Congestive Cardiac Failure in a patient with Systemic Sclerosis: Case Report and Literature Review

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ABSTRACT

BACKGROUND

Systemic sclerosis and other connective tissue diseases are thought to be rare in Nigerians and are not common causes of heart failure compared to hypertensive heart disease. The presence of cardiac involvement in a patient with systemic sclerosis generally portends poor outcome. We therefore present a report of congestive cardiac failure in a patient with systemic sclerosis.

METHODS

The case records of a patient with systemic sclerosis and congestive cardiac failure and a review of the literature utilizing Medline, PubMed and google search engines was utilized.

RESULT

A 63 year old female with ACR criteria for the diagnosis of SSc presented in CCF. Cardiac evaluation revealed findings suggestive of primary cardiac disease of SSc. The presence of CCF in patients with SSc is a poor prognostic marker and cause of mortality and morbidity,

CONCLUSION

Early detection of cardiovascular manifestations should be a priority in systemic sclerosis. To the best of our knowledge, CCF due to SSc has not been reported in Nigerians.

KEYWORDS

Systemic sclerosis; Primary Cardiac Disease; Heart failure; Nigerians

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INTRODUCTION

Systemic sclerosis (SSc) is a chronic autoimmune multi-systemic disorder of unknown etiology characterized by the presence of fibrosis of the skin and visceral organs, predominantly small vessel disease and a systemic inflammatory process.[1] The disease is characterized by thickening of the skin (scleroderma) and distinctive involvement of multiple internal organs, most notably the lungs, gastrointestinal tract, heart, and kidneys[1,2].

The increasing morbidity, mortality and reduced life expectancy accompanying SSc has consistently been associated with the cardio-pulmonary complications of pulmonary arterial hypertension, interstitial lung disease(ILD) and cardiac function impairment[1]. Consequently lung and heart involvement in SSc are the major poor prognostic factors.[1,3]

This recognition of cardio-pulmonary

involvement in the morbidity and mortality of SSc is demonstrated by the findings of Al-Dhaheret al[3] in a Canadian study which reported worse survival rates for patients with cardiac disease and hypertension, with pulmonary arterial hypertension, renal complications, ILD and cardiac complications as the major primary causes of death.[3]

The prevalence and epidemiology of cardiac involvement and cardiac dysfunction in SSc and its impact on mortality and morbidity has been the subject of interest in recent studies.[4]

This interest has been promoted by the contribution of cardiac-related deaths from primary cardiac causes (fibrosis) which is estimated at 15% of all SSc deaths.[4]The need to improve the persistent mortality rates from cardiac disease in contrast to the reduced death rates from renal complications has also stimulated research on the cardiac impact of SSc.[3-6]

The heart involvement in SSc is either primary, related to myocardial fibrosis, or secondarily from pulmonary arterial hypertension (PHT) and systemic hypertension[1,4,5,7,8.]

The consequences of direct cardiac involvement in SSc are Arrhythmias and conduction defects from reentry, inflammation and local fibrosis which may lead to palpitation and syncope. Other effects are pericardial disease from inflammation and effusion which leads to dyspnea and chest pain; and direct myocardial involvement with myocarditis and fibrosis which leads to congestive cardiac failure (CCF)[1,4,5,7,8,9.].

The key elements of cardiac involvement which have been implicated as risk factors for and predictors of morbidity in SScare left ventricular (LV) systolic dysfunction, left axis deviation and pericardial involvement with large effusion.[4-8,9]

These key elements and manifestations of primary cardiac disease in SSc are known to occur at various points in the course of SSc disease. As a result, the opinion that cardiac complications are only associated with long-standing skin involvement are no longer valid as myocarditis, sudden death or cardiac arrhythmias, may occur during the early stage of the disease.[4-8,9]

It is known that LV systolic dysfunction related to myocardial fibrosis and myocarditis resulting in CCF may complicate the clinical course of SSc patients. The diagnosis of CCF may however be missed by clinician's as the features can be disguised by the respiratory and secondary cardiac causes of dyspnea[4,8-11]

It is thus important to ensure adequate evaluation in SScpatients with cardiac failure symptoms, in order to avoid a misdiagnosis of CCF from direct cardiac involvement as corpulmonalesecondary pulmonary arterial hypertension or systemic hypertension from renal disease[10,11].

The importance of avoiding this pitfall in patients with SSc is the fact that

treatment options for CCF from primary cardiac and secondary causes differ, as immunosuppressive and steroids are indicated in patients with CCF from myocarditis[4,8].

Ssc is thought to be rare among Nigerians and even Africans[12-14] though recent studies have shown that it is not as rare as previously thought.[14-16]In settings like Nigeria where SSc is considered a rarity the diagnosis of CCF from primary cardiac disease is therefore more likely to be over looked and under diagnosed.

The objective of this report is to present a case of CCF in a patient with SSc in Nigeria in order to increase the knowledge and index of suspicion as diagnostic facilities are more available.

CASE REPORT

Mrs O. J. a 63yr old petty trader presented with three months history of bilateral leg swelling, dyspnoea at rest; paroxysmal nocturnal dyspnoea, orthopnea, palpitation, unproductive cough and right hypochondrial pain. She was neither a known hypertensive nor diabetic. Six months earlier, she had noticeda non-pruritic rash in the arms which later spread to involve the axilla, shoulders, neck, face, and the anterior chest wall with areas of hypo pigmentation over the face, neck and the upper trunk. There was no loss of sensation in the hypopigmented regions.

On examination, she had salt and pepper rash on the face, neck, arms and upper trunk. There were hypopigmented patches on the chest with alopecia areata. (Figure 1)

She was in respiratory distress with a pulse rate off 110beats per minute and thickened arterial wall but no locomotor brachialis. Blood pressure was 110/70 mmHg and the jugular venous pressure(JVP) was raised to angle of the jaw at 12cm/H_2O. The precordium was normoactive with the apex beat located at the fifth left intercostal space, lateral to mid clavicular line without an apical and left parasternal heave. There was S3 gallop rhythm with grade 3/6 non radiating apical midsystolic murmur.

The electrocardiogram showed sinus tachycardia with occasional Premature Ventricular Complexes and inferolateral ischemia. – Figure 2

Echocardiography showed dilatation of all four chambers with an Ejection fraction of 38%. There was grade III diastolic dysfunction, moderate mitral regurgitation, dilated pulmonary artery and thickened pericardium. These findings indicated marked systolic dysfunction and diastolic impairment of restrictive pattern. (Figure 3)

Her ESR was 44mm/hr while Anti-nuclear antibody and anti-topoisomerase antibody were also negative. The Pulmonary function test showed a restrictive pattern.

Serum electrolytes, renal function indices, liver enzymes and lipid profile were with normal limits, while serum uric acid was elevated 801umol/l.

A Skin biopsy was taken for histology and this revealed a section of skin tissue with atrophic epidermis. The dermis was thickened by broad bands of hyalinized collagen bundles that appeared loose in the papilary dermis and compact in the reticular dermis with extension to the subcutaneous tissue. The dermal appendages also appeared atrophic. There were a few blood vessels with thickened wall and collagen deposit around them.

The findings were consistent with SSc as the patient's clinical features of Proximal diffuse (truncal) sclerosis (skin tightness, thickening, non-pitting induration) and evidence of pulmonary restriction and fibrosis met the American College of Rheumatology (ACR) criteria for the diagnosis of Scleroderma.[17]

The patient was treated for CCF with frusemide, spironolactone, lisinopril, digoxin, prednisolone, wafarin and enoxparin. She however developed bleeding from the skin 8

days after commencement of steroids. She died in the course of treatment from cardio-pulmonary insufficiency.

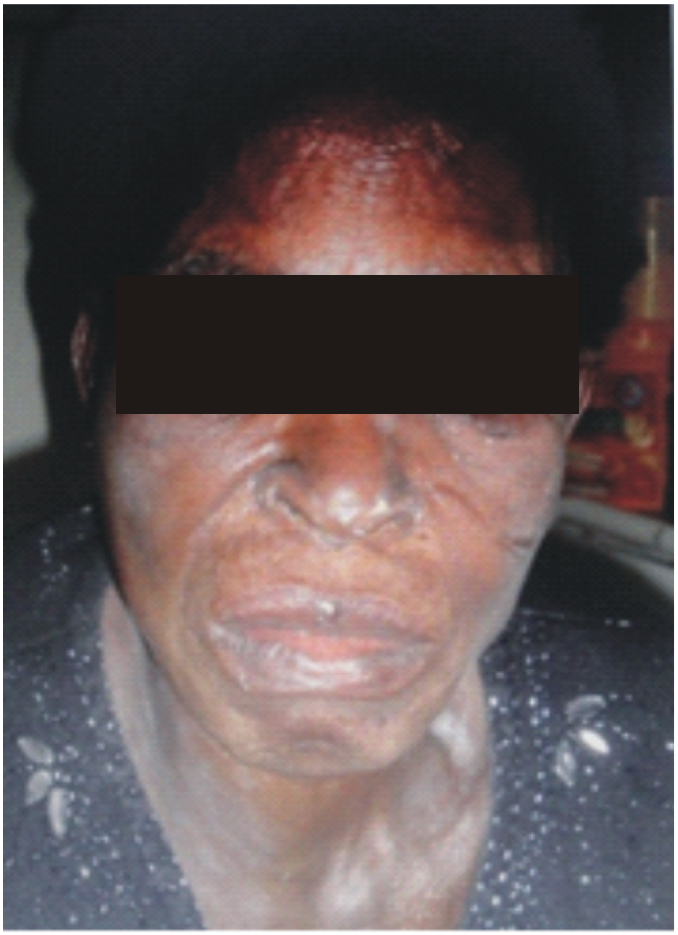

Figure 1 –Hypopigmentation and salt and pepper rash on the face

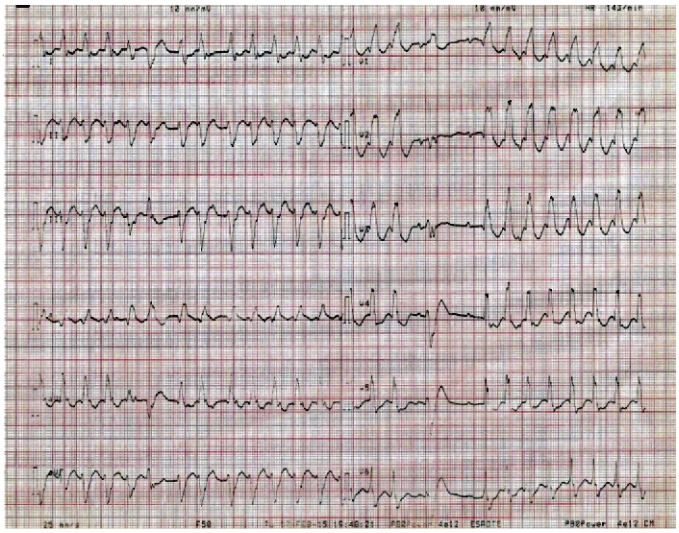

Figure 2 – ECG showing tachycardia and Premature Ventricular Complexes

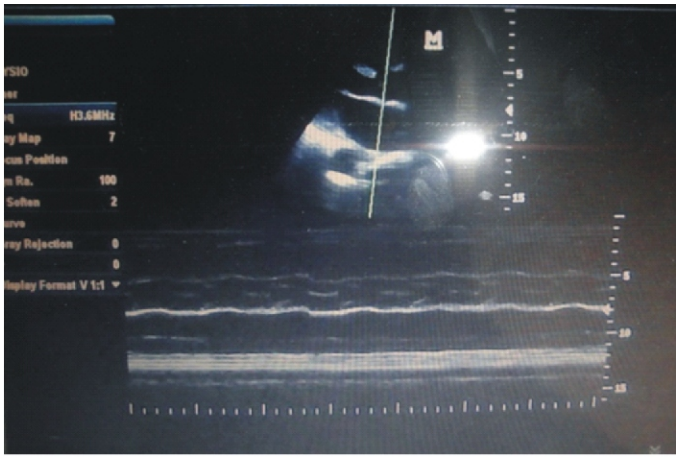

Figure 3 –Echocardiography showing dilated left atrium and thickened pericardium.

DISCUSSION

Systemic sclerosis was first reported in a Nigerian by Ladipo et al in 1976[12]. The case was mistaken for Leprosy due to its affectation of peripheral nerves as suspected in this case.

In 1979, Jacykl[13] reported another case and described its rarity in Africans. Since then many more reports and studies of SSc have been published from Nigeria but with minimal emphasis on the cardiac manifestations of this disease.[14-16]

The incidence of SSc differs among different populations with an incidence of 3.7 per million per year in the United Kingdom and 18.7-22.8 per million per year in the USA.[14]

There is a paucity of community based data from black Africa and most of the data on SSc are from hospital based studies. A study by Adelowoet al[14] in Nigeria reported a scleroderma prevalence of 1.1% out of 1,250 rheumatology cases over a 5-year period (2001-2006) with a total of 14 cases. The majority 85.7% of the patients were females compared to males 14.3%, while the age range of the cases was between 26-69 years with a mean of 40.3years[10]. The index patient in this report was a female aged 63 years.

The cardiac effects of SSc are known to be diverse[1,4]. Though only relatively recently recognized; cardiac involvement is a major manifestation of SSc[4,8]. The cardiac

involvement in SSc is considered a serious consequence as the presence of cardiac involvement generally signifies a poor outcome for the patient;[1,4,8,18] especially as individuals who develop clinically apparent myocardial manifestations are recognized to be at greater risk of clinical deterioration[8,9,18]. Therefore the monitoring of myocardial involvement represents an important aspect of their disease management[1,4].

The cardiac involvement in SSc can generally be divided into direct cardiac effects and the indirect effect of other organ involvement such as pulmonary hypertension and renal crisis[4,8,18]. The direct cardiac effects can involve the myocardium, coronary arteries, pericardium and the conduction system[4,5,8,18].

Vlachoyiannopoulos *et al*[19] in a review article retrospectively analyzed the clinical files of 254 patients over 4 years. They estimated the mortality rate to be 2% per year, and the incidence of cardiac disease to be between 7% in lcSSc and 21% in dcSSc patients. Similar findings have been reported in an African population by Ilovi and Oyoo[15] in Kenya who found a prevalence of 22% for cardiac involvement in patients with SSc. It has also been suggested that the use of nuclear cardiology imaging will reveal a higher estimate of cardiac involvement in patients with Ssc[7].

In the majority of SSc patients, cardiac manifestations may remain subclinical and are usually undetected[4,8]. These early cardiac manifestations can then progress silently to myocardial fibrosis and may also manifest as arrhythmia, left and right heart dysfunction and cardiac failure, pericardial disease, valvular disease and sudden death.[4,5,8]

The relatively short course of 6months from the onset of disease to the presentation with CCF and the resultant mortality in our patient exemplifies the early and silent onset of cardiac complications of SSc. In addition the adverse outcome of mortality which is associated with cardiac manifestations in SSc[1,3,4] is also illustrated by the presented index case.

The presentation and outcome of our reported case also indicates the variability of the clinical course in SSc as well as the connection of skin sclerosis with cardiac disease[4,8].

The patient in our report presented with arrhythmias (PVCs), cardiac ischemia, pericardial disease and ventricular dysfunction which are all features of primary cardiac involvement thus strengthening the diagnoses of CCF in this patient rather than a secondary event such as cor-pulmonale.

Kane et al[20] studied 29 patients with systemic scleroderma who underwent a complete cardiovascular work-up including physical examination, electrocardiogram, chest x-ray and Doppler-echocardiogram. Hypertension was observed in 20.7% of the patients while heart disease was observed in 14 (48.3%) of patients. Myocardial disease was the most frequent form of cardiac disease in 37.9% of the patients followed by pericardial disease and valve disease seen in 13.8% of the cases each. Rhythm and conduction disorders were found in 2 (6.9%) and 8 (27.6%) of the patients respectively.

Baduiet al[21] in a study based on non-invasive cardiac evaluation among 20 patients with progressive SSc reported that 16 (80%) of the patients had some form of cardiovascular complications and abnormalities on electrocardiography (ECG) while 45% of them showed some kind of abnormality on echocardiography.

Meuneet al[22] studied 100 consecutive patients presenting with SSc without pulmonary arterial hypertension or clinical manifestations of heart failure. All patients underwent standard echocardiography. He reported that patients with SSc had a wider mean left atrial diameter, a smaller LV ejection fraction, higher pulmonary artery pressures and diastolic dysfunction as also seen in our patient.

In our patient the electrocardiogram showed sinus tachycardia with occasional premature ventricular complexes and inferolateral ischemia.The echocardiography showed dilatation of all four chambers with an Ejection fraction of 38%, grade III diastolic dysfunction, moderate mitral regurgitation and thickened pericardium.

These features are in keeping with the findings of the studies from Kane et al[20], Badui et al[21]and Meune et al[22]above and further confirm the evidence of primary cardiac complication of SSc in the reported case.

These clinical manifestations of SSc cardiac disease reflect the underlying conditions of myocardial necrosis and fibrosis and may at times mimic ischemic heart disease due to atherosclerosis[8,9]. If myocardial injury is extensive enough, it may lead to dilated hypodynamic ventricles and a syndrome resembling idiopathic dilated cardiomyopathy may be simulated as seen in our patient who had dilatation of all four cardiac chambers on echocardiography.

In general, myocardial fibrosis is considered to be the hallmark of cardiac involvement in SSc[1,4,8,18]. The fibrosis which is patchy and involves all levels of the myocardium bears no direct relation to large or small vessel occlusion or other anatomic abnormalities[4,8,9]. Consequently all levels of the myocardium may be unpredictably involved with the right ventricle affected as often as the left. It is thus possible that the right ventricular involvement seen in this patient may be a result of this process and not a secondary event from pulmonary hypertension.

Systolic and/or diastolic dysfunction can occur as a result of myocardial fibrosis but the role of ongoing low grade myocarditis in this process is less well characterized[1,4,8,19]. Overt congestive heart failure occurs in more advanced disease, but systolic dysfunction is often clinically occult. Diastolic dysfunction is found in more than half of patients with scleroderma, even in the absence of myocardial ischemia, as it correlates with the severity of cutaneous disease[4,8]. Our patient had significant systolic and diastolic dysfunction and extensive skin involvement in keeping with this association as earlier highlighted.

The prevalence of atherosclerotic coronary artery disease is not increased in SSc[1,4,8]. However, in patients with scleroderma and coronary disease, the likelihood of coronary vasospasm is significantly higher than in the general population.[1,4,8,18] It is possible that coronary involvement in scleroderma is not in the epicardial vessels, but rests in small arterial segments as coronary angiograms are normal in patients with exercise-induced perfusion defects suggesting that abnormal resistance to flow is at the level of the microcirculation or myocardial interstitium [8,18,23].The patient in this report had features of inferolateral ischemia.

Pericardial abnormalities in scleroderma include fibrinous pericarditis, fibrous pericarditis, pericardial adhesions, constrictive pericarditis and pericardial effusions.[8,24] Asymptomatic pericardial effusions commonly occur in scleroderma and are frequently associated with pulmonary hypertension and may be the presenting feature of pulmonary hypertension in scleroderma. Large pericardial effusions can lead to pericardial tamponade and are a marker for poor outcome[8,24]. If an inflammatory component is thought to be the cause of the effusion, immunosuppression therapy can markedly reduce the volume of the effusion[8,24]. Moreover, if clinical heart failure is present, the effusion can be reduced with diuresis[8,24]. There was evidence of pericardial thickening in our patient in keeping with pericardial fibrosis.

Conduction defects and arrhythmias are seen frequently in scleroderma patients and are thought to be a result of fibrosis or ischemia of the conduction system.[4,5,8,18] The patient we presented had PVCs on the ECG. The conduction defects in patients with SSc are

significant as they have been linked with higher risk for sudden cardiac death which may occur from ventricular arrhythmias.[4,5,8,18]

Prior studies using echocardiography as well as studies on autopsy samples have suggested a relatively minor valvular involvement in SSc.[4,5,8] Shortening of the chordae tendinae of the mitral valve, mitral valve prolapse, mitral and aortic regurgitation and mitral and tricuspid valvevegetation's have all been reported.[4,5,8]The finding of mitral valve regurgitation in our patient is in keeping with the outcome of earlier studies.

At present, no treatments have been demonstrated to alter the natural history of primary cardiac involvement in patients with SSc.[4,5,8,26]

Although there is limited evidence in respect of specific therapeutic options, treatment of early abnormalities with calcium channel blockers such as Nifedipine and Nicardipine; and angiotensin-converting enzyme inhibitors (Captopril) may improve myocardial microcirculation, perfusion and function[25,26].

Ameliorating damage through tight control of systemic hypertension and early aggressive management of pulmonary hypertension are obviously important to prevent secondary cardiac damage[4,8,26].

Short-term treatment with the dual endothelin receptor antagonist bosentan has been shown to simultaneously improve myocardial perfusion and function.[26,27] It remains to be seen if long-term treatment might result in additional remodeling effects.[27]

When left ventricular function is impaired standard therapies such as ACE inhibition and vasodilating β-adrenoceptor blockade (if tolerated)should be used aggressively.[8,26]In addition implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy (CRT) may be applied as indicated.[8,26] In patients with CCF and fluid retention diuretics can be used to improve symptoms and when patients presenting with acutely deteriorating cardiac failure and persistent troponin leakage, indicative of active myocarditis aggressive cytotoxic therapy and immunosuppressive therapy with can be administered until troponin negativity is achieved.[26]

The patient in this case was placed on standard heart failure regimen and steroids. She however presented in an acute and critical state and all the implemented remedies could not save the patient.

The presence of clinical cardiac involvement in SSc is a harbinger of a poor prognosis[28]. Cardiac disease in SSc is associated with a 70% mortality at 5 years[28,29]. In general, higher risk findings in patients with SSc include clinical heart failure, poor RV function, pulmonary arterial hypertension, low cardiac index, high right atrial pressure, and documented ventricular arrhythmia[8,28]. Most of these features of poor prognosis were present in our index case, who died in the course of treatment.

CONCLUSION

Cardiovascular manifestations are frequent but often latent in patients with SSc. This finding emphasizes the importance of routine cardiovascular work-up in all patients with scleroderma.

We recommend that cardiovascular screening which should include ECG, echocardiography, chest radiograph and B-type natriuretic peptide concentrations should be done biannually inSSc patients, in order to anticipate the development of cardiac symptoms.

Although there is limited evidence in respect of specific therapeutic options, treatment of early abnormalities with calcium channel blockers and angiotensin-converting enzyme inhibitors may improve myocardial perfusion and function[18].

It is important to evaluate SScpatients with features of heart failure for primary cardiac

disease of SScwithout assumption that it is corpulmonale and other secondary causes of CCF.

LIMITATION

There is no photographic microscope in our centre.

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