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ORIGINAL RESEARCH

Systemic sclerosis (Scleroderma) among adults attending the Rheumatology Clinic of a Tertiary Institution

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Abstract

Background: Systemic sclerosis is a multi-systemic autoimmune disorder characterised by the generation of autoantibodies, massive deposition of collagen and other matrix substances in the connective tissues and alterations of the microvasculature.
Methods: This was a prospective study of all the cases of scleroderma seen between January 2012 and June 2015 at the Rheumatology Clinic of the Olabisi Onabanjo University Teaching Hospital. All the patients with the diagnosis of scleroderma were included. Excluded from the study were patients with other skin lesions not typical of scleroderma.
Results: Six hundred and six patients with rheumatologic disorders were seen over the study period but eight of them had scleroderma. All the eight cases of scleroderma were females. The age range was 36-52 years with a mean age of 45 years (SD ± 11.4 years). All the cases had arthritis and diffuse skin lesions. Other features included sclerodactyly, microstomia and salt and pepper skin appearance in all the eight cases while Raynaud's phenomenon and leg ulcers were not frequent. Inflammatory marker (erythrocyte sedimentation rate) was significantly elevated in all the cases. Renal and cardiovascular complications were the leading causes of death.
Conclusion: Diffuse systemic sclerosis is a more serious disease than the limited form. Early referral of patients with skin lesions suggestive of scleroderma to a specialist centre is recommended as symptomatic treatment helps to improve the quality of life.

Keywords: *Auto-antibodies, Collagen deposition, Connective tissues disorders, Organ dysfunction*

Introduction

Systemic sclerosis (SSc) is a multi-systemic disease. The clinical course and the prognosis vary with the extent of microangiopathy as well as the degree of involvement of the skin and internal organs. [1] The hallmark of SSc is excessive collagen deposition and accumulation on the skin and the internal organs. [2]

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]The pathogenesis of the disease includes immune dysregulation, endothelial dysfunction and excessive fibrous tissue deposits on the skin and internal organs. [3] There are two major subsets of this disease; limited cutaneous scleroderma and diffuse cutaneous scleroderma. In limited cutaneous scleroderma, fibrosis affects the hands, arm and the face mainly. Raynaud's phenomenon usually precedes fibrosis for many years, pulmonary hypertension occurs commonly and anti-centromere antibodies are seen in 50 to 90% of cases. [4] On the other hand, diffuse cutaneous scleroderma is a rapidly progressing disease which typically involves a wider area of the skin and affects one or more internal organ. [5]

The pathogenesis of systemic sclerosis (scleroderma) is complex and remains incompletely understood. Immune activation, vascular damage, and excessive synthesis of extracellular matrix with deposition of increased amounts of collagen are all known to be important in the development of this illness. [6] Scleroderma can lead to severe dysfunction and failure of any and multiple internal organs. The kidneys, oesophagus, heart and the lungs are commonly affected. [7] Drugs such as prostanoids, endothelin-1 and phosphodiesterase inhibitors are useful in the treatment of pulmonary arterial hypertension and digital ulcers. [8] Renal complications can be managed with angiotensin-converting enzyme inhibitors (ACEI). [9] Stem cell transplantation seems to be promising in restarting the immune system to limit fibrosis and restore micro-vasculature. [10]

Scleroderma is believed to be rare among blacks, hence, the aim of this study was to determine the prevalence of this disorder in a population of Nigerians.

Methods

This was a prospective study of all the cases of scleroderma seen over a period of three and a half years (January 2012 to June 2015). These were adult patients who attended the Outpatient Clinic of the Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria. All the patients with the clinical diagnosis of scleroderma were included and those whose skin lesions were not typical of scleroderma were excluded.

The demographic characteristics of the patients were obtained. A detailed history was taken and systemic physical examination was done with the emphasis on the lung, heart and the kidneys. Relevant ancillary laboratory and radiologic investigations were done as available. Skin biopsy was done in only one patient who presented with the scleroderma-like skin lesion.

Case definition

Scleroderma (systemic sclerosis) was defined according to the 1980 classification criteria of the American College of Rheumatology (ACR): the presence of one major criterion or two or more minor criteria. The major criterion was proximal scleroderma while the minor criteria included sclerodactyly, digital pitting scars of the fingertips and bibasilar pulmonary fibrosis.

Medications

All the patients received medications to prevent complications of internal organ involvements. Angiotensin enzyme inhibitors to prevent scleroderma renal crisis and proton pump inhibitors to prevent reflux of acidic gastric contents into the lungs were prescribed. Intermittent antibiotics were also given to prevent bacterial overgrowth from the stasis of the intestinal contents. Anti-fibrotic drugs (such as D-penicillamine and anti-cytokines) were also prescribed. Treatment of cardiac failure was instituted in patients with heart failure while the patient with scleroderma renal crisis had three sessions of renal dialysis.

Results

Six hundred and six patients with rheumatologic diseases were seen over the study period (January 2012 to June 2015). There were 372 females and 234 males, with a female to male ratio of 1.6:1. There were eight scleroderma cases representing 1.17% of the total rheumatologic diseases seen over the period. All the patients with scleroderma were females. The age range was 36-52 years with a mean age of 45 years (SD± 11.4yrs).

Arthritis and skin manifestations were common to all the cases while other manifestations were as depicted in Table I. The skin lesions were diffuse in all the patients. Commonly encountered skin lesions included alternating hypopigmentation and hyperpigmentation (salt and pepper appearance), microstomia and sclerodactyly which were seen in all the patients. (Figures 1 and 2) The least seen skin lesions were leg ulcers and Raynaud's phenomenon. Table II shows the skin manifestations of scleroderma in this cohort.

Erythrocyte sedimentation rate (ESR) was uniformly elevated in all the patients. Anti-nuclear

antibody was elevated in all the patients, six patients showed the speckled pattern while 2 patients showed the peripheral pattern. The anti-topoisomerase antibody was detected in all the patients. All the patients also showed the restrictive pattern on pulmonary function test. Carbon –monoxide diffusion capacity was not however done because it was not available locally. Cardiovascular system evaluation revealed one patient with massive cardiomegaly while another two had marginal cardiomegaly on Chest-X-ray. The patient with massive cardiomegaly also presented in heart failure. Electrocardiogram of two patients revealed atrial ectopics. Two patients, however, had pleural effusion on Chest-X- ray while one patient had pulmonary fibrosis. A patient presented with scleroderma renal crisis secondary to oral steroid given at a private clinic.

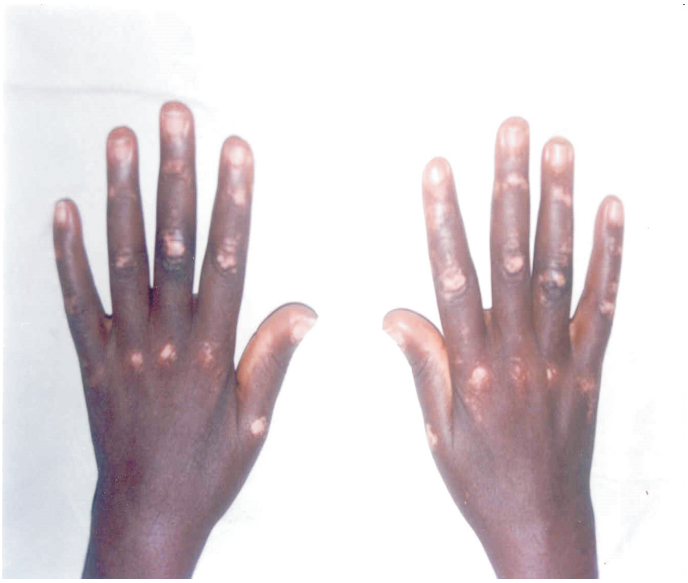

Figure 1: Hypopigmented skin lesions on the dorsum of hands in scleroderma.

Table I: Organ involvement associated with scleroderma in the studied patients.

Organ	*Presentation*	*Number*	*Percentage*
Gastrointestinal	Retrosternal pain	7	87.5
	Dysphagia	5	62.5
Cardiovascular	Cardiomyopathy	1	12.5
	Pericardial effusion	3	37.5
Renal	Renal crisis	1	12.5
Neurology	Convulsion	1	12.5
	Headache	2	25
Respiratory	Dry cough	4	50
	Exertional dyspnea	2	25
	Pleural effusion	2	25
	Pulmonary fibrosis	1	12.5

Table II. Skin manifestations encountered in scleroderma patients seen.

Skin manifestation	*Frequencies*	*Percentage*
Oedema	4	50
Skin fibrosis	3	37.5
Digital pulp ulcer	7	87.5
Salt and pepper appearance	8	100
Microstomia	8	100
Puckered mouth	6	75
Sclerodactyly	8	100
Leg ulcer	1	12.5
	1	12.5

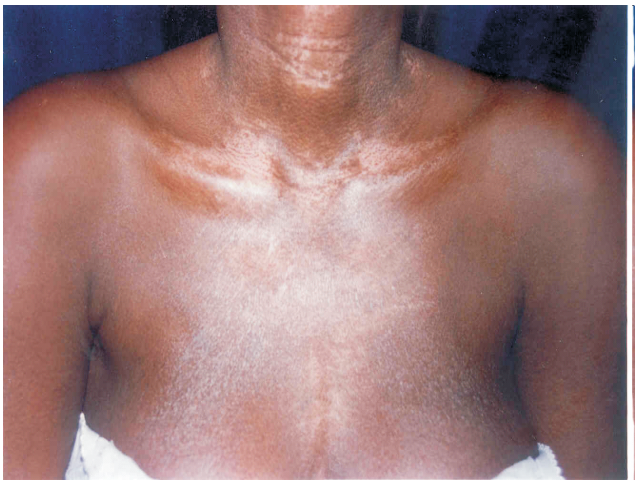

Figure 2: Salt and pepper (hypopigmentation interspersing hyperpigmentation) distribution of skin changes in scleroderma.

Morbidity/mortality

Four patients are still being followed up in the Outpatient Clinic. The patient with scleroderma renal crisis died during the first admission after the third session of renal dialysis. The patient with massive cardiomegaly also died during the third admission episode. Two patients defaulted from follow- up care.

Discussion

Scleroderma, as earlier documented in the literature, is a rare disease. This study also confirmed the previous findings of the rarity of the disease as systemic sclerosis constituted only 1.17% of all rheumatologic disorders seen over a period of three and a half years. The study conducted by Adelowo *et al* in a privately-owned rheumatology clinic also showed a finding of 1.1% of all rheumatology disorders. [11] Some of the missed cases may, however, be visiting dermatologists, since there is a paucity of Rheumatologists in the country. All the cases seen in the present study were females. Several kinds of literature have documented female preponderance and the outcome of this study agreed with the earlier literature. [12] The mean age of our patients (45 years) was however slightly lower than 51.5 years which was reported among the Caucasians. [13]

All the eight patients with scleroderma had the diffuse type of the disease. Adelowo had earlier reported eight cases (57.1%) of diffuse scleroderma out of fourteen cases seen in the privately-owned rheumatology clinic.[11] In that series, there were three cases of limited disease (21.4%), two undifferentiated types and one sine scleroderma.[11] This pattern of distribution suggests the rarity of limited scleroderma among Nigerians. Raynaud's phenomenon is not commonly seen among black Africans. [4] The authors are of the opinion that because of the thick, dark skins of Blacks, the colour changes characteristic of Raynaud's may be difficult to recognise. The finding of only one patient with Raynaud's phenomenon in the present study confirmed the difficulty in recognising the tri-phasic skin changes of Raynaud's phenomenon among Blacks.

Pulmonary fibrosis was detected on plain X-ray of the chest in two of our patients. Bi-basal fibrosis is one of the minor criteria for the classification of scleroderma but it is not an early finding on chest x-ray. In well-equipped centres, high-resolution Computerized Tomographic Scan is the preferred investigation [14] Respiratory complications are the leading causes of death in systemic sclerosis.[15] Carbon monoxide diffusion test is expected to be abnormal in more than 70% of cases,[16] but it was not available at our facility during the course of this study.

One patient presented with scleroderma renal crisis (characterised by the abrupt onset of moderate to severe hypertension, proteinuria, and progressive renal failure) and she eventually died despite the institution of renal replacement therapy. Kidney involvement used to be the leading cause of death until the detection of angiotensin converting enzyme inhibitors (ACEI) and the angiotensin receptor blockers. [9] Renal complications as causes of mortality in scleroderma now rank next to lung involvement. [17] Patients with diffuse skin involvement carry a high risk of acute renal crises. [18] ACEI has been shown to significantly improve the five-year survival of systemic sclerosis patients because they limit kidney failure and prolong survival. [9]

Echocardiography detected slight pericardial effusion in the same patient that presented with cardiomyopathy. However, pericardial effusion is known to be more common among patients with limited scleroderma. Although cardiac involvement in scleroderma is common, it is rarely clinically significant. [19] Clinically manifested forms have been described in 20-25% with a 70% mortality after five years. [18] However, autopsy evidence of cardiac involvement is in the range of 30-80% of patients. [20] All the layers of the heart can be affected in scleroderma. [21]

The gastrointestinal manifestation was second to skin manifestations in our patients. There were 87.5% of patients with retrosternal pain while 62.5% presented with dyspepsia. The gastrointestinal system is frequently involved in systemic sclerosis; the oesophagus is involved in more than 85% of cases with resultant dysphagia and reflux oesophagitis. [22]

The neurological manifestations in the form of headache and convulsion were observed in only one of our patients. These were possibly secondary to uraemia from the scleroderma renal crisis, because in general, central nervous system (CNS) involvement due to systemic sclerosis is rare. [23]

All the patients in the present study had positive

anti-nuclear antibodies (ANA). The speckled ANA pattern, which was more frequent in this study, has generally been commonly described in diffuse scleroderma. [24]

Conclusion

Systemic scleroderma was not a common finding among adults with rheumatologic disorders in Sagamu, Nigeria. The prognosis in systemic sclerosis depends on the involvement of internal organs, particularly the lung, kidneys and the heart. Severe organ involvement often occurs in the early course of diffuse systemic sclerosis. Therefore, patients of scleroderma should be diagnosed early, monitored closely and be commenced on potential disease-modifying therapies early.

Authors' Contributions: OSA conceived and designed the study. OOA and BOB collected and analysed the data. OSA did literature search and reviews. All the authors participated in the drafting of the manuscript.

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