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FOUR CASES OF SCLERODERMIA ASSOCIATED WITH DISEASE OF THE THYROID GLAND.

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I PURPOSE in this communication to describe four cases of sclerodermia associated with disease of the thyroid gland.

One patient (Case 4) has suffered from myxœdema for seventeen years, and the sclerodermia developed while the symptoms of myxœdema have been entirely controlled by thyroid treatment. This observation I believe to be unique. In the other three cases the sclerodermia is associated with Graves' disease.

I have notes of 22 cases of sclerodermia seen during recent years in private practice and at the London Hospital, 18 of which were females and 4 males. Besides those now put on record there was 1 case of pure guttate type, reported by Silva Jones (1), 1 of band form on the thigh and leg with guttate lesions on the trunk (2), 15 of morphœaic sclerodermia, and 1 of the diffuse type. Of the 22 cases, 4 were associated with affections of the thyroid gland.

CASE 1: *Sclerodermia of legs associated with Graves' disease.*—Mary S—, single, consulted me at the London Hospital on December 20th, 1909. She was then aged 22 years, and had passed all her life in Essex. She attended the hospital on account of an ulcer on the left leg. The ulcer had been in existence for several months and had failed to respond to the usual methods of treatment. When I first saw her it was evident that the ulcer was a secondary phenomenon. The lower half of the left leg was in a condition of sclerodermia and the ulcer had resulted from a slight injury. The

sclerodermia extended the whole way round the lower half of the left leg. Its upper margin was fairly well defined, but there was no lilac colour such as is usually present in morphœa. The sclerosed skin was pale, tough, and could not be pinched up. There were no telangiectases and no pigmentation. Over the middle of the area on the shin there was an ulcer the size of a two-shilling piece with a shelving edge and a base covered with flabby granulations. There was also an area of sclerodermia about the size of the palm over the middle of the inner side of the right leg.

General condition.—On examination the patient was a thoroughly well-developed young woman, the skin was pale, and the mucous membrane of the lips and gums showed there was distinct anæmia.

The eyes were slightly prominent and von Graefe's sign was present.

The tongue was protruded without tremor.

The thyroid gland was enlarged and prominent. The carotid arteries showed visible pulsation in the neck. Tachycardia was present on every occasion the patient was examined, the pulse-rate varying from 112 to 120 per minute. The heart-sounds were normal and the apex was not displaced.

Fine tremor was well marked in the hand. There was no evidence of visceral disease, and the Wassermann reaction was negative.

Progress.—The patient attended the hospital at rather irregular intervals until this year. The ulcer proved exceedingly difficult to heal, and many different applications were used, both of a stimulating and antiseptic character. Stimulant doses of X-rays were also given. The ulcer has at last healed after prolonged rest, but it is quite possible that it may break down again.

General treatment.—As benefit has been reported by the thyroid treatment in cases of sclerodermia, I gave the patient two courses of thyroid extract, but without benefit to the ulcer or to the skin condition. The general condition appeared to be made worse, the tachycardia and tremor increasing.

From July, 1914, to the end of that year, the swollen thyroid gland was treated by X-rays through an aluminium screen, and this treatment had a definite effect upon the general symptoms and may have contributed to the healing of the ulcer, but it had no appreciable effect upon the sclerodermia.

CASE 2. *Sclerodermia of trunk with Graves' disease.**—G. F—, aged 22 years, single, came to the London Hospital on December 21st, 1915, on the recommendation of Dr. Smulian. She had suffered from measles and scarlet fever in childhood, she had never had rheumatism. For some years she has had a swelling in the neck, and two months ago she noticed some white patches on the front of the chest. The thyroid gland is very large, the eyeballs are prominent, there is a fine tremor of the hand and tongue, there is no excessive sweating, but the patient complains of flushing. The pulse rate had been as high as 128. She states that she has been very irritable of late, micturition is somewhat frequent, and there is some increase in the quantity of the urine passed. The patient sleeps well, the bowels are opened regularly without medicine.

Sclerodermia.—There is a large oval patch extending obliquely across the left clavicle. Its surface is of ivory whiteness and remarkably smooth. It is surrounded by a lilac margin about a finger's breadth in width. Extending from it towards the middle line are numerous small spots of the same character. There is another area of smaller dimensions over the right side in the middle of the sternum, and numerous macular areas below it. On the back there are two oval patches, one situated at the level of the spine on the left scapula is about the size of a five-shilling piece, and there is a somewhat larger patch at a slightly lower level along the base of the right scapula. There are a few macular areas on each hip, just above the trochanters. The *tâche* is obtained very easily, and the patient is anæmic and obviously of a nervous temperament. She suffers frequently from headaches, and the pupils are dilated. The Wassermann reaction is negative. The skin of the arms shows common Keratosis follicularis.

CASE 3. *Symmetrical Sclerodermia associated with Graves' disease.* Mrs. X—, aged 59 years. Symmetrical pear-shaped patches of sclerodermia on each leg, the apex of each being upwards and at the head of the fibula. On the right thigh, about the middle of the posterior surface, was a small patch also oval in shape, but not more than three-quarters of an inch in length. The lilac edge of the white patches was well marked. There were tachycardia, some proptosis and pro-

* Shown at the Royal Society of Medicine (Dermatological Section), January 20th, 1916 (see p. 69).

minence of the thyroid gland. A history of heat and flushings was also given and the *tâche* was well marked.

This patient was only seen once. The Wassermann reaction was not examined. There was no history or evidence of syphilis. The patient was a wasted, nervous woman.

CASE 4. *Sclerodermia of both legs developing in a myxœdematous patient taking thyroid.**—Alice M—, a married woman, came under my care at the London Hospital on October 29th, 1900. She was then aged 42 years. She had had six children, who were in good health, and one miscarriage. She had been in failing health for nearly two years before I saw her, and had been admitted into a provincial cottage hospital as possibly suffering from cancer of the liver. She came to the Skin-Department of the London Hospital on account of a dry eczematous condition of the hands. It was immediately obvious that she was suffering from myxœdema. The skin was dry, the hair had been falling out freely and was then very thin, there was a pink flush on each cheek, and the rest of the skin had a characteristic waxen appearance. The lips were thickened, and the patient complained of feeling cold. She was rather deaf, and her speech was slow. She stated that she had not perspired for a long time. On examination the thyroid gland could not be felt, the fingers, on palpating, coming directly down on the trachea.

Progress.—This patient has attended my department for the past fifteen years, and throughout has taken thyroid extract. At first I began with a very small dose, and increased it until the patient complained of flushing, palpitation, etc., *i. e.* until I had demonstrated the reaction to thyroid. I then diminished the dose until I could keep the symptoms entirely in control, and for years the patient has taken 1 gr. of the thyroid extract three times a day. In passing it is interesting to note that the patient shows a remarkable sensitiveness to the drug. During the long period she has been under my care she has twice complained of the tablets doing her no good, and on inquiry each time I have found that a temporary change has taken place in the source of supply of the drug.

The patient has enjoyed good health and her skin gave no trouble

* Shown at Royal Society of Medicine (Dermatological Section), December 16th, 1915 (see p. 46).

until about a year ago. She has complained from time to time of "rheumatic pains," in the lower extremities chiefly.

Present condition.—The patient is now aged 56 years. She shows no sign of myxœdema. She is rather fresh-coloured, brisk in her movements, and her speech is not affected. There is no evidence of pulmonary, cardiac or hepatic disease. The bowels act only with the use of saline aperients. The urine is of normal character.

The Wassermann reaction is negative.

Sclerodermia.—For a great part of the past year the patient has noticed that the skin on the lower half of both legs has been very hard, and she has had "rheumatic" pains in these parts. An area of sclerodermia extends from below the middle of each leg to just above the instep. The skin is rather more yellow than the rest of the integument, it is very tough, feels like hide, and cannot be pinched up. There are no telangiectases, but below the sclerosed areas there is on each side of both feet a very large plexus of dilated veins, which I presume to be due to pressure of the sclerodermia on the venous trunks of the leg. The area affected on the right leg is more extensive than that on the left, but in either it forms a band which envelops the limb.

The obvious interest of this case is the development of sclerodermia in a patient suffering from myxœdema, which disease has been controlled for many years by thyroid extract.

The *pathogenesis of sclerodermia* is still obscure, and the most cursory survey of the literature shows that this cutaneous affection occurs in connection with such a variety of conditions that it is difficult to believe that many of the casual relationships which have been suggested can be accepted. Heller (3) advanced the hypothesis that sclerodermia is due to a general or local lymphatic obstruction, and in support of this contention a case associated with obstruction of the thoracic duct was reported. Hoppe-Seyler (4), impressed with the occurrence of the disease in two children from the same place, suspected an infectious origin. No micro-organisms have been demonstrated in the cases examined, but it is worthy of note that the disease has been seen as a sequel to scarlatina (Pringle), diphtheria (Marsh), erysipelas (Chauffard), infectious tonsillitis, pneumonia, tuberculosis, influenza, malaria, measles, etc. Many

references are given by Luithlen in this connection, and their number justifies the suggestion of Dana (5) that any infectious disease may be followed by sclerodermia. The most generally accepted is that it is a tropho- or angiotropho-neurosis, caused by changes in the nervous system (Lewin and Heller (6)). The peculiar distribution seen in some cases of morphœic sclerodermia supports this contention. It is more difficult to accept this hypothesis in cases of diffuse sclerodermia, which may possibly have a different cause. Jacquet (7) has described changes in the spinal cord, "myélite cavitaire," in sclerodermia, but Mott (8) failed to find any evidence of disease. J. L. Steven (9) found atrophy of the grey matter of the anterior horn of the cord on the same side as an area of localised sclerodermia.

Degeneration of the peripheral nerves and of the cord has been described by various authors (*vide* Luithlen (10)), but there appear to be no recent observations. Brissaud (11) maintained that the skin affection depended upon disease of the sympathetic, and its occasional association with anomalies of pigmentation may be held to be in support of the hypothesis, but there is no conclusive evidence.

Another hypothesis is that sclerodermia is the result of extensive endarteritis. In this connection it is interesting to note its occasional co-existence with Raynaud's disease. Cases are recorded by Hutchinson (12). Favier (12) collected fourteen cases with this association.

This naturally opens up the question of the possibility of there being a syphilitic basis in some cases of sclerodermia, as some cases of Raynaud's disease have been shown to have a positive Wassermann reaction. In Luithlen's article in Mracek's Handbuch (10) there are numerous references to the treatment of sclerodermia by anti-syphilitic remedies during the latter half of the nineteenth century (Rilliet, Arning, Cohn, etc.), and one (Curzio) in the eighteenth century. Lustgarten (13) first recorded a positive Wassermann reaction in a case of sclerodermia, and Whitehouse (14) had the blood examined in seven cases. In five of the diffuse type three gave a strongly positive reaction, one faintly positive, and one negative. Jeanselme and Tourraine (15) describe the case of a woman, aged 48 years, with sclerodermia of the face, trunk, and extremities, whose blood gave a positive Wassermann reaction and who improved

remarkably under anti-syphilitic treatment. In this case there was marked cerebro-spinal lymphocytosis. Brocq, Fernet, and Maurel (16) also reported a case of diffuse and rapidly-spreading sclerodermia in the course of secondary syphilis. The patient was a male, aged 32 years; his blood gave a positive Wassermann reaction, but the cerebro-spinal fluid was negative to the last.

In Osler's Case V (17), in which there was sclerodermia associated with Graves' disease, the patient had had syphilis ten years before, but had been treated for five years.

Three patients described in this communication had a negative Wassermann reaction.

Sclerodermia associated with Affections of the Thyroid Gland.

Luithlen (10) states that Eulenberg was the first to record the co-existence of sclerodermia and Graves' disease. The thesis of Samouilson (18), "De la co-éxistence de la sclérodermie et des altérations du corps thyroide," deals with the literature to 1898. Roques (19) in an article on "Opotherapy in Sclerodermia" states that of 31 cases in which the state of the thyroid gland was mentioned there were clinical signs of the organ being affected in 22. In 14 cases the thyroid was described as being small or imperceptible. In 8 cases it was hypertrophied. In 9 cases it was reported as being normal. It seems probable that local conditions may have some influence on the frequency of the co-existence of these conditions, for Dittisheim (20) found 8 cases of sclerodermia in 17 cases of exophthalmic goitre, *i. e.* in 47 per cent. Osler's Case V (17) was a male patient, aged 40 years, with an advanced stage of Graves' disease with remarkable sclerodermia of both legs. The patient had had a severe attack of syphilis ten years before. The same author's Case VII, a male, aged 49 years, suffering from sclerodermia of the hands, fingers, and cheeks, suffered from tachycardia, but there was no evidence of thyroid hypertrophy.

Thyroid atrophy, according to Roques' collection of cases, appears more common than hypertrophy. In Singer's case (21) one lobe of the thyroid was much reduced and fibrous; in Hektoen's case (22) the gland was atrophic and only weighed 14 grm. In Uhlenhuth's case (23) the organ had completely disappeared. Bouchet and Dujol (24) also describe a recent case associated with thyroid atrophy.

The co-existence of serious disease of the thyroid gland with sclerodermia naturally suggested treatment of the cutaneous condition by thyroid extract. Roques (*loc. cit.*) collected 67 cases in which this form of opotherapy had been practised. The results were as follows:

Cures	4	5·97 per cent.
Improvement	32	47 ,,
No effect	31	46 ,,

I have used thyroid extract in the treatment of a number of cases, and I agree with Osler's statement that "thyroid extract has no specific action in sclerodermia as it has in myxœdema. In no case did the skin of the affected regions become softened or regain its normal consistence." Other observers quoted by Roques have been more fortunate, and perhaps the most remarkable case of all is one reported in 1912 by Nicolas and Moutot (25). The patient was a child aged 3 years, and the lesions were in plaques. Cure was *complete* in four months.

Association of Sclerodermia with Affections of the other Ductless Glands, etc.

Cases are on record in which Addison's disease has co-existed with sclerodermia. But in considering this association it is important to bear in mind Osler's caution that increase in the pigment of the skin is a very striking feature in sclerodermia. It occurred in 144 of the 508 cases collected by Lewin and Heller (6). Alquier and Touchard (26) quote cases in which Addison's disease and sclerodermia co-existed. Winfield (27) also described an interesting case in a woman aged 52 years in whom there was diffuse sclerodermia with Addison's disease and Raynaud's phenomena. *Sclerodermia with acromegaly* has been recorded by Alquier and Touchard (26) and by L. Wernie (28).

Renon (29), believing sclerodermia to be due to polyglandular insufficiency, recommended thyro-ovarian treatment. Dupré and Kahn (30) followed the same lines, but without benefit, in cases of sclerodermia associated with Raynaud's disease. Schwerdt (31), on the assumption that sclerodermia is the effect of an intestinal toxine which the affected mesenteric glands cannot neutralise, gave mesenteric gland (0·3 grm. a day) in certain cases.

The consideration of these observations shows that our knowledge of the cause of this interesting condition is limited. I think we may leave out of account lymphatic obstruction as a cause. It appears probable that one type, the localised band variety of morphœa, has a nerve basis, and they would be properly considered to be trophoneuroses. Have we any ground for looking upon sclerodermia as due to thyroid disease? It is true that a certain proportion of the cases are associated with affections of this gland, but there is nothing to warrant the conclusion that alterations in the activity of the gland or of its secretion are actually causative of sclerodermia. The very fact that sclerodermia has been known to occur both in thyroid atrophy and thyroid hypertrophy makes one cautious, and my fourth case, in which the sclerodermia developed in a myxœdematous patient under thyroid treatment, seems sufficient to negative the view that sclerodermia develops as a result of deficient or excessive thyroid secretion. It is impossible to exclude the effects of changes in the character of the secretion. Possibly also the sclerodermia and the thyroid changes may cover a common cause, at present unknown.

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ROYAL SOCIETY OF MEDICINE.

DERMATOLOGICAL SECTION.

Meeting held December 16th, 1915, Dr. J. H. STOWERS, President of the Section, in the Chair.

Dr. E. G. GRAHAM LITTLE showed a case of *Granuloma annulare with a widespread follicular eruption.* The patient was a young officer in good health. For about a year he had noted the eruption on his hands and knees. This was in the form of a ridge of white nodules closely aggregated together and arranged in the ringed distribution so typical of the disease described by Radcliffe-Crocker under this name. There were several such small rings on a patch at the base of the middle and ring-fingers on the dorsum of each hand. The skin included within the ridge was of a bluish tinge, showing no atrophy or other change. On the knees the eruption was less diffuse but equally characteristic. Itching was very moderate. The case offered many dissimilarities clinically as compared with the patient brought forward by the same exhibitor at the last meeting of the Section, a little girl, who showed the variety of the disease known as Erythema elevatum diutinum. The follicular eruption in the present case, which was