Myocardial Involvement in Generalized Scleroderma*

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Introduction

Generalized scleroderma is no longer considered strictly a dermatosis, but rather a disease of the connective tissue of various organs and systems. The pathological changes characterizing scleroderma have been thoroughly described and reviewed by Beerman.4 Of recent years, numerous investigators1,3,4,6-7,9,12,14,16-17,19-22 have emphasized the frequency of myocardial and pericardial involvement in generalized scleroderma. In fact, Weiss et al.22 pointed out that in their series of nine cases, three presented cardiovascular symptoms several years prior to the development of skin lesions and concluded that scleroderma heart disease is a clinical and pathological entity. Consequently, both the internist and dermatologist must be aware of the possibility of cardiovascular involvement in this disease. The purpose of this communication is to present an additional case of scleroderma heart disease.

Case Report

First Admission:

L. J., a 50 year old colored male, entered the Cardiovascular Section of Kennedy Veterans Administration Hospital, March 8, 1947, with a chief complaint of shortness of breath. The onset of his present illness dated back one year when he noted exertional dyspnea which increased in severity so that at the time of admission he was having definite orthopnea. He also complained of soreness beneath the anterior chest wall and pain in the right axilla. He was conscious of constant palpitation. For approximately a year he had noted a productive cough which had become more severe in the two months preceding admission. There was no history of hemoptysis or dependant edema. The history by systems revealed only that he had a penile lesion prior to World War I. The past medical, social, and family history was otherwise non-contributory.

Physical Examination: The patient was a well developed and well nourished negro male with evident dyspnea. The pertinent findings were limited to the cardiovascular system. The heart sounds at the base were faint and tachycardia was present. The blood pressure was 140/88. There were inconstant and scattered musical rales over the entire posterior chest but most prominently at the bases where they were more pronounced on deep expiration. The liver was slightly enlarged.

Laboratory Studies: Serological tests for syphils were positive. A blood count was normal except for a differential revealing 65 per cent lymphocytes, and a heterophile test was positive 1:28. Electrocardiographic studies (Figure 1) showed elevation of the ST segments over the right side of the heart.

Clinical Course: He was seen by the cardiac consultant who felt that all symptoms were adequately explained by a diagnosis of bronchial asthma. He was treated with aminophyllin and adrenalin and improved. He was discharged with diagnoses of bronchial asthma and latent syphilis.

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Second Admission:

He was readmitted to the cardiovascular section, February 6, 1948. He had done fairly well until two months prior to admission when he noticed swelling of his feet and ankles toward evening. This was followed by swelling of the arms and face. He also complained of fever, soreness in his arms, legs and most of his joints. His fever subsided but the joint and muscle pains continued up to admission. Attacks of dyspnea persisted.

Physical Examination: The patient was still well developed and nourished. Fundoscopy revealed slight tortuosity and narrowing of the retinal vessels. The ability to open his mouth was restricted to 60 per cent of normal, and he stated that this had been present for several weeks. The percussion note over the chest was hyperresonant. Asthmatic wheezes were audible at both bases and there were decreased breath sounds at the apices. The blood pressure was 115/76. A² was equal to P² which was accentuated. The cardiac sounds were of good quality and occasional extrasystoles were present. The liver was palpable one fingerbreadth below the costal margin. There was no edema of the legs, arms or face. The joints were clinically normal.

Laboratory Tests: The urinalysis was negative and a Fishberg test revealed a
concentration of 1.022. The serological tests for syphilis were again positive. The blood count and hemoglobin were normal, but the differential revealed 44 per cent neutrophils, 48 per cent lymphocytes and 8 per cent eosinophils. The sedimentation rate (Westergren) was 23 mm. per hour. X-ray film and fluoroscopy of the lungs and heart were normal except for a suggestion of prominence of the pulmonary conus in the right anterior oblique position. Joint x-ray films were normal but minimal calcifications were present in the arterial walls in the legs.

Clinical Course: While in the hospital he ran a low grade fever. Symptomatic treatment for the asthmatic state gave satisfactory relief. An electrocardiogram taken February 6, 1948, showed a low voltage and clockwise rotation (Figure 2). A second tracing taken February 25, 1948, however, showed the sudden appearance of incomplete right bundle branch block (Figure 3). At this time it was felt there was enough evidence to make diagnoses of acute rheumatoid arthritis and cor pulmonale. He was discharged following therapy and was instructed to report to his local health department for treatment of latent syphilis.

Final Admission:

He was readmitted on June 6, 1948, with progression of joint and muscle pains. For two weeks preceding this admission, he was unable to walk or attend to his personal toilet.

Physical Examination: He appeared chronically ill, was lucid, oriented, and cooperative, but had difficulty in opening his mouth. There was wasting of the shoulder girdle muscles. The chest was hyperresonant to percussion and asthmatic wheezes were heard over both lung fields. Examination of the heart revealed weak and distant sounds. The rate and rhythm were normal. P2 was louder than A2. The blood pressure was 118/80. The remainder of the examination was negative except for moderate tenderness of the muscles and joints of both the upper and lower extremities.

Laboratory Data: The blood count was within normal limits. The sedimentation rate was 24 mm. per hour. Urinalysis was not remarkable. NPN was 23 mgm. per cent. The total protein was 6 grams with an A/G ratio of 1. Serological tests for

FIGURE 3: This electrocardiogram was taken approximately two and a half weeks following the tracing in figure 2. The three standard leads do not reveal any gross change. However, there is a marked change in the CF leads. Incomplete right bundle branch block is now present.
syphilis were repeatedly positive in low titer. The spinal fluid examination was normal. Liver function tests, blood electrolytes and urinary 17 ketosteroids were within normal limits. The sputum was negative for acid-fast organisms. Chest x-ray films showed evidence of only pulmonary emphysema, and a barium enema was negative. KUB films revealed only calcifications of pelvic vessels. An esophagram demonstrated a dilated esophagus with markedly diminished peristalsis. Joint x-ray films again were negative except for minimal osteoarthrosis of the spine. An electrocardiogram taken June 10, 1948, showed a disappearance of the right incomplete bundle block seen February 25, 1948, and in addition showed a supraventricular premature systole with aberrant conduction (Figure 4). A final tracing taken October 14, 1948, showed further lowering of the voltage with more frequent supraventricular premature systoles in addition to an increase in the duration of the QRS interval to 0.12 seconds (Figure 5).

Clinical Course: On admission this was felt to be a case of rheumatoid arthritis or possibly fibrositis. However, it was soon noted that the skin was becoming shiny and inelastic and that the facial expression was masklike. Generalized scleroderma was suspected at this time. On palpation of the arms and legs there was a distinct leathery feel of the skin and subcutaneous tissues. It was at this time that the esophagram revealed the dilated esophagus with only slight peristalsis. However, chest x-ray films revealed no definite heart or lung changes. A biopsy of the skin from the anterior abdominal wall was reported as consistent with generalized scleroderma. He ran a slowly progressive downhill course with occasional elevations of temperature to 101 degrees F. An extensive course of penicillin given for his latent syphilis did not affect his failing health. Physiotherapy afforded only slight symptomatic relief. During the last month of hospitalization, severe dysphagia developed with frequent regurgitation of food which was often blood.

FIGURE 4: The incomplete bundle branch block seen in figure 3 is no longer present. The voltage has decreased even further. The transition point is now present in V6. A supraventricular premature beat with aberrant conduction is seen in V4.
stained. He became absolutely helpless, being unable to raise his hands from the bed. He continued in this state of inanition and quietly expired on October 27, 1948.

Necropsy: Examination of the body disclosed loss of much subcutaneous fat and a thin, smooth, shiny skin which had lost its elasticity. The skin was stretched over the bony prominences and showed cracking and scaling in some areas. There was generalized muscle wasting; the pectorals were thin, atrophic and pale. Over the sacrum was a large decubitus measuring 6 cm. in diameter.

Each pleural cavity contained 200 cc. of clear yellow fluid. There were a few fibrinous interlobar adhesions. The pericardial sac contained 100 cc. of a similar fluid. Section of the lungs revealed moderate congestive changes and a few emphysematous blebs.

The heart weighed 180 grams and showed edema of the subepicardial fat. In the left and right ventricular walls were depressed, scarred areas measuring up to 1 x 0.3 cm. The valve measurements were normal, but along the edges of the mitral and tricuspid valves were healed verrucous lesions. The myocardium was firm, and the scars noted on the surface extended in some areas through the entire thickness of the wall. The uninvolved left ventricular wall measured 1.2 cm.; the right 0.4 cm. The coronary vessels were moderately sclerotic and tortuous but their lumina were patent.

The kidneys each weighed 100 grams. The capsules stripped with difficulty. The cortico-medullary demarcation was indistinct and the cortex measured approximately 0.5 cm. The calyces, pelves and ureters were not remarkable.

The esophageal mucosa showed numerous irregular plaque-like whitish elevations and areas of ulceration. There was moderate thickening and firmness in the esophageal wall.

FIGURE 5: This tracing was taken four months following figure 4. The voltage in the standard leads continues to decrease. A supraventricular premature beat is present in Lead 2 and Lead 3. A nodal premature beat is seen in aVf. The S waves in Lead 3, aVf and V5 and V6 are now greatly slurred.
The remainder of the necropsy revealed only moderate testicular atrophy and gynecomastia.

**Microscopic Study**: The sections from the skin disclosed atrophy of the epidermis and an increase in the number of collagen fibers in the dermis. These fibers were thick, dense, often fragmented, and stained deeply with eosin. Skin appendages were decreased in number and atrophic. Small collections of fat cells were caught in the dense scar and showed an embryonic appearance. Small vessels were concentrically thickened.

In the lungs there was an increase in collagenous material in the interalveolar septa and peribronchial scarring. The small branches of the pulmonary arteries showed moderate to marked concentric thickening and decrease in size of the lumen.

Sections from the heart disclosed moderate epicardial fibrosis which contained flecks of calcified material and a few round cells. Similar calcifications have been noted by Durham⁵ (Figure 6). Throughout the myocardium there was a general increase in connective tissue, varying from slight interstitial cellular fibrosis (Figure 7) to large, dense, hyaline scars (Figure 8). Frequently the large areas of scarring were hyalinized in the center and more cellular at the periphery where the connective tissue strands interlaced with and often imprisoned small groups of myocardial fibers. These trapped fibers exhibited fracturation, vacuolization of cytoplasm, and other degenerative changes. Nearby were scattered hemosiderin-laden macrophages and occasional chronic inflammatory cells. The distribution of the scarring was diffuse and had no constant relation to the coronary vascular tree. Often the areas of fibrosis contained numerous small patent vessels (Figure 8). The small arteries demonstrated both intimal and medial concentric thickening to a marked degree, and the capillaries had a prominent endothelial lining. The muscle fibers in the uninvolved areas of the myocardium showed no significant changes.

In the kidney sections stained with hemotoxylin and eosin there was noted only slight increase in intercapillary hyaline material, but the true extent of this deposition was brought out by the periodic-acid Schiff stain. Only occasional intralobular arteries revealed concentric hypertrophy, and afferent arterioles with thickening or fibrinoid necrosis were rare.

The esophageal lining was ulcerated in many areas. The underlying wall was thickened by dense fibrosis which involved the muscle layers.

Sections from striated muscle showed changes somewhat similar to the lesions in the heart. Many of the fibers were atrophic or degenerating. Many had lost their striations and were hyalinized and fractured. Dense bands of hyaline and cellular connective tissue coursed through the sections and scattered collections of lymphocytes were present.

**Discussion**

Brock⁶ in 1934 reported a case of generalized scleroderma in which the cause of death was congestive failure due to myocardial fibrosis. In 1943 Weiss et al. summarized the findings in nine cases of generalized scleroderma in three of which cardiac symptoms preceded the skin changes by two years. Goetz et al.⁸-¹⁰ in 1942, 1945 and 1951 emphasized the frequency of myocardial changes in this disease. In recent years Mathiesen and Palmer,¹⁴ East and Oram,⁶ Spain and Thomas¹⁹ and Ries¹⁷ have contributed additional studies on scleroderma heart disease. Several investigators²,¹³ have reported pericarditis occurring in scleroderma heart disease. Pericardial fibrosis was prominent in the patient presented in this case report.

It is interesting that this case presented cardiovascular symptoms ap-
Figure 6: Heart. Right Auricle showing fibrous thickening and areas of calcification in epicardial region. (H & E x 100).

Figure 7: Heart. Left Ventricle showing cellular and hyalin fibrosis. Many groups of muscle fibers are being surrounded by the cellular fibrous tissue (H & E x 100).

Figure 8: Heart. Left Ventricle showing fibrosis. Note patent small blood vessels and trapped degenerating myocardial fibers. (H & E x 200).
proximately a year before the actual diagnosis became apparent as in three of the cases of Weiss et al.,22 and the case of Spain and Thomas.19 Increasing dyspnea is the most common presenting symptom in scleroderma heart disease, being present in every case reported in the literature. This is probably due mainly to the progressive myocardial fibrosis and partly to the changes in the lungs. Chest pain, such as experienced by the patient, is a frequent occurrence.6,14,22 No explanation has been given for its origin, though it probably is the result of the pathological changes in the myocardium or pericardium. During the progress of the disease, P\(^2\) increased in intensity. This has been emphasized by Weiss et al22 in their series.

Numerous changes have been reported in the electrocardiogram in scleroderma heart disease.1,7,12,14,16,22 The most frequent finding is low voltage. Arrhythmias such as auricular or ventricular premature systoles, auricular fibrillation, various degrees of AV block, and bundle branch block have been noted. This patient presented low voltage, supraventricular premature systoles, and a transient episode of right bundle branch block. Incomplete bundle branch block was present in three of Gil's seven cases.7

Both the gross and microscopic pathological findings were typical of those described in generalized scleroderma.4 The changes were most pronounced in the heart, esophagus, skin and muscle, but a generalized increase in connective tissue was present also in the lungs and kidneys.

In the heart the pathological changes showed different stages of development. These changes were not found in the distribution of any one large coronary vessel such as may follow occlusion of an artery. The changes were diffuse throughout the myocardium indicating generalized involvement of focal areas and smaller vessels. These vessels showed marked concentric thickening and were of the small artery size or smaller. The sequence of the changes in the heart consist first of focal edematous cellular and vascular fibrosis. This gradually becomes more compact and finally resolves into a dense hyaline scar. Often the process remains active about the periphery of the involved areas and myocardial fibers are trapped and degenerate and disappear. Whether the vascular changes precede the focal scarring is not known, but possibly the same underlying mechanism is active in both the vessels and myocardium at the same time. Primary vascular involvement is suggested by the fact that numerous patients with scleroderma have previously exhibited Raynaud's phenomenon. No inflammatory changes in the arteries or arterioles were observed in this case. Though the etiology of scleroderma remains obscure, the changes in the heart present a distinct pathological picture. There was no granulomatous inflammation, gummatous changes, or marked inflammatory reaction to suggest luetic myocarditis,18 and the aorta demonstrated none of the changes of syphilis. The findings of progressive lowering of blood pressure and low voltage in the ECG tracings are easily explained by the progressive diffuse scarring in the hearts of patients with scleroderma. The various other ECG changes must follow involvement of specific areas.

This patient had no significant urinary findings during life and yet
revealed kidney lesions to a limited degree, similar to those described by Moore and Sheehan.15

SUMMARY
A case of diffuse scleroderma (progressive systemic sclerosis) with autopsy is presented and discussed. Symptoms of heart disease were the first to appear and were followed by involvement of joints, muscles, skin and esophagus. The related literature is reviewed.

RESUMEN
Se presenta y se discute un caso de escleroderma difuso (esclerosis general progresiva). Los síntomas cardiacos fueron los primeros en aparecer y fueron seguidos de afección de las articulaciones de los músculos de la piel y del esófago. La literatura al respecto se revisa.

RESUME
L’auteur rappporte et discute une observation de sclérodermie diffuse avec autopsie. Les premiers symptômes furent des troubles cardiaques qui suivirent une atteinte des articulations, des muscles, de la peau et de l’oesophage. Cette observation est suivie d’une revue de la littérature.

REFERENCES