Musculoskeletal	Mucocutaneous	Serositis	Neurological	Renal
1	Yes	Yes	Yes	No	No	No
2	Yes	Yes	Yes	No	No	Yes
3	Yes	Yes	Yes	Yes	No	Yes
4	Yes	Yes	Yes	No	No	Yes
5	Yes	Yes	Yes	Yes	No	Yes
6	Yes	Yes	No	No	No	No
7	Yes	Yes	Yes	No	No	Yes
8	Yes	Yes	No	Yes	No	No
9	Yes	Yes	Yes	No	No	No
10	Yes	Yes	No	No	No	No
11	Yes	Yes	Yes	No	No	No
12	Yes	No	No	Yes	Yes	Yes

**Interquartile range (IQR).*

of the 11 patients tested had reduced complement. Only 1 patient was tested for anti-cardiolipin, anti-b2GP-1, and lupus anticoagulant, and all results were negative. The mean baseline Mex-SLEDAI was 12.4 ±5.6.

The most commonly used drugs were prednisolone in every patient and hydroxychloroquine in 10 (83%) patients. Only 3 (25%), 2 (16.7%), 2 (16.7%), and 1 (8.3%) patients were using methotrexate, tacrolimus, rituximab, and azathioprine, respectively. About 7 (58.3%) patients were prescribed mycophenolate mofetil and 8 patients were on hydroxyurea.

Most (83%) patients improved clinically; however, 2 (16.7%) were on maintenance hemodialysis, while the other 2 had chronic recurrent DVT and interstitial lung disease, respectively. Other details on the laboratory and treatment profile are shown in Table II.

Discussion

Our study showed the coexistence of SLE and SCD in 4.7% of the 256 cases of SLE diagnosed over the study period. This confirms the rarity of such an association, particularly in a population with a large burden of sickle cell disease. In the largest literature review on the topic, Robazzi et al. [14] reviewed 45 cases of this coexistence over 50 years since the first report by Wilson et al. [24] in 1964. In the same vein, in the analysis of a large cohort of 304 adults with SCD, 1 patient (0.03%) had lupus among 15 documented to have systemic autoimmune diseases [15].

Our series is the largest in homogeneous black populations, as previous reports were mostly from outside Sub-Saharan Africa [10–15]. To date, no fewer than 65 cases have been reported in the literature. The rarity may be related to the low level of awareness of this association as well as the diagnostic challenges that may be encountered due to the overlapping clinical and laboratory features of both conditions. The mean age at diagnosis of our patients (28.5 years) is higher than the 23 years reported in the analysis of 45 cases by Robazzi et al. [14]. This may be due to the inclusion of only adults in our study, in contrast with that of Robazzi et al. [14], which included 17 children with an age range of 4 to 63 years, compared to our age range of 18 to 45 years.

It is noteworthy that 4 children with the coexistence of SCD and systemic autoimmune disease from our hospital have been reported by Faleye et al. [25]. Two children among the 4 had lupus. As most reports were case series, there is variation in the duration of illness before diagnosis. We observed a delay in diagnosis as the mean duration of illness was 5 years before diagnosis. This reflects a general delay in diagnosis reported in previous lupus studies across Africa.

The aforementioned diagnostic challenges associated with the presence of both conditions may also contribute to delayed diagnosis. Given that all our patients were diagnosed with SCD before the diagnosis of lupus, diagnosis may also be missed in community and secondary health settings where the possibility of lupus is less likely to be considered in patients with musculoskeletal symptoms.

We documented baseline musculoskeletal and constitutional symptoms in all our patients, observing serositis in 33.3% and mucocutaneous manifestations in 66.7%. Renal manifestations were noted in half and neurological manifestations in one-sixth of our patients. The largest review to date, of 45 SCD-SLE patients drawn from 19 case reports and case series, showed articular manifestations in 76%, renal manifestations in 46.7%, and serositis in 40% of the SCD-SLE patients [14]. These data are comparable with our findings. However, in contrast to our study, neurological and cutaneous manifestations were documented in 27% and 37.8% of the reviewed SCD-SLE cases, respectively [14]. Due to limited data, the true frequency, patterns, and peculiarities of clinical manifestations of SLE-SCD are difficult to determine at the moment.

Anemia of any type is common in both conditions. Although autoimmune hemolytic anemia is characteristic of lupus, there is a rare report of its association with SCD regardless of lupus [26]. Hematological manifestations were found in 41.7% of our patients, compared to 36% reported in previous studies [14]. Cytopenias rather than leucocytosis and thrombocytosis may distinguish lupus from SCD.

The acute-phase reactants, such as ESR and CRP, were elevated in all our patients. Elevated ESR is common in untreated lupus and may be an indicator of associated inflammatory or infectious conditions in the presence of sickle cell disease. This is because, in isolated SCD, high and low ESR is possible with chronic anemia and difficulty in rouleaux formation by sickle-shaped red cells, respectively [27]. Unlike ESR, CRP is a specific marker of inflammation, and it is not affected by the level or morphology of red cells. It is elevated in sickle cell crisis, articular lupus, and lupus serositis [27, 28]. However, CRP may be normal in lupus, and this has been suggested to be due to CRP polymorphism, autoantibodies against CRP, and interferon-induced suppression of CRP levels [28].

An isolated SCD is associated with higher levels of antinuclear antibody and anti-phospholipid (APL) markers compared with the control, probably due to alloimmunization from recurrent blood transfusion, chronic antigen stimulation, and subsequent immune activation from recurrent infection [29–31]. Whether the presence of these antibodies predicts the development of overt lupus or anti-phospholipid syndrome in the future remains to be determined [30, 31]. All our patients had positive ANA with predominant speckled patterns, and one had recurrent deep vein thrombosis in the absence

Table II. Laboratory profile and treatment of SLE patients with sickle cell disease

Laboratory profile													
Hematologic investigations													
Case	Hematocrit/ SS [%]	WBC [/ml]	Platelet count [/ml]	Lymphocytes [/ml]	ESR [mm/h]	CRP [mg/dl]	Positive Coombs test	Anemia	Leucopenia [< 3,000/ml]	Thrombo-cytopenia	Pancyto-penia	High ESR [> 20 mm/h]	High CRP [> 7.5 mg/dl]
Mean (SD)	18.8 (4.6)	5954 (4945.3)	181667 (146885.1)	1425.3 (659.8)	90.3 (26.2)	53.9 (37.7)							
1	22	3200	152,000	1200	90	53	No	Yes	No	No	No	Yes	Yes
2	17	2500	90,000	850	120	106.7	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3	13	1250	75,000	612	110	85	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4	19	12000	225,000	1800	75	21.4	No	Yes	No	No	No	Yes	Yes
5	15	2700	92,000	2000	105	59	No	Yes	Yes	Yes	Yes	Yes	Yes
6	25	3800	150,000	1650	80	17.4	No	Yes	No	No	No	Yes	Yes
7	18	8200	140,000	1600	45	9.2	NA	Yes	No	No	No	Yes	Yes
8	20	15000	170,000	1220	100	103.2	No	Yes	No	No	No	Yes	Yes
9	16	2400	111,000	912	103	42.5	No	Yes	Yes	No	No	Yes	Yes
10	19	13200	530,000	2500	50	18.1	No	Yes	No	No	No	Yes	Yes
11	28	6100	415,000	2310	76	24.7	NA	Yes	No	No	No	Yes	Yes
12	13	1100	30,000	450	130	106.9	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Renal investigations					
Cases	UPCR [/g/24 h]	Proteinuria (dipstick)	Active urine sediment	Serum creatinine [mg/dl]	Reduced eGFR [< 60 ml/1.73 m^2]
Median (IQR)	1.1 (2.4)			1.5 (6.3)	
1	0.32	Yes	No	0.6	No
2	3.6	Yes	Yes	1.8	No
3	1.8	Yes	Yes	10.7	Yes
4	2.1	Yes	Yes	12.5	Yes
5	2.9	Yes	No	6.2	Yes
6	0.16	No	No	1.1	No
7	2.4	Yes	Yes	1.5	No
8	0.09	No	No	1.4	No
9	0.12	No	No	1	No
10	0.04	No	No	1.3	No
11	0.18	No	No	0.7	No
12	7.2	Yes	Yes	15.8	Yes

Table II. Cont.

Autoantibody profile										
Case	Positive ANA	ANA titer	ANA patterns	Anti-dsDNA (+)	Anti-Smith (+)	Reduced complements	Anticardiolipin	Anti-b2GP-1	Lupus anticoagulant	Baseline Mex-SLEDAI
Total										12.4 (5.6)
1	Yes	1 : 640	Speckled	Yes	Yes	No	NA	NA	NA	8
2	Yes	1 : 5,120	Speckled	Yes	Yes	Yes	NA	NA	NA	13
3	Yes	1 : 5,120	Homogeneous	Yes	No	Yes	NA	NA	NA	18
4	Yes	1 : 1,280	Speckled	Yes	Yes	Yes	NA	NA	NA	17
5	Yes	1 : 5,120	Speckled	Yes	Yes	Yes	Negative	Negative	Negative	21
6	Yes	1 : 640	Speckled	No	Yes	No	NA	NA	NA	10
7	Yes	1 : 640	Speckled	Yes	Yes	No	NA	NA	NA	12
8	Yes	1 : 1,280	Speckled	No	Yes	No	NA	NA	NA	10
9	Yes	1 : 1,280	Speckled	No	Yes	NA	NA	NA	NA	6
10	Yes	1 : 160	Speckled	Yes	No	No	NA	NA	NA	8
11	Yes	1 : 320	Speckled	Yes	No	NA	NA	NA	NA	5
12	Yes	1 : 5,120	Speckled	Yes	Yes	Yes	NA	NA	NA	21

Treatment and clinical outcome									
Case	Prednisolone	Hydroxychloroquine	Methotrexate	Azathioprine	Mycophenolate mofetil	Cyclophosphamide	Tacrolimus	Rituximab	Clinical outcomes
1	Yes	No	Yes	No	No	No	No	No	Clinical improvement
2	Yes	Yes	No	Yes	No	No	Yes	No	Clinical improvement
3	Yes	Yes	No	No	Yes	Yes	No	No	Maintenance hemodialysis
4	Yes	Yes	No	No	Yes	Yes	No	No	Clinical improvement
5	Yes	Yes	No	No	Yes	Yes	No	No	Chronic recurrent DVT
6	Yes	Yes	Yes	No	No	No	No	No	Interstitial lung disease
7	Yes	Yes	No	No	Yes	No	Yes	Yes	Clinical improvement
8	Yes	Yes	No	No	Yes	No	No	No	Clinical improvement
9	Yes	No	No	No	Yes	No	No	No	Clinical improvement
10	Yes	Yes	Yes	No	No	No	No	No	Clinical improvement
11	Yes	Yes	No	No	No	No	No	No	Clinical improvement
12	Yes	Yes	No	No	Yes	Yes	No	Yes	Maintenance hemodialysis

ANA – antinuclear antibodies, DVT – deep vein thrombosis.

of APL markers. Similarly to lupus, SCD is associated with a higher risk of thromboembolism than controls [32], and the coexistence of both will certainly increase the risk in such patients. Besides APL, other risk factors for thrombosis in lupus include disease activity, premature and accelerated atherosclerosis, and chronic inflammation [33]. Anti-ds-DNA and extractable nuclear antibodies are not frequent in isolated SCD [15] and may be used as immunologic indicators of the coexistence of lupus with SCD. Anti-ds-DNA and extractable nuclear antibodies were documented in 75% and 58.3% of our patients, respectively. A variable percentage of these antibodies was reported in various case reports and case series [10–15]. Apart from the diagnostic challenge of such an association, there are a few management challenges as well. The management of SLE-SCD stems from the management of isolated lupus, as there are no randomized controlled trials available to develop guidelines for management.

The use of hydroxychloroquine may increase the risk of retinopathy in patients with SLE-SCD associations. A baseline maculopathy assessment was done in the majority of our patients, and only 2 had pre-existing maculopathy that precluded the use of hydroxychloroquine. Despite the known adverse effects of steroids, they appear to be effective in the control of the disease in the active phase but particularly increase the risk of vaso-occlusive crisis, infection, avascular necrosis, and osteoporosis [34]. Hydroxyurea as a routine drug for certain SCD patients may mask manifestations of autoimmune conditions, including SLE, in undiagnosed subjects due to its immunosuppressive effects, leading to missed and delayed diagnoses. In addition, hydroxyurea may mask hydroxychloroquine-induced maculopathy in SCD-SLE subjects due to its link with the prevention of SCD retinopathy [35].

Despite reports of the tolerability of disease-modifying anti-rheumatic drugs, including biologics, there are a few instances of exacerbations of SCD and the development of infections requiring hospitalization in those on these medications [15, 34].

While 2 patients are on maintenance hemodialysis, one on lifelong anticoagulation due to chronic recurrent DVT, and another with interstitial lung disease, others have had significant clinical improvement. Our SLE-SCD series confirmed the existence of this coexistence in Nigerian patients. Constitutional symptoms and musculoskeletal, as well as mucocutaneous manifestations, are more frequent with high levels of lupus antibodies.

Study limitations

As there are limited data on this topic and most studies are case reports and case series with low levels of evidence, our findings cannot be generalized and should be interpreted with caution. We were unable to determine any difference between the clinical and laboratory profiles of SLE-SCD and isolated SLE. Furthermore, it remains to be determined whether the association is a mere coincidence or a true association. Large-scale longitudinal cohorts and case-control studies would be able to address the aforementioned limitations.

Conclusions

Heightened consideration for the possibility of the co-existence of SLE is warranted in SCD patients with musculoskeletal symptoms unresponsive to standard SCD treatment, such as inflammatory synovitis, hair loss, mouth/oral sores, facial rash, nephrotic syndrome, photosensitive rash, cytopenias, and positive SLE-specific autoantibodies. We hope this report will raise diagnostic suspicion and ensure early diagnosis and prompt initiation of effective treatment to prevent multiorgan dysfunction and damage that may ensue from the co-occurrence of these diseases.

Disclosures

Conflict of interest: The authors declare no conflict of interest.
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Ethics approval: The study was approved by the National Health Research Ethics and Committee of Nigeria (NHREC) as the data and study center was part of the Nigeria Multicenter Retrospective Lupus Cohorts and Registry, approval number: NHREC/01/01/-2007/26/01/2022.
Data availability: The data that support the findings of this study are available on request from the corresponding author (G.J.O.).

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