

THE HEART IN SCLERODERMA

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The following case is of such rarity as to be worth recording in some detail. Although generalized scleroderma, itself a rare disease, may on occasion involve the heart muscle, even if only microscopically, a careful search has shown that only nine examples have been recorded in which the cardiac lesion was gross and directly responsible for death from heart failure. The rarity of this condition is shown by the fact that Weiss (1939) in an article on diseases of the heart and aorta that are not well recognized, in which he described some fifty rare conditions involving the heart, made no mention of scleroderma. In a later paper Weiss *et al.* (1943) recorded nine cases of scleroderma with cardiac involvement, six of which died with generalized congestion. In three of them the cardiac symptoms preceded the skin changes by two years. Among a series of cases which Brock (1934) analysed in an attempt to draw a distinction between dermatomyositis and scleroderma, there was one in which the cause of death was heart failure. Heine (1926) also recorded such a case, and, more recently, Mathisen and Palmer (1947) have published details of one.

CASE REPORT

The patient, a captain in the Merchant Navy, aged 49, stated that since about October 1945 he had noticed his hands and feet had become numb and white on exposure to cold, but quickly improving with warmth. There had been also a very gradual onset, of indefinite date, of muscular weakness and stiffness of his joints, which by May 1946 had become quite noticeable. The weakness was first noticed in the muscles of the calf of the left leg on climbing ladders on board ship, and progressed without remissions to involve successively the thighs, forearms, neck, trunk, and abdomen, till finally he found his jaws became tired when chewing and he would have to pause with food held in his mouth.

At about the time the weakness became pronounced, he began to experience dyspnoea on exertion and swelling of the ankles, and three months later he noticed a sensation of retro-sternal constriction, which was brought on by effort and also occurred while in bed at night. The pain on effort was relieved immediately by rest and the pain at rest was relieved by drinking water. He experienced a severe attack of "indigestion" in May 1946. He estimated that he had lost at least two and a half stone in the past year.

Apart from pneumonia in 1931, and in the same year a severe attack of seborrhœic dermatitis, which recurred mildly from time to time especially in hot weather, there was nothing of note in the past history. He had never been frostbitten, had served in the Merchant Navy since 1913, smoked twenty cigarettes a day, and drank moderately.

There was nothing relevant in his family history.

Physical Examination. When first seen early in August 1946 he was of good physique but still somewhat over weight in spite of his loss. The face was blank and remarkably expressionless. The skin looked smooth and shiny with an ivory pallor; the creases were ironed out; the lips were rigid. The facial movements were small and slow and seemed to be made with effort because of the thickening of the skin.

Examination of the cardiovascular system revealed that the heart sounds were distant, the rhythm was regular, the rate was 60, and no murmurs could be detected. There was no jugular engorgement. A small sacral pad of œdema was present. The blood pressure was 120/78. A skiagram of the heart showed a progressive generalized enlargement, particularly of the left ventricle (Fig. 2, see p. 171). In an electrocardiogram on August 20, the P-R interval was prolonged to 0.28 sec., left axis deviation was present, the QRS complex was a little widened and slurred, T I was low, and there was slight depression of the S-T segment in lead IVF. An occasional auricular premature beat was present (Fig. 1A). The respiratory system and central nervous system were normal.

The abdominal wall was remarkably thick so as to give an effect like orange peel, and firm pressure only could produce pitting, which filled up slowly. Neither the spleen nor liver could be felt. The muscles of the anterior abdominal wall were so weak that the patient was unable to sit upright without pulling himself up with his arms. All movements of the arms were weak, and he could not raise them to the back of his head without working his fingers along his temples. Extension of the elbows was limited to 10 degrees, but flexion was unimpaired. All movements of the wrists and small joints of the hands were limited. The skin and subcutaneous tissue were thickened and inelastic, almost brawny in feel, and this was more obvious towards the forearms and fingers, the hands showing the typical appearance of sclerodactyly. The legs showed changes similar to those in the arms. Pulsation in the dorsalis pedis artery was palpable in both feet. The upper edge of the trapezius muscle on both sides was strikingly hard and fixed, resulting in a "hide-bound" effect, feeling almost as though it were carved out of wood.

Progress. On August 26, 1946, he developed suddenly an acute attack of urticaria with much swelling which involved the scalp, face, shoulders, and flexures of the forearm. A papular element appeared and became pustular in the beard area. Four days later gallop rhythm of the left ventricular type was noticed, his lumbar œdema increased, the œdema spread from his legs to his thighs, scrotum, and abdominal wall, and fine moist râles appeared at both lung bases. It was evident that heart failure was coming on rapidly. Bradycardia with frequent extrasystoles and occasional coupling then appeared and persisted in spite of discontinuing digitalis, the pulse falling to 46 and the auricular beat being audible at times. Partial heart block with dropped beats was, therefore, present. By September 16 complete heart block was present, and further flattening of T I and T II had occurred and T IVF had become inverted. Left ventricular premature beats were present (Fig. 1B). On October 14, the pattern was much the same. Complete heart block persisted until death.

During September his urinary output fell and the response to neptal was poor. He was given a neutral diet with low sodium intake and unrestricted fluids, and although his urinary output improved for a few days, he again developed oliguria. On September 30 he began to complain of dysphagia and this continued and became extreme just prior to his death. A fortnight before he died he developed a peculiar mental disturbance consisting of much depression during the day, mainly because he experienced some delay in remembering names of objects, and at night there was much talking and some shouting.

On October 23 a second extremely acute exacerbation of the urticaria occurred and the patient presented an enormous "ballooned-up" appearance, resembling the famous advertisement for "Michelin" tyres. The urticarial rash became hæmorrhagic and serum exuded from the pressure areas and from many other minute excoriations on the trunk and legs. The rigid skin caused extreme pain and discomfort for it would hardly stretch to accommodate the œdema. Morphia scarcely gave any relief and he died the following day.

Treatment. The urticarial attacks were treated with adrenalin and benadryl with no material effect. A penicillin course was tried but was also ineffective. Digitalis for his heart failure was disappointing, organic mercurial diuretics did not appreciably increase the urinary



FIG. 1.—(A) Electrocardiogram taken on 20/8/46 showing latent heart block.
(B) Electrocardiogram taken 16/9/46 showing complete heart block.

volume, and although a neutral diet with a low sodium intake appeared at first to increase his urinary output, the effect was very short-lived.

INVESTIGATIONS

Blood Counts. These were repeated on several occasions and showed persistently a moderate polycythæmia and polymorphonuclear leucocytosis. A typical count (August 19, 1946) was: red blood corpuscles 7.56 million per c.mm.; hæmoglobin 130 per cent; white blood corpuscles 12,800 per c.mm. (polymorphs 78 per cent, metamyelocytes 6 per cent lymphocytes 11 per cent, eosinophils 3 per cent, mononuclears 2 per cent).

X-ray examination of œsophagus, stomach, and duodenum, and of forearms, legs, and thighs showed no abnormality.

Chemical Investigations. Fæcal fat estimation. This showed, on repeated examination, an excess of unsplit fat, a typical result (September 17, 1946) being: total fat 27.1 g. per 100 g. of dried fæces; split fat 7.2 g. and unsplit fat 19.9 g. per 100 g. of dried fæces.

Plasma proteins. These were at first (August 10, 1946) normal—7.7 g. per 100 ml. and later (September 28, 1946) fell to 5.66 g. per 100 ml., the albumen being 3.06 g. and the globulin 2.60 g. per 100 ml.

Urinary creatinine. This was persistently raised, for example on August 25–26, 1946, the total daily output was 1590 mg. and preformed creatinine was 1010 mg.

Serum calcium. This was a little low—8.1 mg. per 100 ml.

POST-MORTEM EXAMINATION

Apart from the widespread and characteristic changes due to scleroderma described above there was much anasarca due to heart failure. Watery fluid streamed from the cuts. The skin, subcutaneous tissues, and the underlying muscles were very pale and indurated and cut as though the knife were blunt. The most striking changes were seen in the cardiovascular system. The heart was moderately enlarged (weight: 370 g.) and a small pericardial effusion was present. The ventricles were much dilated. The muscle looked pale brown and lacked resilience. The myocardium cut with the same resistance as the skeletal muscle, and the atrophied fibrous muscle presented an appearance which was striking and best described as "stringy." The heart valves and coronary arteries were normal, and not affected by the fibrosis. The liver showed classical nutmeg changes, the spleen was indurated, cyanotic, and fibrous, and the kidneys were much swollen and indurated by passive congestion.

Microscopic Findings. (Dr. H. A. Magnus.) Pieces of tissue from all organs were submitted for histological examination. All the endocrine glands were normal, except the testis which showed spermatogenesis arrested in the stage of spermiogenesis. The striking changes seen in the heart, subcutaneous tissue, striated and non-striated muscle will be described in detail; the other organs examined, including the pancreas, showed no unusual changes apart from congestion.

Heart Muscle. Six blocks were sectioned from various parts of the heart. They all show a uniform histological picture. Scattered throughout are very numerous areas of fibrosis; the majority of these are small but just visible in the section with the aid of a hand-lens (Fig. 3 and 4). Each area of fibrosis has an irregular outline and the muscle fibres seem to taper away at the edge. Sometimes remains of isolated fibres can be seen in the centres of fibrotic patches. The heart muscle fibres show a considerable degree of brown atrophy, and collections of similar pigment are scattered about in the areas of fibrosis. All the small branches of the coronary vessels are quite healthy; in many areas there is an increased vascularity of the fibrous tissue (Fig. 5). There is no cellular infiltration of the heart apart from small numbers of eosinophils in the fibrous tissue. Sections impregnated by silver for reticular fibres show no new formation of fibrils in the scarred areas. Frozen sections stained by Sudan IV for fat show small quantities to be present in the muscle fibres.

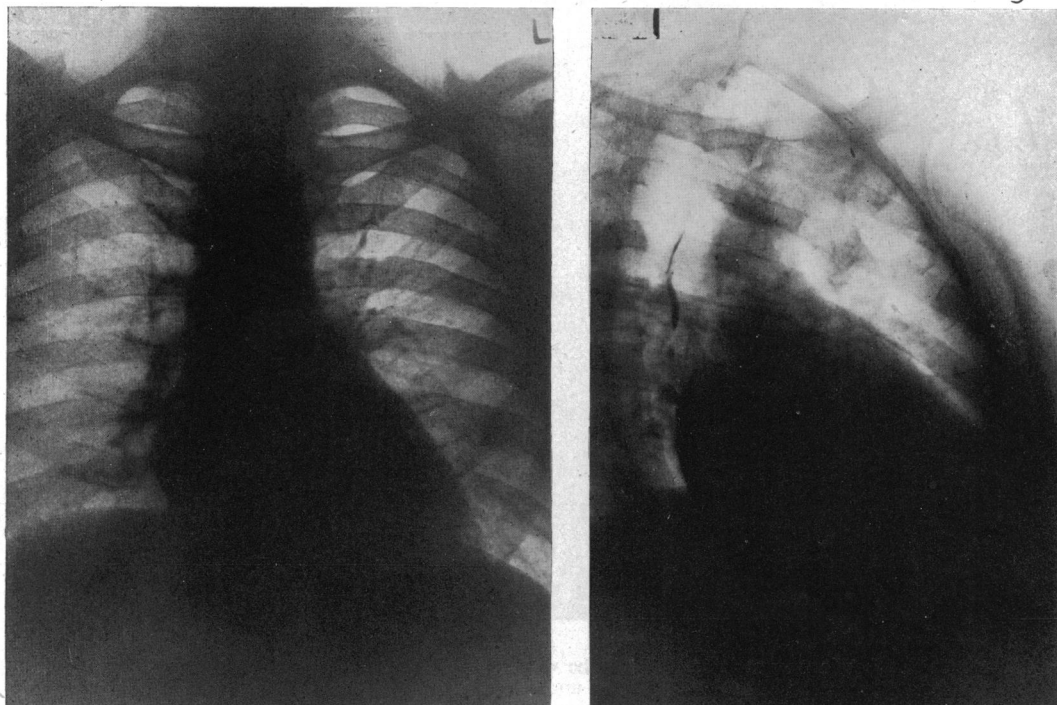
Skin and Subcutaneous Tissue. Apart from some vacuolation of cells the epidermis shows little change, but in all the sections examined there is a striking increase in the amount of collagenous tissue present in the corium. It extends from immediately beneath the epidermis to an average depth of 4 mm. The collagenous tissue is very dense and almost acellular; the blood vessels show no abnormality; the elastic tissue is still present but is fragmented (Fig. 6).

Striated and Non-striated Muscle. The most severe changes are present in muscle from the abdominal wall and the forearm. Here the fibres are undergoing a form of coagulative necrosis. They vary greatly in size and shape; the majority have lost their striations and the cytoplasm is granular; in some areas the fibres have almost disappeared. The nuclei have either disappeared or have been exuded from the fibres. There is a remarkable absence of cellular infiltration in the interstitial tissue and in the sections examined there is no proliferation of collagenous tissue between the muscle bundles. The blood vessels are normal (Fig. 7 and 8).

Similar but less severe changes are present in the muscle of the tongue, pharynx, œsophagus, and intestinal wall.

DISCUSSION

Scleroderma, if it is sufficiently generalized, may on rare occasions be associated with changes in the heart in some degree, but it is exceptional for these changes to be so great as to cause heart failure and death. Only nine such reported examples have been found.



A

B

FIG. 2.—(A) Postero-anterior skiagram of the heart, showing generalized enlargement particularly of the left ventricle.

(B) Right oblique view.

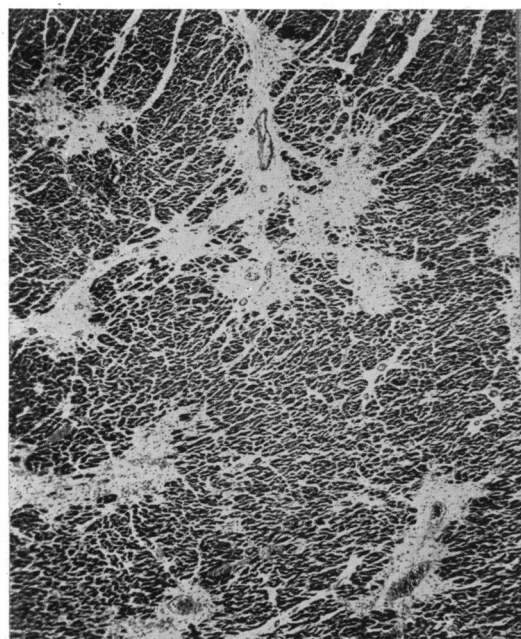


FIG. 3.

FIG. 3.—A low-power view of the myocardium showing the numerous small scattered areas of fibrosis. Hæmatoxylin and eosin. Magnification: $\times 24$.

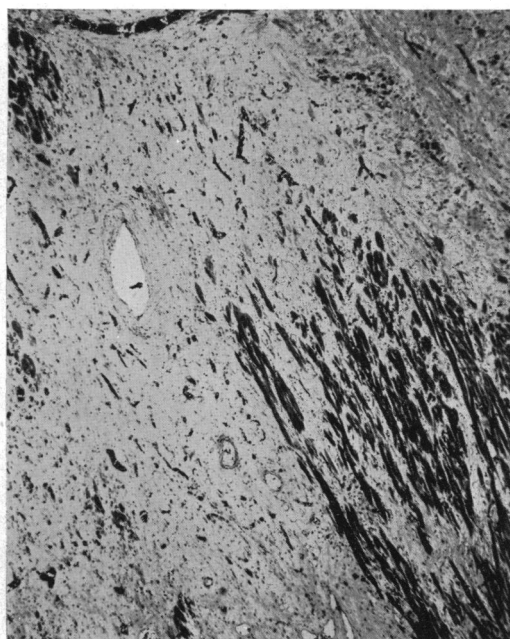


FIG. 4.

FIG. 4.—An area of fibrosis showing the irregularity of its edge and the absence of any inflammatory reaction. Hæmatoxylin and eosin. Magnification: $\times 24$.

N**



FIG. 5.

FIG. 5.—An area of collagenous tissue showing the well-developed blood supply. Near the centre there are several isolated muscle fibres. Hæmatoxylin and eosin. Magnification: $\times 55$.

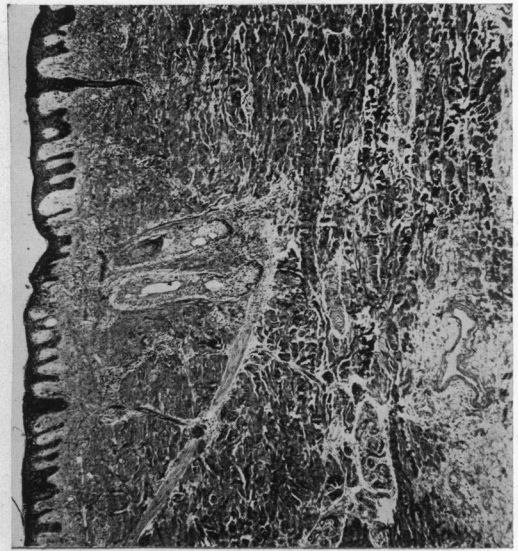


FIG. 6.

FIG. 6.—A low-power view of skin and subcutaneous tissue showing the zone of dense fibrous tissue in the corium, and the absence of any cellular reaction. Hæmatoxylin and van Gieson. Magnification: $\times 21$.

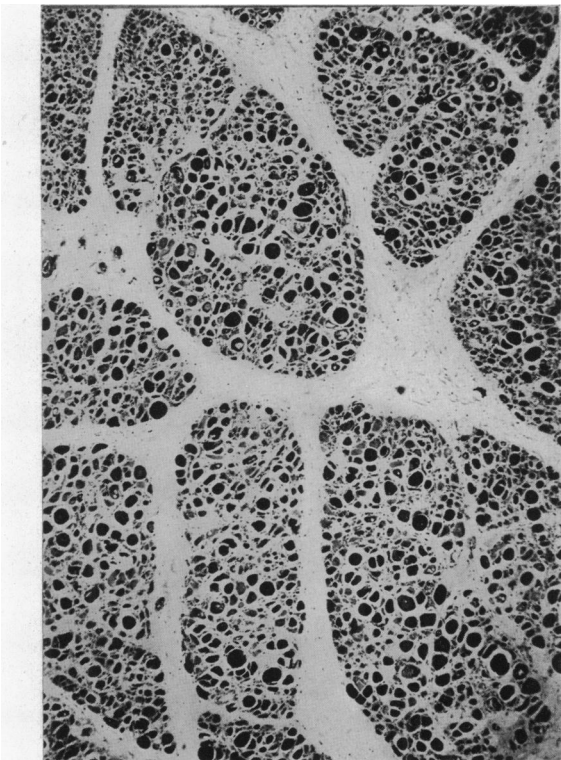


FIG. 7.

FIG. 7.—A low-power view of part of a rectus abdominis muscle showing the great variation in the size of the fibres and the complete absence of cellular infiltration of the interstitial tissue. Hæmatoxylin and eosin. Magnification: $\times 27$.

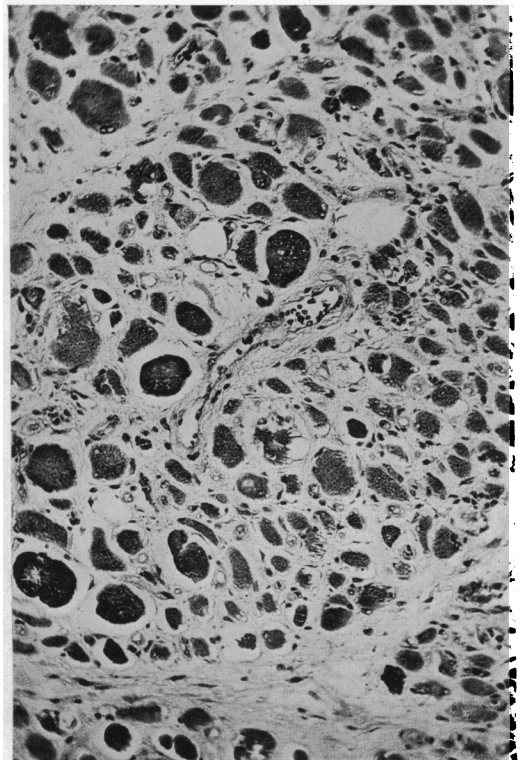


FIG. 8.

FIG. 8.—A higher power view of a rectus abdominis muscle showing the structureless appearance of the muscle fibres many of which have almost disappeared. Hæmatoxylin and eosin. Magnification: $\times 63$.

The course of the disease is extremely variable. It may be fulminating, with death resulting in a few weeks, or the progress may be extremely slow or remain stationary for years, death resulting from some other disease. The case recorded died within a year of onset.

The heart almost always fails with normal rhythm, auricular fibrillation having been recorded only once, by Weiss *et al.* (1943). The picture which our case presented was of left-sided failure, accompanied by gallop rhythm, and gradually superseded by right-sided failure, and that is the usual one. Some degree of heart block is common, but this is the first example we can find of scleroderma progressing from partial heart block to complete heart block. With such an interference with myocardial structure, the presence of heart block is not to be wondered at. Considering the amount of cardiac muscle that was replaced by this peculiar fibrous tissue, and that the skin was also heavily infiltrated with it, it is rather surprising that the electrocardiogram deflections were of such good voltage. In a case recorded by Petrácěk and Šilink (1937) there was simple bradycardia with a pulse rate of 54 a minute. Weiss *et al.* (1943) are of the opinion that the skiagram of the heart in these cases presents a suggestive triangular shape, somewhat resembling the shadow seen in pericardial effusion or sometimes in myxœdema, but the configuration of the heart in our case was in no way typical although there was some selective enlargement of the left ventricle. The impression gained at autopsy, that the enlargement was due to dilatation and not hypertrophy, was borne out by the weight of the heart (370 g.). No organic cause was discovered post-mortem for the dysphagia experienced by our patient, although cases have often been recorded where obstruction could be seen a few centimetres above the diaphragm. It is tempting to presume that the obstruction was neurogenic in origin and that the sensation of præcordial constriction experienced by our patient was of œsophageal origin. Certainly the coronary arteries were unaffected. The patient of Mathisen and Palmer (1947) also experienced mild præcordial pain, which was relieved by rest, and this substernal tightness and constriction recurred a week prior to death and was more evident when she was excited. Weiss *et al.* (1943) consider that the pathological process consists essentially of a primary overgrowth of fibrous tissue, with secondary destruction of cardiac muscle fibres which are infiltrated and pushed aside, and Mathisen and Palmer (1947) also believe that the fibrotic areas encroach upon and destroy the adjacent myocardial fibres. But from study of sections, we are of the opinion that, for some unknown reason, the cardiac muscle fibres disappear in patches and their place is filled up by this new tissue. In Fig. 7 and 8 it will be seen that many muscle fibres are structureless and disappearing, yet there is a complete absence of cellular infiltration of the interstitial tissue. Our conception might be summarized by the title of one of Strauss's tone poems, namely "Death and Transfiguration." This interpretation of the histological picture would explain the complete absence of involvement of even the finest branches of the coronary vessels. The significance of the polycythæmia, which was also present in the case recorded by Petrácěk and Šilink (1937) but in none of the cases of Weiss *et al.* (1943), is not clear. Possibly anoxæmia might have arisen as a result of the fixity of the thoracic cage which was present; cases have been recorded with radiological evidence of involvement of the lungs, for example that of Mathisen and Palmer (1947), but in our patient the lung fields were clear.

Treatment of the cardiac failure was disappointing, as might be expected from the nature of the process. The presence of excess unsplit fat in the fæces suggested that the pancreas was affected. This biochemical finding has been noted by other observers, and Sellei (1934) has recommended raw pancreas by mouth to alleviate the condition. This was administered to our patient but without effect; microscopically there was no evidence of pancreatic involvement.

SUMMARY

A case of generalized scleroderma is described in which the degree of involvement of the

cardiac muscle was so great as to produce complete heart block and to be directly responsible for death from heart failure. The few other reported cases are reviewed.

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