Lupus myocarditis, a reversible cause of heart failure in sub-Saharan Africa: a case report

Odunlami G[1], Olaosebikan H[2], Ogunlade O[3], Ajibade A[4]

[1]*Rheumatology Unit, Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), PMB 5538, Ile-Ife, Osun State, Nigeria*
[2]*Rheumatology Unit, Department of Medicine, Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria.*
[3]*Cardiology Unit, Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Osun State, Nigeria*
[4]*Rheumatology Unit, Somerset NHS Foundation Trust, United Kingdom*

Corresponding author
Dr. Gbenga Odunlami, Rheumatology Unit, Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), PMB 5538, Ile-Ife, Osun State, Nigeria. Email: godunlami31@gmail.com

Abstract

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with multisystemic involvement and varied clinical courses. It has a predilection for women in their reproductive ages. It is more common in sub-Saharan Africa than was previously reported. While pericarditis is a relatively common cardiac manifestation of lupus, myocarditis is a rare but potentially life-threatening manifestation. Myocarditis may present as heart failure amid other multisystemic manifestations. Therefore, a high index of suspicion is required for early diagnosis and prompt management to prevent fatal complications. We hereby present a 24 year old female who presented at our rheumatology clinic with generalized lymphadenopathy and inflammatory polyarthritis. She subsequently defaulted clinic follow-up until she presented five months later at the emergency department with sepsis, serositis, lupus myocarditis, and acute heart failure with reduced left ventricular ejection fraction. She was commenced on intravenous antibiotics and within days of methylprednisolone therapy, she experienced a dramatic improvement in her cardiac symptoms.

Key words: Systemic lupus erythematosus, Myocarditis, Heart failure, Sub-Saharan Africa

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that is characterized by inflammation of multiple organ systems with a myriad of clinical manifestations. Cardiac involvement is found in about 50% of patients with lupus, affecting the heart components[1,2]. However, myocardial involvement is relatively rare and may present as heart failure with associated extracardiac manifestations[1,2]. The frequency of myocarditis presenting as acute heart failure is rarely reported in sub-Saharan African studies on heart failure probably because these studies focused only on chronic heart failure. The important causes of heart failure in those studies include hypertension, cardiomyopathies, rheumatic heart disease, endomyocardial fibrosis, and HIV-induced cardiomyopathy[3,4]. The prevalence of SLE in sub-Saharan Africa according to a meta-analysis of recent studies shows that it is much higher than it was previously reported[5,6]. This is probably due to increasing diagnostic capacity, environmental factors (pollution, viruses, smoking, western lifestyle), and poverty[6]. In addition, SLE reported in sub-Saharan Africa also share some clinical and demographic characteristics with African descendants living outside Africa in terms of early age at diagnosis, female predominance, and protean manifestations including myocarditis[6,7]. Therefore, the purpose of this case report is to raise awareness of lupus myocarditis as an important reversible cause of acute heart failure in sub-Saharan Africa.

Case report

The index case is a 24 year old woman who presented in March, 2019 at the Rheumatology Clinic of the Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife on account of progressive and painless right post-auricular swelling and multiple inflammatory joint pains involving her toes, ankles, feet, knees, wrists, elbows, shoulders, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints with associated swelling in the affected hand joints, ankles, and wrists. She also had low-grade fever, but no fatigue or weight loss. Other systemic history was insignificant. She was not a known hypertensive or diabetic. There was no family history of autoimmune disease.

General physical examination showed non-tender, mobile, and rubbery axillary and inguinal lymphadenopathy. There was also a mass on the right side of her neck, in the post-auricular area, measuring 4cm by 4cm, non-tender, mobile, and rubbery, perceived to be

an enlarged lymph node. Musculoskeletal examination findings were in keeping with inflammatory polyarthritis of the affected joints. Examination of other systems was essentially normal. An assessment of SLE was made to rule out lymphoma, rheumatoid arthritis, and viral polyarthritis.

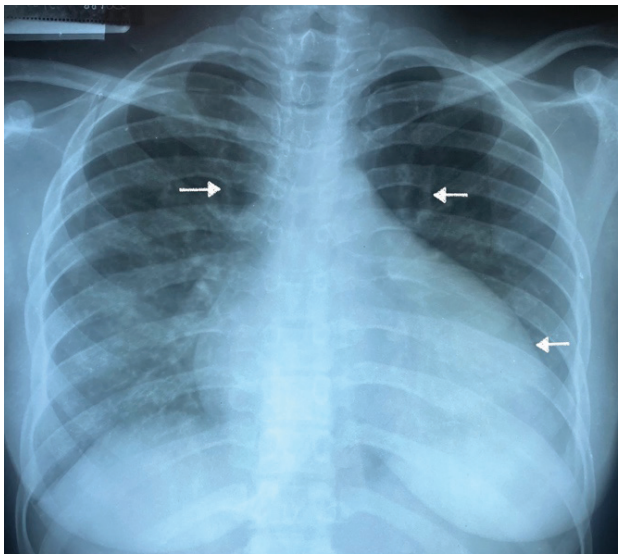
Complete blood count showed Packed Cell Volume (PCV) of 30% and the Erythrocyte Sedimentation Rate (ESR) was 132mm/hr. C-Reactive Protein (CRP) was also raised, 45.3-g/L (0 -10-g/L). Plain hand radiograph, viral screening, serum electrolytes, urea, and creatinine; urinalysis, and urine microscopy were all normal. Antinuclear Antibody (ANA), Anti-double stranded Deoxyribonucleic Acid (Anti-dsDNA), Rheumatoid Factor (RF), anti-Cyclic Citrullinated Peptide (Anti-CCP), and biopsy of the neck mass were ordered but the patient declined.

The patient was lost to follow-up until she presented five months later with high-grade fever, watery diarrhoea, nocturnal cough productive of whitish sputum, exertional dyspnoea, orthopnoea, and paroxysmal nocturnal dyspnoea. There was no associated abdominal or leg swelling, no history of exercise intolerance or post-exertion squatting in childhood.

Respiratory examination revealed tachypnoea, and coarse crepitation in the middle and lower lung zones bilaterally. Cardiovascular examination revealed tachycardia, displaced apex beat in the left 6th intercostal space, anterior axillary line, diffuse, with S1, S2, and S3 gallop rhythm.

Repeat full blood count showed PCV of 20.6%, leucopenia (3700/μL), and lymphopenia (700/μL). Sputum, blood, urine, and stool culture yielded no growth. Serum procalcitonin was highly elevated. Chest radiograph showed cardiomegaly with upper lobe diversion of vascular markings and non-homogeneous opacities in the right middle and lower lung zones, and mild left-sided pleural effusion (Figure 1).

Figure 1: Chest plain radiograph on admission showing cardiomegaly and upper lobe diversion of vascular markings



Electrocardiogram (ECG) showed sinus tachycardia, left atrial enlargement, left ventricular hypertrophy, and widespread T-wave inversion in anterolateral leads (Figure 2). Echocardiography revealed mild pericardial effusion, dilated left ventricle with hypertrophied interventricular septum and the left ventricular posterior wall, reduced Left Ventricular Ejection Fraction (LVEF) of 30%, and left ventricular diastolic dysfunction. The heart valves were normal. Antinuclear antibody titre was 1:5120, Anti-ds-DNA was> 200 (0 – 25U/ml). Rheumatoid factor and anti-CCP were negative. A lymph node biopsy showed no evidence of lymphoma. Fasting lipid profile, fasting blood glucose and two-hour postprandial glucose were also normal.

Figure 2: ECG on admission showing left ventricular hypertrophy, left atrial enlargement, and T-wave inversion of the anterolateral leads

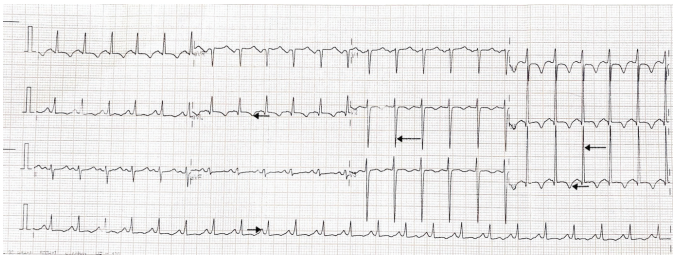
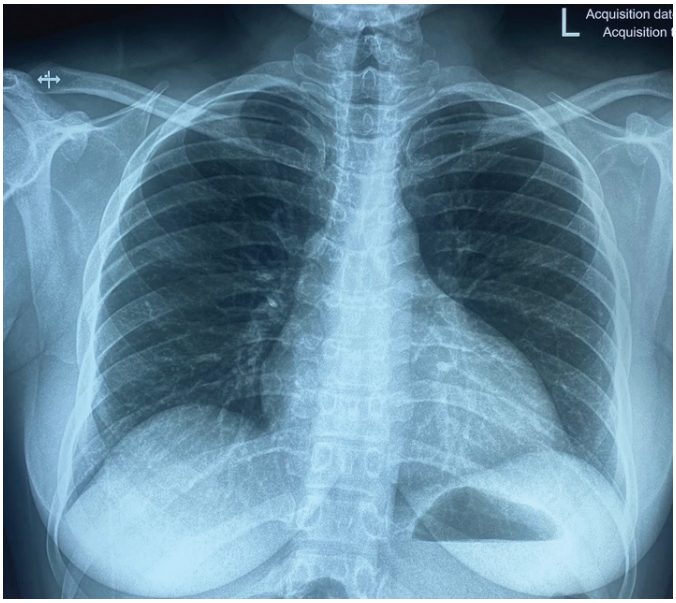


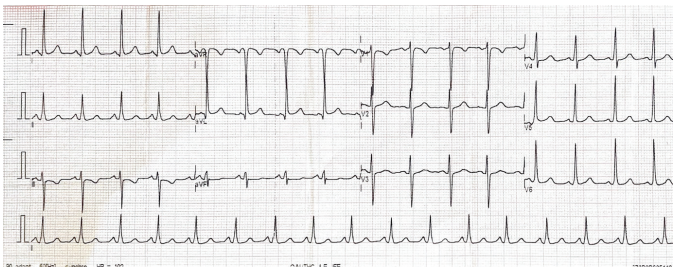
Figure 3: Repeat chest plain radiograph at 3 year follow-up showing dramatic structural reversal of the earlier changes



Using the 2012 Systemic Lupus Erythematosus International Collaborating Clinics Criteria (SLICC), a diagnosis of SLE complicated by heart failure with reduced ejection fraction(New York Heart Association class IV) and sepsis from chest focus was made. She was treated with intravenous antibiotics for sepsis with serial serum procalcitonin monitoring while anti-failure regimen with oral spironolactone, telmisartan, frusemide, and bisoprolol was commenced. The patient had two pints of blood transfused and was pulsed with methylprednisolone

500mg daily for three days followed by oral prednisolone, intravenous cyclophosphamide regimen for induction therapy, and then oral mycophenolate mofetil for maintenance therapy. Within a week after completing pulse steroid therapy, there was a dramatic improvement in her cardiac symptoms and she was subsequently discharged for follow-up. Echocardiography was repeated 6 months later and was completely normal with LVEF of 58%. Anti-failure regimen was then discontinued and serum anti-dsDNA was serially monitored until it was normal. She is presently on low-dose prednisolone, hydroxychloroquine, azathioprine, and calcium/vitamin D supplement. The generalized lymphadenopathy has also completely resolved. Repeat chest radiograph and ECG that were done on follow-up showed signs of significant improvement (Figures 3 and 4).

Figure 4: Repeat ECG, done at 3 year follow-up showing complete normalization of the earlier changes



Discussion

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune, multisystemic connective tissue disease characterized by the elaboration of auto-antibodies targeting nuclear antigens, highly variable clinical presentations, disease course, and prognosis[8]. The global prevalence of SLE ranges from 20 – 70 per 100,000 with a higher prevalence in African Americans and a female-to-male ratio of 7-15:1[8,9]. Cardiac manifestations in SLE can involve the pericardium, myocardium, endocardium or valves, coronary arteries, and the conducting system[2]. While pericarditis is the commonest cardiac manifestation of lupus, myocarditis is a rare, life-threatening condition, presenting as acute heart failure and it usually occurs as part of generalized lupus activity[2,10]. Clinical lupus myocarditis usually presents with fever, dyspnoea, tachycardia, and congestive heart failure. The most common features include left ventricular dysfunction, non-specific ST/T-wave changes, segmental wall motion abnormalities, and decreased ejection fraction found in >80% of patients with myocarditis[11]. Other features include cardiomegaly, diastolic dysfunction, arrhythmias, and conduction defects[12,13]. In addition, left ventricular hypertrophy with/without atrial hypertrophy or ectopic ventricular beat could be an important feature of lupus myocarditis among black Africans[14]. A study done in South Africa on lupus myocarditis suggested that absolute lymphopenia and reduced LVEF at presentation were predictors of mortality[7]. Anti-Ro (SSA) and anti-RNP have been associated with lupus myocarditis[12,15]. Furthermore, markers of myocardial injury such as troponin I and creatine kinase may be raised in lupus myocarditis with the former being more sensitive[16]. Coronary artery disease in this patient is unlikely considering the age and absence of the traditional risk factors and classical features. Patients usually respond dramatically well to pulse steroid and strong immuno suppressives such as cyclophosphamide, mycophenolate mofetil, and rituximab with favourable outcome as it was with this case[10,12].

Anaemia of chronic disease, increased ESR, serositis, inflammatory arthritis, and lymphadenopathy are common manifestations of SLE and usually indicate an active disease[11]. Studies in Africa show that while polyarthritis, serositis, and alopecia are common presentations in lupus patients, skin manifestations are not as common as was reported in the literature[5,17]. SLE is an immunosuppressive disease; therefore, patients with active disease are predisposed to infection with both typical and atypical pathogens. Causes of immunosuppression in lupus include CD4 lymphopenia and immunosuppressive drugs. Infection is a major cause of mortality in SLE and therefore, it should be aggressively managed[6,11]. Although there are conflicting reports about the correlation between CRP and lupus activity, CRP is elevated in arthritis, serositis, lupus nephritis, and myocarditis.

Antinuclear antibody is a useful screening test for connective tissue disease because of its high sensitivity (>90%). However, it has a low positive predictive value for SLE because of its lower specificity. However, anti-dsDNA is highly specific (>95%) for lupus[11].

Lupus myocarditis is associated with high mortality. The newer and highly sensitive non-invasive imaging modalities such as cardiac magnetic resonance imaging, speckle tracking echocardiography, and 18F-fluorode oxyglucose positron emission tomography are emerging in the diagnostic evaluation of both clinical and subclinical forms of lupus myocarditis. It remains to be seen whether subclinical myocarditis is a predictor of fulminant myocardial disease or if early therapeutic intervention can modify the disease course and prevent the evolution of a clinical disease[7,18].

Limitations of this study include the inability to obtain echocardiographic images for this case report due to the limited memory of the echocardiographic machines. Furthermore, other important diagnostic investigations such as cardiac enzymes and connective tissue disease screening panel could not be done due to financial constraints and poor insurance coverage in a poor resource setting.

Conclusions

Systemic lupus erythematosus is the commonest connective tissue disease in black Africans and emerging studies in sub-Saharan Africa suggest that its prevalence may be similar to that reported among African-Americans. Furthermore, lupus runs a more aggressive course among

black Africans which correlates with the finding that the African-American race is an independent risk factor for lupus myocarditis. Therefore, lupus myocarditis should be considered especially in a young black woman who presents with florid symptoms of acute heart failure with extra cardiac manifestations in the absence of traditional risk factors for heart failure. SLE is a multisystemic disease that requires a multi-disciplinary approach to management to optimize outcome. Lupus myocarditis is a reversible cause of heart failure among black Africans if diagnosed early and prompt therapeutic intervention is instituted. The outcome of treatment is generally favourable and life-saving.

Disclosure: The authors hereby disclose no conflict of interest in writing this case report.

References

1. Doria A, Iaccarino L, Sarzi-Puttini P, Atzeni F, Turriel M, Petri M. Cardiac involvement in systemic lupus erythematosus. *Lupus.* 2005; **14**:683–686..
2. Moder KG, Miller TD, Tazelaar HD. Cardiac involvement in systemic lupus erythematosus. In: Mayo Clinic Proceedings. *Elsevier* 1999; **74**: 275–84.
3. Gallagher J, McDonald K, Ledwidge M, Watson C. Heart failure in Sub-Saharan Africa. *Cardiac Failure Review.* 2018; **4**:21-24.
4. Agbor VN, Essouma M, Ntusi NAB, Nyaga UF, Bigna JJ, Noubiap JJ. Heart failure in sub-Saharan Africa: A contemporaneous systematic review and meta-analysis. *Int J Cardiol.* 2018; **257**:207–215.
5. Adelowo O, Bello M. Systemic autoimmune diseases: not so rare in black Africans. *State of Immunity.* 2014; **9**:74-79.
6. Essouma M, Nkeck JR, Endomba FT, Bigna JJ, Singwe-Ngandeu M, Hachulla E. Systemic lupus erythematosus in Native sub-Saharan Africans: A systematic review and meta-analysis. *J Autoimmun.* 2020; **106**:102348
7. Du Toit R, Herbst PG, van Rensburg A, du Plessis LM, Reuter H, Doubell AF. Clinical features and outcome of lupus myocarditis in the Western Cape, South Africa. *Lupus.* 2017; **26**:38–47.
8. Fava A, Petri M. Systemic lupus erythematosus: diagnosis and clinical management. *J Autoimmun.* 2019; **96**:1-3.
9. Oku K, Atsumi T. Systemic lupus erythematosus: nothing stale her infinite variety. *Mod Rheumatol.* 2018; **28**:758-765.
10. Chen PY, Chang CH, Hsu CC, Liao YY, Chen KT. Systemic lupus erythematosus presenting with cardiac symptoms. *Am J Emerg Med.* 2014; **32**(9):1117–19.
11. Johannes WJ Blisma, Eric Hachulla. Eular Textbook on Rheumatic Diseases. Sofia T, George B, Caroline G, Dimitrios TB, editors. Systemic Lupus Erythematosus: Pathogenesis and Clinical Features. London: *Br Med J.* 2016; **531**-557
12. Marc CH, Ellen MG, Allan JS, Josef SS. Rheumatology 7th. Daniel JW, Michael HW, Jose AG, Gerald E, Ricard C, editors. Clinical Features and Management of Non-renal and Non-central Nervous System Lupus. P*hiladelphia: Elsevier;* 2019:**1111**-1178
13. Pinamonti B, Alberti E, Cigalotto A, Dreas L, Salvi A, Silvestri F, *et al.* Echocardiographic findings in myocarditis. *Am J Cardiol.* 1988; 62:285-291.
14. Yaméogo NV, Tougouma SB, Zabsonré J, Kologo KJ, Tiemtore WS, Kagambega LJ, *et al.* Cardiovascular damage during lupus in black African subjects. *J Cardiol Cardiovasc Med.* 2018; **3**:31-34.
15. Logar D, Kveder T, Rozman B, Dobovisek J. Possible association between anti-Ro antibodies and myocarditis or cardiac conduction defects in adults with systemic lupus erythematosus. *Ann Rheum Dis.* 1990; **49**:627-629.
16. Smith SC, Ladenson JH, Mason JW, Jaffe AS. Elevations of cardiac troponin I associated with myocarditis: experimental and clinical correlates. *Circulation.* 1997; **95**:163-168.
17. Adelowo OO, Oguntona OA. Pattern of systemic lupus erythematosus among Nigerians. *Clin Rheumatol.* 2009; **28**:699-703
18. Perel-Winkler A, Bokhari S, Perez-Recio T, Zartoshti A, Askanase A, Geraldino-Pardilla L. Myocarditis in systemic lupus erythematosus diagnosed by 18 F-fluorodeoxyglucose positron emission tomography. *Lupus Sci Med.* 2018; **5**:e000265.