

PULMONARY FIBROSIS IN GENERALIZED SCLERODERMA

REVIEW OF THE LITERATURE AND REPORT OF FOUR FURTHER CASES

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Generalized scleroderma is not a disease of the skin alone. This was originally shown by Lewin and Heller as early as 1894, when they produced a monograph on the subject, and reviewed the 451 cases which had been recorded in the literature before that date. As regards the respiratory system, several cases were recorded in which dyspnoea was a prominent symptom, but the authors correlated this with sclerodermatous changes in the skin and muscles of the chest wall, and it is of interest to note that there is no record of any case in which involvement of the lungs themselves was detected clinically. This is in accord with the general experience that symptoms of respiratory insufficiency are not commonly encountered, even in those cases in which gross pulmonary fibrosis has subsequently been shown to be present. However, in their post-mortem series of twenty-four cases, there is mention of at least two in which generalized pulmonary fibrosis was found.

Since that time there have been many case reports recording involvement of various viscera in cases of generalized scleroderma, notably the lung, the myocardium, and the oesophagus, but also the thyroid, the kidneys, and other organs. Hektoen in 1897 reported a case in which the thyroid and the myocardium were involved and in which there were also changes in the pituitary. Masugi (1938) and Talbott and others (1939) recorded involvement of the kidneys. In 1943 Weiss and others thoroughly reviewed the subject of myocardial fibrosis in association with generalized scleroderma, and reported nine additional cases. Lindsay and others in the same year dealt with the oesophageal changes, describing five cases and reviewing the literature from that aspect. Bevens in 1945 reported two cases in which the

process of fibrosis extended throughout the whole of the intestinal tract, and in which were present both pulmonary and myocardial fibrosis and also changes in the thyroid gland.

On the subject of pulmonary fibrosis in association with generalized scleroderma there are fewer reports. Although the association of the two is well-recognized, search of the available literature reveals only seventeen cases. In most of these the condition was proved to be present by examination of post-mortem material, but in four cases the evidence was radiological only. Lewin and Heller (1894), as has been noted above, did not report any cases in which the pulmonary fibrosis was actually recognized during life, but in at least two of the 24 autopsies reviewed by them there was macroscopic and histological evidence of it. Matsui (1924), in his description of the clinical and post-mortem findings in six cases of generalized scleroderma, reported three in which pulmonary fibrosis was found to be present. In addition he made mention of the histological findings in one museum specimen of the disease, and this also showed a degree of generalized fibrosis. In none of these cases were there any significant clinical symptoms of pulmonary involvement.

Since that time cases showing the association of the two conditions have been reported by Murphy and others (1941), Linenthal and Talkov (1941), Weiss and others (1943), Jackman (1943), Bevens (1945), and Getzowa (1945). It is of interest to note, although not particularly surprising, that in three cases at least (Bevens, 1945; and Weiss and others, 1943) the radiograph of the chest during life did not reveal any significant abnormality even though histological evidence of widespread fibrosis was found in the post-mortem material.

THE PRESENT SERIES

The four cases which form the basis of this report show a remarkable similarity in their chest radiographs. The appearances are those of a diffuse fibrosis which is obviously generalized and yet at the same time predominantly basal in distribution. Before outlining the case histories, it might be profitable to consider the natural history of the average case of generalized scleroderma.

Generalized scleroderma is twice as common in women as in men. It usually begins between the third and fourth decade, and is usually preceded by the Raynaud syndrome. The course may be rapid or slow, progressing to death in a matter of months or extending over many years. Spontaneous recovery is recorded but is rare. At first there is oedema and induration of the dermis, and only later does this progress to the more widely recognized shiny atrophic skin, which frequently shows pigmented areas. In the early stages muscle weakness is a prominent feature, and there may also be myalgia and arthralgia. As the active stage passes, the more familiar muscle wasting and contractures develop, together with the shiny and inelastic skin.

In the three women seen by us scleroderma was fairly advanced. It was preceded for several years in all three by the Raynaud phenomenon, and in one by calcinosis. In the one man, the scleroderma was definite though early.

CASE 1.—This patient, a single woman, was first seen by us in June, 1943, when she was 45 years old and when Raynaud's disease had been progressing for three years. During that time she had also felt increasing breathlessness on exertion, and had lost over 42 lb. (19 kg.) in weight. The hands were swollen and somewhat cyanosed, and the skin showed early changes characteristic of generalized scleroderma. No abnormal physical signs were discovered in the chest, but the radiograph showed some basal fibrosis. In May, 1946, owing to an increase in the severity of the Raynaud symptoms, a right cervical preganglionic sympathectomy was performed. This resulted in improvement in the symptoms, and two months later sympathectomy was in consequence performed on the left side. The skin at this time showed very definite sclerodermatous changes, which were most severe in the hands but which also involved the face and arms. Apart from some increase in the exertional dyspnoea, there were no symptoms referable to the chest. The radiograph showed considerable increase in shadowing throughout both lung fields. Since that time the patient has been remarkably free from symptoms of the Raynaud type, but both the skin and the lung changes have steadily progressed. The vital capacity is now 27 per cent of normal, and the radiograph (Plate XXIVa) reveals

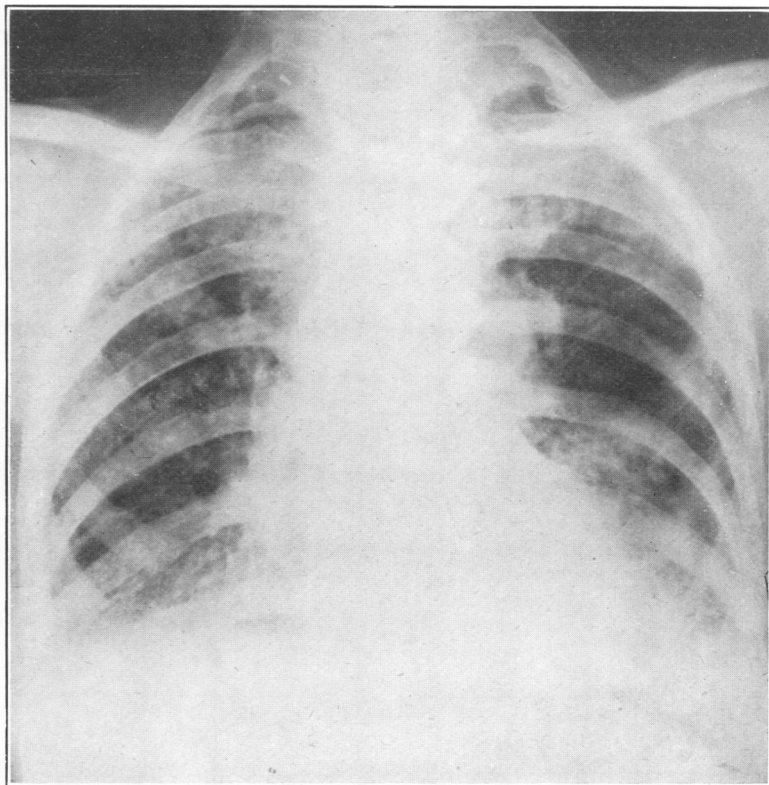
very considerable fibrosis, most severe in the lower zones. Many rales are audible throughout the lungs, and the patient is only able to walk along the level and at a very slow rate, owing to the great dyspnoea resulting from the slightest effort. Repeated and exhaustive search for evidence of tuberculosis throughout the whole period of her observation has revealed nothing. The Mantoux reaction is negative to 1 mg. O.T. The possibility of the effects of chronic lung irritants has also been excluded.

CASE 2.—This patient, an unmarried woman, was first seen in June, 1938, when she was 48 years old. She had been suffering for twenty years from attacks of the Raynaud phenomenon. On examination there were trophic ulcers on the fingers, and the skin of the hands was smooth and atrophic. Radiographs of the limbs revealed large masses of calcium in the muscles of the calves and forearms. A diagnosis of Raynaud's phenomenon with sclerodactylia and calcinosis was made, and on account of the severity of the symptoms a right cervical sympathectomy was performed. This resulted in considerable relief of symptoms, and in consequence the operation was performed on the left side six months later. Blood calcium and phosphorus were within normal limits, as was the calcium balance. A radiograph of the chest showed some basal fibrosis.

In March, 1939, the patient began to have Raynaud symptoms in the legs, and in consequence a bilateral lumbar sympathectomy was performed which again resulted in considerable relief. She was not seen again until June, 1946, when she said she had suffered from general debility and lassitude for the past year. She also complained of exertional dyspnoea. She had difficulty in swallowing unless her food was fluid or finely divided. Her skin was atrophic and thin, and there were abnormal areas of both pigmentation and depigmentation over the hands and forearms. A few small subcutaneous nodules were present over the middle third of the left ulna; these discharged chalky material from time to time. Apart from the skin changes, there were no significantly abnormal physical signs. A radiograph (Plate XXIVb) of the chest showed the fibrosis, which was known to have been present in 1938, to have increased considerably; it was generalized, although still predominant at the bases. The sputum was negative for tubercle bacilli. The erythrocyte sedimentation rate (Westergren) was 5 mm. in the first hour. The blood Wassermann and Kahn tests were negative. The patient died at home soon after discharge from hospital. No post-mortem examination was obtained.

CASE 3.—A man, aged 55 years, in October, 1947, complained of gradually increasing exertional dyspnoea over a period of three years. He had also noticed loss of weight over the same period, which he thought amounted to 2 or 3 st. (12 to 19 kg.). He coughed a little, sputum was scanty only, and there was no haemoptysis. The texture of the skin had changed, but only on direct questioning did the patient

(a)



(b)

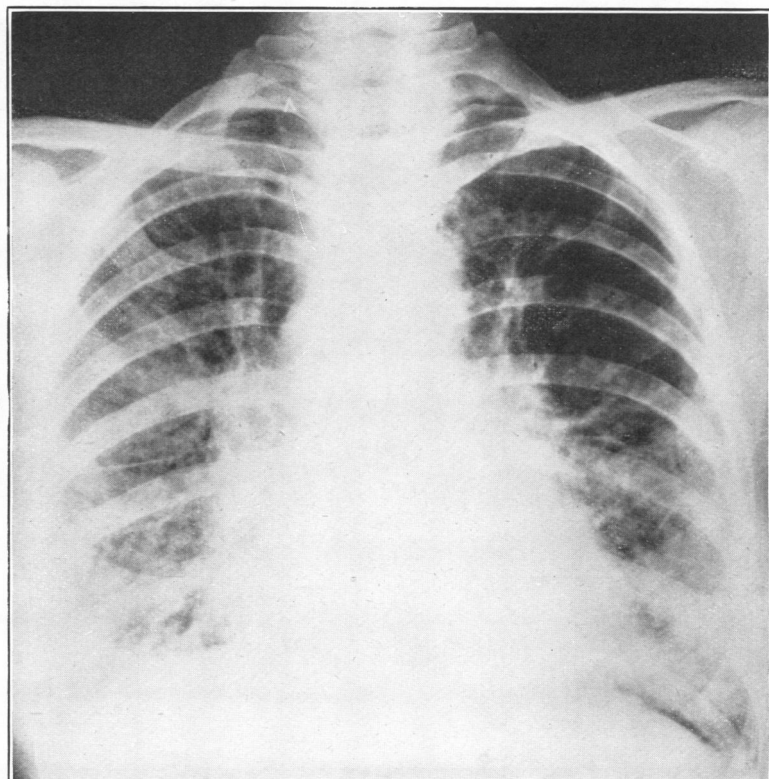
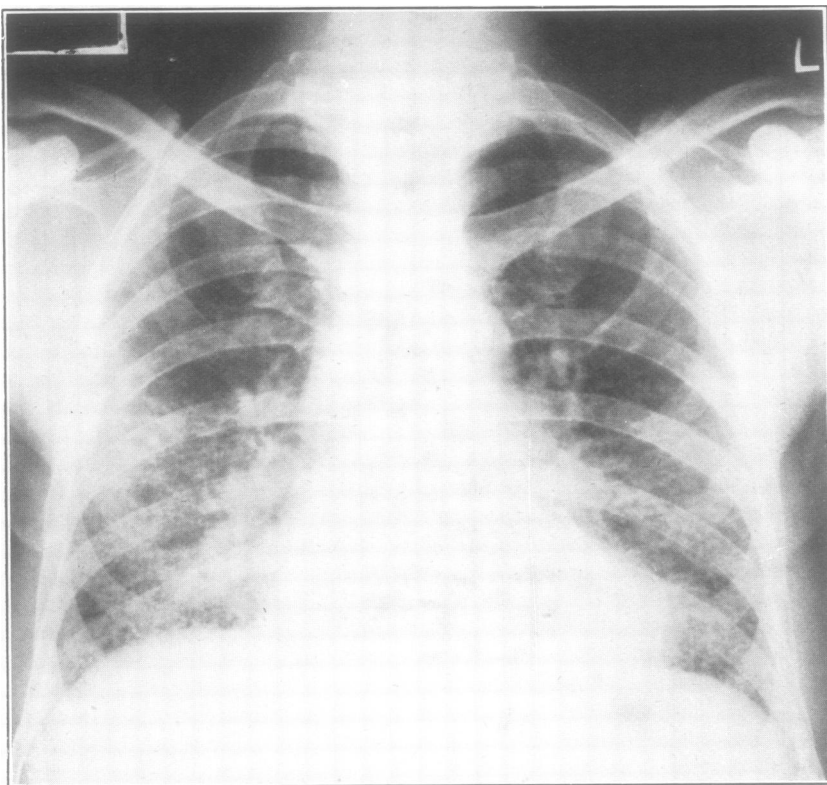
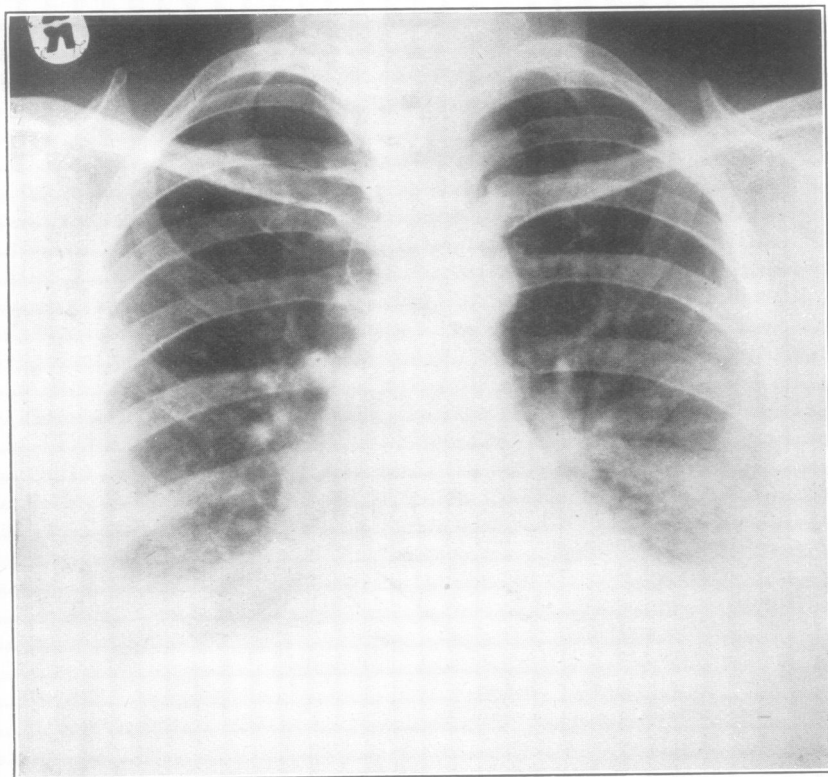


PLATE XXIV.—(a) Radiograph of Case 1, showing considerable fibrosis. (b) Radiograph of Case 2, showing generalized fibrosis.



(a)

PLATE XXV.—(a) Radiograph of Case 3, showing widespread interstitial fibrosis predominantly basal in distribution, and a calcified primary complex in the right lung. (b) Radiograph of Case 4, showing generalized fibrosis, predominant in the lower zones.



(b)

admit that temperature changes affected his hands, which readily became blue and cold in the winter. The full Raynaud syndrome was not present. There were no other symptoms. The skin of the face and hands was firm and leathery, with loss of the subcutaneous fat. The skin just above and below the clavicles and above the pubis showed lesser degrees of this same change. The feet and legs were slightly affected and the back was spared. There were also areas of increased pigmentation with depigmented spots below the clavicles. There was some clubbing of fingers and toes. There was also some diminution of the percussion note and air entry at the bases of both lungs. A radiograph (Plate XXVa) showed evidence of widespread interstitial fibrosis which was predominantly basal in distribution; a calcified primary complex was present in the right lung. Sputum was negative for tubercle bacilli. The Mantoux reaction was positive to 0.0002 mg. purified protein derivative. The blood Wassermann and Kahn tests were negative.

CASE 4.—A Polish Jewess, married and aged 48 years, first noticed thirteen years before the present examination that the tips of her fingers became bleached on stretching the fingers, and that little festering spots appeared. Since that time the skin had become progressively tight. Soon after this the symptom complex became more definitely of the Raynaud type. Five years before examination she noticed her lips becoming thin, and about the same time she began to feel some shortness of breath on exertion.

She was found to be a very nervous individual, and she said she had always been "highly strung." When asked about her health she concentrated upon her mental illness and appeared somewhat indifferent to the physical changes in the skin.

The skin of the hands, forearms, face, and neck showed generalized scleroderma. The trunk was also affected, but less so. Legs and feet were relatively clear. Examination of the chest revealed a few scattered rales only. Radiography, however, showed generalized fibrosis, predominant in the lower zones, and similar to that found in the other cases (Plate XXVb).

DISCUSSION

It seems likely that, in those cases of generalized scleroderma in which radiography reveals a diffuse irregular shadowing throughout both lung fields, there is an increase in the pulmonary connective tissue which represents a visceral manifestation of the disease. The majority of the recorded cases have no pulmonary symptoms apart from progressive exertional dyspnoea, which may become extreme in the terminal stages.

That the pulmonary condition can exist in the absence of detectable dermatological changes, or at least may precede these changes, is suggested

by the fact that an exactly comparable radiological picture has been observed in cases in which the clinical picture is that of the Raynaud phenomenon only (Linenthal and Talkov, 1941). This is a point of the greatest importance in the interpretation of chest radiographs in cases exhibiting the Raynaud phenomenon, and possibly also in those which reveal generalized fibrosis for which there is no other satisfactory aetiological explanation.

Generalized scleroderma is by no means a single clear-cut disease, even if its occurrence as an occasional sequel to the Raynaud phenomenon be taken into account. Many authors have shown its association with several other conditions, notably calcinosis (Thibierge and Weissenbach, 1911; Durham, 1928; Prosser Thomas, 1942) and dermatomyositis (Dowling and Griffiths, 1939; Banks, 1941). Dowling (1940) in a most convincing paper discussed the arguments in favour of considering generalized scleroderma and dermatomyositis as expressions of the same disease. He stressed the fact that in both conditions generalized myasthenia is a prominent symptom, progressing to muscle wasting and subsequent fibrosis. That a myopathic state exists in both is supported by the raised creatinine output which is to be found in some cases of both conditions. On this line Dowling goes even further and offers the suggestion, with some supporting evidence, that thyroid dyscrasia may also bear a close relationship to generalized scleroderma, calcinosis, and dermatomyositis.

If the association of these three conditions is accepted, the question arises whether generalized pulmonary fibrosis may occur in conjunction with all of them. Search of the available literature has not revealed any reports of pulmonary fibrosis having been noted in conjunction with dermatomyositis, nor in any case of pure calcinosis (Brooks, 1934); pulmonary changes have been reported only in cases which later developed scleroderma. However, the possibility of its occurrence should be borne in mind.

The occurrence of arthralgia as a not uncommon feature in the course of the development of scleroderma is of interest to us in view of the fact that we have a further case whose chest radiograph bears a striking similarity to those of the four cases described above, showing generalized fibrosis which is somewhat more marked in the lower zones. It is not accompanied by symptoms or signs referable to the chest, with the exception of very marked clubbing of the fingers and toes. This patient has progressive arthritis of the rheumatoid type, which is of considerable severity,

but he shows no evidence of generalized scleroderma. A further point of interest is that he had a thyroidectomy performed for Graves' disease some eight years previously. He still retains his exophthalmos.

SUMMARY

The association of progressive pulmonary fibrosis with generalized scleroderma is well recognized. The literature on this association is reviewed and four further cases are described.

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