Echocardiographic Patterns in Scleroderma*

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The echocardiograms of two patients with sclerodermatous cardiac disease are described. In one patient the pattern was that of a congestive cardiomyopathy with ventricular dilatation and reduced wall motion. In the second patient the pattern was that of an infiltrative cardiomyopathy with thickened walls and reduced wall motion in the absence of ventricular dilatation. Echocardiographic studies are useful in the early detection of pericardial involvement and primary or secondary myocardial involvement by scleroderma and in following the progression of the disease process.

In recent years, echocardiography has emerged as an important noninvasive method of studying cardiac disease. There have been no reports describing the echocardiographic abnormalities seen in sclerodermatous cardiac disease. Two patients are presented who had sclerodermatous involvement of the heart confirmed by autopsy. The echocardiograms of these patients are described.

METHODS

The echocardiographic examination was performed according to the method described by Feigenbaum. The patients were studied with an ultrasonic scope (Hoffrel Ultra Sonoscope 101) using a 2.25-MHz 7.5-cm focused transducer positioned along the left sternal border in the fourth intercostal space. Strip-chart recordings were obtained with a recorder (Honeywell Visiorder 1856).

CASE REPORTS

CASE 1

A 30-year-old black man was admitted to Barnes Hospital in December 1974. The patient had developed Raynaud's phenomenon and the cutaneous changes of scleroderma three years prior to admission. One year prior to admission, he had developed progressive dyspnea on exertion. Several weeks before admission, the patient had developed orthopnea and paroxysmal nocturnal dyspnea. Medications included digoxin, spironolactone, and furosemide.

The patient appeared to be chronically ill. The apical pulse rate was 84 beats per minute, the respiratory rate was 40/min, and the blood pressure reading was unobtainable. The skin was tight and smooth over the digits. There was jugular venous distention to the angle of the jaws at 90° but no Kussmaul's sign. Examination of the chest revealed bibasilar rales and dullness to percussion. Cardiac examination showed a diffuse apical impulse at the anterior axillary line and a loud gallop rhythm with a third heart sound. Abdominal examination revealed an enlarged liver with a 15-cm total span. There was marked pitting edema to the knees.

An electrocardiogram showed low QRS voltage and atrial fibrillation. A chest x-ray film revealed marked cardiomegaly, bilateral pleural effusions, and pulmonary vascular redistribution.

The patient was treated with large doses of furosemide, with minimal response. A Swan-Ganz catheter was inserted. The mean pulmonary wedge pressure was 31 mm Hg. The mean right atrial pressure was 13 mm Hg. The patient deteriorated rapidly and died 24 hours after admission.

Echocardiogram. An echocardiogram was obtained four months prior to the patient's death. Aortic motion was markedly reduced. The left atrium was mildly enlarged (4.4 cm). There was delayed closure of the mitral valve compatible with elevated left ventricular end-diastolic pressure (PR-AC interval, 0.04 second). The left and right ventricles were enlarged, with left ventricular diastolic dimension of 4.0 cm and right ventricular diastolic dimension of 3.0 cm.

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<td>Ejection fraction, percent</td>
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The ventricle was dilated (Fig 1; Table 1). The interventricular septum had a normal thickness and slight paradox motion. Septal thickening was reduced (normal, greater than 30 percent). The left ventricular posterior wall was normal in thickness and also moved poorly. The ejection fraction (18 percent) was markedly depressed.

**Autopsy Findings.** At autopsy, there were dense deposits of collagen in the skin, heart, and esophagus. The heart weighed 550 gm. There was gross dilatation of all chambers, particularly the right ventricle. The left ventricle was 1.8 cm thick, an increase from 0.9 cm four months earlier by echocardiogram. The discrepancy in the thickness of the ventricular wall may be due in part to further progression of the disease process or to the fact that different portions of the left ventricle were measured by autopsy and echocardiograms. The right ventricle was 0.8 cm thick. Microscopically, there were many areas of full-thickness replacement of muscle cells by fibrous tissue. The remaining muscle cells were hyperplastic with bizarre nuclei.

**Case 2**

A 56-year-old white woman was admitted to the Jewish Hospital of St. Louis in December 1974. Four months prior to admission, she developed diffuse myalgias, proximal muscular weakness, and progressive edema of her lower extremities. She was unable to close her fingers because of edema. She also complained of dyspnea at rest.

On physical examination the vital signs were normal. The skin was diffusely edematous and erythematous. The jugular veins were normal. Pulmonary examination revealed a few bibasilar rales. A loud pulmonic second sound and an apical gallop rhythm with a fourth heart sound were heard on cardiac examination. There was marked proximal muscular weakness and tenderness. The fingers were edematous. There was tense pitting edema of the lower extremities to the knees.

An ECG revealed low limb-lead voltage and left atrial enlargement. A chest x-ray film showed moderate cardiomegaly and mild interstitial fibrosis. Pulmonary function tests

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**Figure 1.** Echocardiogram at left ventricular level, showing dilated right and left ventricular chambers. RV, Right ventricle; IVS, interventricular septum; LV, left ventricle; LVP, posterior left ventricular wall; and P, pericardium.

**Figure 2.** Normal left ventricular echocardiogram. IVS, Interventricular septum; RV, right ventricle; LV, left ventricle; and LVP, posterior left ventricular wall.
revealed moderate restriction, with a marked decrease in diffusing capacity. Findings from biopsies of skin and muscle were compatible with a collagen disorder, either scleroderma or dermatomyositis. The patient was given therapy with prednisone (60 mg daily), with subsequent marked improvement in the cutaneous inflammation. The muscular weakness remained unchanged at the time of the patient's discharge from the hospital.

The patient was readmitted in March 1975 with progressive weakness, dyspnea, and confusion. The skin was now thick and leathery. There was a marked jugular venous distention. There was no Kussmaul's sign or paradoxical pulse. Examination of the lungs revealed bibasilar rales. Cardiac examination revealed a left ventricular heave and a loud summation gallop. There were no focal neurologic signs.

The ECG was unchanged. A chest x-ray film revealed an interval increase in the size of the cardiopericardial silhouette and pulmonary congestion. The patient was treated with digoxin, furosemide, dexamethasone, and cyclophosphamide, without improvement. She became progressively obtunded and azotemic and died ten days following admission.

Echocardiogram. An echocardiogram was obtained during the patient's first hospitalization in December 1974. Findings from the left ventricular study were normal (Fig 2). The percentage of systolic thickening of the ventricular septum was normal (Table 1). There was a moderate-sized pericardial effusion.

A repeat echocardiogram was performed nine days prior to death. Aortic motion was markedly reduced (Fig 3). The aortic valve cusps opened and closed slowly, suggesting a low state of flow. The left atrium was not enlarged. The pulmonary valve echocardiogram was compatible with pulmonary hypertension. The anterior mitral valve leaflet had a reduced opening velocity, indicative of elevated initial left ventricular diastolic pressure. The interventricular septum and posterior left ventricular wall were now hypokinetic and thickened (Fig 4). The ejection fraction had fallen from 79 percent three months earlier to 37 percent; there was now no septal systolic thickening (Table 1). The

Figure 3. Echocardiogram of aortic root, showing markedly reduced aortic motion. AAR, Anterior aortic root; rcc, right coronary cusp; ncc, noncoronary cusp; PAR, posterior aortic root; and LA, left atrium.

Figure 4. Echocardiogram showing thickened, poorly moving septum and posterior wall, and moderate-sized pericardial effusion. RV, Right ventricle; IVS, interventricular septum; LV, left ventricle; AMV, anterior mitral valve leaflet; LVP, posterior left ventricular wall; E, epicardium; and P, pericardium.
left ventricular chamber was unchanged in size. The pericardial effusion was increased.

**Autopsy Findings.** At autopsy the heart weighed 500 gm. The left ventricle was 1.6 cm in thickness and the right ventricle 4 mm in thickness. There were small recent intramural infarcts in the posterior septum and posterior diaphragmatic wall. Microscopically, there were numerous small infarcts of various ages. Some were acute, with eosinophilic clumping of the myocardial cytoplasm. Others were resolving, with resorption of fibers and residual segmented macrophages. The extensive degeneration of muscular fibers was accompanied by increased interstitial fibrosis and edema. Several vessels showed fibrinoid material in the walls. There was marked atherosclerotic involvement of the medium-sized coronary arteries. The pericardial cavity contained 125 ml of straw-colored fluid. The remaining pathologic findings were compatible with scleroderma.

**DISCUSSION**

In scleroderma the myocardium characteristically shows proliferation of connective tissue and cellular degeneration of varying degrees. In case 1, fibrosis predominated pathologically, whereas in case 2, there was marked degeneration of muscular fibers with less prominent fibrosis. The myocardial necrosis seen was of the contraction-band type reported in scleroderma, as opposed to the coagulative type seen in ischemic damage. The vasculature may show intimal proliferation of the small arteries and arterioles. It is as yet unclear how the fibrosis, cellular degeneration, and vascular lesions in scleroderma are interrelated. Pericarditis, with or without effusion, is common.

Involvement of the myocardium in scleroderma represents a secondary cardiomyopathy as classified by Goodwin. Of the four types of cardiomyopathy described (hypertrophic, congestive, obliterative, and restrictive or infiltrative), two are represented by our patients. Case 1 is typical of the clinical syndrome of congestive cardiomyopathy. The echocardiogram demonstrates ventricular dilatation and reduced wall motion. The reason for the slight paradoxical septal motion is unclear but may be due to the ultrasonic beam traversing the superior part of the septum. One of the examples reported by Goodwin et al as congestive cardiomyopathy is a case of scleroderma. In their case, as in our first case, the pattern of myocardial restriction did not occur. As diffuse myocardial fibrosis was the cause of these patients' heart failure, restriction of ventricular filling, rather than ventricular dilatation, might have been expected.

The clinical course and echocardiogram of case 2 correspond to an infiltrative cardiomyopathy. The echocardiogram demonstrates reduced wall motion and a striking increase in the thickness of the septal and posterior wall over a period of three months, suggesting "pseudohypertrophy" of the myocardium due to edema or to infiltration with fibrous tissue, or both. Also, in contrast to the first case, there is no ventricular dilatation, suggesting restriction of ventricular filling. This same echocardiographic pattern has been reported in amyloid heart disease. It is possible that this pattern represents early cardiac involvement by scleroderma, which progresses to a pattern of congestive cardiomyopathy if the patient survives.

The pericardial effusion seen in case 2 was not hemodynamically significant clinically, and the echocardiogram did not show the abnormalities in motion of the anterior mitral valvular leaflet during cardiac tamponade described by D'Cruz et al, however, reduced anterior and posterior wall motion has been reported during cardiac tamponade.

The echocardiogram is helpful in the early detection of cardiac involvement by scleroderma. It may detect primary involvement, as in the two patients presented. The echocardiogram also detects secondary involvement of the heart when the lungs or kidneys are involved. The echocardiogram is also useful in following the progression of the disease process, as our second case illustrates. Because of the high incidence and seriousness of cardiac involvement by any of the connective tissue diseases, it is suggested that echocardiographic studies be used in the routine evaluation of these patients, even in the absence of cardiac symptoms.

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**REFERENCES**

Pedantic purists and perfectionists remind us that nitroglycerin, CH₂NO₃ CHNO₃ CH₂NO₃, is not a nitro compound, rather it is glycerol trinitrate. It was discovered by Ascanio Sobrero (1812-1888) of Turin, Italy, who was made subsequently life-time adviser at one of Nobel’s factories. Nitroglycerin is an inflammable, explosive, thick liquid of pale yellow color and sweet burning taste and very sensitive to shock. It is an essential component of the most widely used detonator, dynamite, invented and so named by the Swedish Alfred Bernhard Nobel (1833-1896). The essential feature of his invention was the reliable control of the intensity and velocity of detonation and of its initiation. Currently there are some one hundred different explosives in this category and under this label. According to the Encyclopedia Americana, Cayne, BS (ed), New York, Americana Corporation, 1976, the ingredients of modern dynamite are glycerin-ethylene glycol nitrates, ammonium nitrate, sodium nitrate, and combustible pulps, such as wood meal, starch, rye flour, and sugar cane pith. “It is packaged in cylindrical paper cartridges 2–20 cm in diameter and 20–91 cm in length. The heat liberated by the explosion of dynamite amounts to 900 to 1,200 calories per gram, depending on the nitroglycerin content.” Dynamite is used for mining, quarrying, tunnel, ship-channel, bridge and dam construction, land clearing, harbor improvements, and in rocket propellants. Alfred Nobel was not only a genius excelling in chemistry but also a talented entrepreneur, a versatile connoisseur in social, cultural and scientific endeavors, and a generous humanitarian. He was of less than average height, physically frail, in delicate health, and a lover of melancholic temperament. Even so, on occasions, he was congenial, and a witty conversationalist. Nobel’s name has become immortalized by his last will written in his own hand in 1895. “The whole of my remaining realizable estate shall be dealt with in the following way. The capital shall be invested in safe securities and shall constitute a fund the interest on which shall be annually distributed in the form of prizes to those who, during the preceding year, shall have conferred the greatest benefit on mankind.” Awarding of Nobel prizes began in 1901. They pertain to achievements in physics, chemistry, physiology and medicine, literature, and peace. W. Murrell of England (Lancet 1:80 and 1:113, 1879) first introduced nitroglycerin for the treatment of angina pectoris. Its current extensive use attests to its clinical value. Acute and chronic poisoning with nitroglycerin has been observed in industrial workers, as listed in the Merck Index, Stieber, PC (ed): The Merck Index (8th ed), Rahway, NJ, Merck & Co, 1968: Nausea, vomiting, abdominal cramps, headache, mental confusion, delirium, bradycardia, bradycardia, paralysis, convulsions, methemoglobinemia and cyanosis, circulatory collapse, death. Several noncardiac diseases may simulate angina pectoris. It is known that nitroglycerin causes relaxation of the muscles of the gastrointestinal tract, the biliary passages, gall bladder, sphincter of Oddi, the ureters and of bronchi. Angina may cease with rest spontaneously; in some instances it may be relieved by a placebo or by the psychologic influence of the physician, nevertheless nitroglycerin is considered a potent remedy in angina pectoris. As to the mechanism of its action, Gorlin, R et al (Circulation 19:705, 1959) recorded no increased coronary blood flow by nitroglycerin in patients with diseased coronary arteries. Others made confirmatory observations. Parker, JO et al (Am J Cardiol 27:59, 1971) measured coronary blood flow by means of krypton 85 technique and found no demonstrable effect of nitroglycerin on coronary blood flow in patients with coronary artery disease. The consensus is that in patients with angina pectoris the therapeutic efficacy of sublingual nitroglycerin is attributable to reduction of left ventricular oxygen requirement through reduction of peripheral vascular tone, with consequent venous pooling, and through reduced left ventricular volume.

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