Scleroderma Heart Disease

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Generalized progressive scleroderma is characterized by visceral involvement concerning which there are many important reviews in the literature (Beigelman et al., 1953; Leinwand et al., 1954; Oram and Stokes, 1961). Weiss et al. (1943) firmly established scleroderma heart disease as a clinical entity. Oram and Stokes (1961) summarized the cardiac manifestations, which include myocardial failure, pericarditis, chronic cor pulmonale, various arrhythmias, and incidental findings such as cardiomegaly, cardiac murmurs, and electrocardiographic anomalies.

The clinical, electrocardiographic, and necropsy findings in two cases with cardiac involvement are reported here. One of us (E.F.) has already published two additional cases with pathological findings in the heart (Roessler and Fletcher, 1963, Figs. 46 and 47).

Case 1

A woman aged 50 had had joint pains and stiffness for about 10 years. At the time the E.C.G. shown in Fig. 1 was recorded she had extensive scleroderma involving the limbs and trunk. She complained of shortness of breath. The heart sounds were normal and there was a basal systolic murmur. Blood pressure was 102/70 mm. Hg, serum calcium 10 mg./100 ml., and serum potassium 4.6 mEq/l. Radiological examination showed extensive soft-tissue calcinosis. X-ray examination of the chest showed a normal heart shadow and extensive fibrosis of the lower lobes of the lungs. Three months after the electrocardiogram was recorded she developed bronchopneumonia and died. No digitalis had been given at any time.

At necropsy the heart weighed 400 g. Both ventricles were hypertrophied. Microscopical sections of the ventricular myocardium showed areas of small haemorrhages and fibrosis with perivascular infiltration by plasma cells and eosinophils. The coronary arteries showed minimal atheroma with no evidence of occlusion of any coronary vessel of significant size. The valves were all normal. Both lungs showed extensive fibrosis.

In Fig. 1 the limb leads show abnormal low voltage, no deflection exceeding 5 mm. in amplitude. There is sinus rhythm, rate 88 a minute. The mean QRS axis is deviated towards the right, with a deep S deflection in lead I and a late R deflection in lead aVR. The P-R interval measures 0.15 sec. and the QRS interval 0.09 sec. The Q-T interval measures 0.37 sec., which is the upper limit of normal for the heart rate. The S-T segments are abnormally depressed in leads II, III, and aVF, with reciprocal slight elevation in leads I, aVR, and aVL. The chest leads show low QRS voltage in lead V1 adjacent to the right ventricle, and also in lead V6 adjacent to the left ventricle. The S-T segments are displaced downwards in leads V1, V2, and V6, and the T waves are negative in leads V3 and V4. The T wave in lead V5 is abnormal in shape.

Comment.—The abnormal S-T segment and T-wave changes indicate myocardial impairment due to the extensive infiltration of the myocardium found at necropsy. The biventricular hypertrophy resulted likely from compensation for the loss of myocardial fibres from progressive fibrosis. The abnormal low QRS voltage recorded in spite of the hypertrophy may reflect changes in the conduction properties of the lungs associated with pulmonary fibrosis. The R deflection in lead V1 is relatively high in amplitude compared with the S deflection, which may be due to right ventricular hypertrophy noted at necropsy. In leads V2, V3, and V4 the QRS voltage is normal or increased, as these leads are adjacent to the "bare area" of the heart with little intervening abnormal lung tissue. The right axis deviation appears to reflect right heart strain associated with extensive pulmonary disease.

Case 2

This patient began to develop multiple joint pains at about the age of 30. They were insidious and progressive, and two years after their onset she had a medical examination in hospital. The only abnormality discovered was a raised blood sedimentation rate. An electrocardiogram was reported as normal. She was next seen in hospital at the age of 40, when she was found to have extensive scleroderma. In the intervening years she had had intensified joint pains and stiffness. She complained of shortness of breath and dysphagia. The facial structures were shrunken and she had a "small mouth." There were flexion deformities of the limbs due to scleroderma. The heart sounds were normal and there was a basal systolic murmur. Blood pressure was 110/70 mm. Hg, serum calcium 10 mg./100 ml., and blood urea 40 mg./100 ml. She died five months after the electrocardiogram (Fig. 2) was recorded. No digitalis had been given.

At necropsy there was a pericardial effusion of blood-stained fluid. The coronary arteries and valves were normal. The heart weighed 370 g. The right ventricle measured 0.7 cm. in thickness and the left ventricle 1.2 cm. Microscopical sections of the myocardium showed diffuse interstitial fibrosis. Both lungs also showed fibrotic changes. The kidneys were normal.

The E.C.G. in Fig. 2 shows sinus rhythm, rate 86 per minute, P-R interval 0.16 sec., QRS interval 0.08 sec. The QRS voltage is normal and the mean QRS axis is normally directed. The S-T segments are abnormally depressed in leads I, II, aVL, and V4 to V7. The high-amplitude R deflection in lead V1 measured 8 mm. is

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greater than the S deflection, and this may reflect right ventricular hypertrophy, as this lead is located at the xiphisternum.

Comment.—The electrocardiogram was recorded five months before death, so that close correlation with the necropsy findings has less meaning. Nevertheless, it is reasonable to assume that the abnormal S-T segment changes reflect myocardial impairment due to the diffuse myocardial fibrosis found at necropsy.

Discussion

These two patients had primary myocardial infiltration and fibrosis associated with advanced scleroderma. They complained of breathlessness, but assessment of this symptom is difficult in view of the pulmonary fibrosis and restriction of respiratory effort in extensive scleroderma. Radiological and auscultatory findings were not particularly helpful. The electrocardiogram alone afforded objective evidence of primary myocardial involvement, as noted in the above comments. The abnormal findings were confined chiefly to S-T segment and T-wave changes, indicating abnormal repolarization of the ventricular myocardium on the basis of extensive myocardial impairment supported by necropsy findings. Windesheim and Parkin (1958) reviewed the electrocardiographic findings in 27 similar cases, of which three showed low QRS voltage and T-wave changes similar to those described above. Pulmonary involvement or metabolic abnormalities in scleroderma may also produce secondary electrocardiographic anomalies, as noted in the interpretations. Neither patient had hypertension to complicate the electrocardiographic findings. The cause of death was probably not related directly to the cardiac abnormality in either case.

Summary

Two cases of generalized progressive scleroderma are described with electrocardiographic and necropsy findings. Cardiac symptoms may be masked by pulmonary involvement. The electrocardiogram gave the most useful objective evidence of the primary myocardial infiltration, confirmed at necropsy, when correlated with the clinical findings. The S-T segment and T-wave changes, however, are non-specific in character, and this requires to be taken into account in generalized scleroderma, which may also be associated with renal hypertension and metabolic imbalance.

References


Medical Memoranda

Fatal Hypercalcaemia Complicating Carcinoma of Breast, Resistant to Cortisone and Phosphate Administration


One in three patients suffering from carcinoma of the breast metastases five years after the menopause may be expected to achieve temporary suppression of these metastases by the use of oestrogens (Taylor, 1956). This therapy is often chosen first in the post-menopausal woman, as it causes less endocrine upset than either androgens or cortisone. The effects of oestrogen therapy are always carefully observed in each patient, as some metastases in the elderly are oestrogen-dependent and flare up on treatment. One of the methods used to detect this dependence has been the increased urinary calcium excretion which occurs (Emerson and Jessiman, 1956), and on occasion hypercalcaemia (Kennedy, Nathanson, Tibbetts, and Aub, 1955). Several authors mention that this complication of therapy may be fatal (Herrmann, Kirsten, and Krakauer, 1949), and eight cases have been recorded (Kleinfeld, 1962). We had the opportunity of observing and treating a similar patient while she was on a fixed dietary intake of calcium in preparation for other metabolic measurements.

Case History

A 66-year-old widow was admitted to hospital for investigation of a three-month history of tiredness, nose bleeds, and nodules in the skin. On questioning she admitted to a mass in the breast which had been present for at least eight years to her recollection.

On examination she was pale, there were multiple skin secondaries stemming from a hard fixed mass in the right breast which had not ulcerated, and bruises on the back and over both knees. The liver was enlarged 3 cm. below the right costal margin. There was no bone tenderness. Blood pressure was 155/90 mm. Hg. Further systemic examination was normal.

Investigations.—Haemoglobin 6.8 g./100 ml.; W.B.C. 4,600/ cu. mm., with 5% myelocytes and 25 nucleated red cells/100 W.B.C.s; platelet count 13,000/cu. mm. Radiographs of chest and spine showed diffuse osteolytic metastatic infiltration involving the ribs, dorsal and lumbar spine, sacrum, and pelvic region. Lung fields were clear. Serum proteins 6.3 g./100 ml., electrophoretic pattern normal. Serum alkaline phosphatase 6.6 K.A. units/100 ml. (normal 3-14) (King and Armstrong, 1934). Serum alanine aminotransferase 15 units/ml. (normal 0-25 units) (Rietman and Frankel, 1957). Plasma calcium 9.7 mg./100 ml. by flame photometry (MacIntyre, 1961). Plasma inorganic phosphorus 3.3 mg./100 ml. (Riske and Subbarow, 1925). Na 143, K 4.3, HCO3 20 mEq/l. Blood urea 42 mg./100 ml. The 24-hour urinary excretion of calcium on admission was 36.5 mg. on a ward diet. Electrocadiogram was normal. Biopsy of skin nodules showed a spheroidal-cell carcinoma infiltrating the dermis and fat.

She was transfused with 4 pints (2.3 litres) of blood, one of the skin nodules was biopsied, and she was started on a calcium balance. Stilboestrol 60 mg./day was given from 11 May 1966, and the progressive changes in the plasma calcium were noted from 15 May. Stilboestrol was discontinued two days later and 150 mg. of hydrocortisone a day was given intramuscularly. On the third day on this regimen with no immediate response, 500 ml. of 1% buffered sodium phosphate was given, and later that day (19 May) the patient died. Details of the calcium balance, electrolytes, and cardiology are given in Figs. 1 and 2.

Post-mortem Findings.—The subject was a wasted female with a large carcinoma which involved most of the right breast and invaded the interstitial tissues and pleura. Metastases were present in the skin of the chest and abdomen, and in the rib, vertebrae, and pelvis. The lymph nodes were not involved. Both lower limbs showed extensive subcutaneous haemorrhages. Only minor abnormalities were noted in the gross appearances of the other organs, including brown pigmentation of the myocardium, oedema and congestion of the lungs, fatty changes in the liver, and nodularity of the thyroid. Four parathyroids were dissected out and noted to be normal in size. Histology showed a poorly differentiated cellular carcinoma of the breast. Sections stained with von Kossa's stain...