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Thyroid Hormones in Generalized Scleroderma

A Controlled Study

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Parameters of thyroid metabolism were analysed in 42 patients with generalized scleroderma and healthy individuals matched with respect to sex and age for comparison. Decreased free thyroxine ($p<0.01$), decreased free triiodothyronine ($p<0.001$), and increased thryoid-stimulating hormone ($p<0.001$) evidenced an associated state of myxoedema in scleroderma. Total thyroxine was normal, and total triiodothyronine was increased ($p<0.01$) probably reflecting binding to abnormal serum proteins in scleroderma. Normal concentrations of reverse triiodothyronine indicated a normal peripheral metabolism of thyroid hormones. Thyroid-stimulating immunoglobulins also analysed were within normal range. Changes in free thyroxine, free triiodothyronine, and thyroid-stimulting hormone were quantitatively small with mean values within normal ranges.

In conclusion, this study evidenced a mild associating myxoedema state in generalized scleroderma. Probably, this reflected slight and subclinical affection of the thyroid. *Key words: Thyroxine; Triiodothyronine; Thyroid-stimulating hormone; Thyroid-stimulating immunoglobulin.* (Received June 24, 1985.)

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In the early fifties, in histological experiments, Asboe-Hansen showed that thyroid hormone and thyrotrophic hormone influence the mucopolysaccharides of connective tissue of skin (1, 2, 3). These findings correlated well with known alterations in myxoedema and malignant exophthalmos.

In scleroderma skin, histological, ultrastructural and biochemical studies accordingly show that acid mucopolysaccharides (later named glycosaminoglycans) are altered, in particular in the hypertrophic and oedematous state of the disease (4, 5, 6, 7). In generalized scleroderma the excretion of glycosaminoglycans in the urine is also increased (8). As a result of these observations, treatment of scleroderma with dextro-thyroxine was tried (9).

It was recently briefly stated that patients with Raynaud's disease have levels of thyroid-stimulatingh hormone approximtely ten times that of controls (10). Schwarz, Schell & Hornstein in a study of 14 patients with generalized scleroderma could not confirm these findings (11). However, some of their patients presented elevated thyroid-stimulating hormone.

In the present study of a larger material of patients suffering from generalized scleroderma, and healthy controls matched with respect to sex and age, a more detailed evaluation of the thyroid physiology including the peripheral metabolism of thyroid hormones was undertaken.

MATERIAL AND METHOD

The study included 42 patients (37 females, 5 males) with a definite diagnosis of generalized scleroderma according to the American Rheumatism Association criteria (12). Their mean age was

Table I. *Analyses of parameters of thyroid metabolism in 42 patients with generalized scleroderma in comparison with matched controls*

		Generalized scleroderma	Matched controls	Conclusion	Normal range
T_4	Mean	105.6	103.6	Normal	57–124 nmol/l
	SD	28.0	22.1		
T_3	Mean	1.696	1.532	Increased**	1.10–2.38 nmol/l
	SD	0.343	0.216		
FT_4	Mean	16.5	19.5	Decreased**	12.6–21.6 picomol/l
	SD	4.91	3.63		
FT_3	Mean	5.73	6.60	Decreased***	4.8–8.3 picomol/l
	SD	1.09	1.37		
rT_3	Mean	0.357	0.374	Normal	0.24–0.57 nmol/l
	SD	0.140	0.087		
TSH	Mean	1.303	0.498	Increased**	<35 milliunits/l
	SD	1.276	0.943		

** $p<0.01$, *** $p<0.001$.

51.3 years (range 18–71). The mean duration of scleroderma was 7.9 years (range 1–22). Thirty-eight patients had Raynaud's phenomenon, 29 had radiological affection of the esophagus, and 15 and 5 had pulmonary affection according to lung function test and radiography of the chest respectively. None of the patients had verified renal affection or uraemia. The patients had been treated with inhibitors of collagen synthesis as described by Asboe-Hansen (13). Thirty-six received penicillamine in combination with glutamine, three glutamine only, one hydralazine, and two klorpromazine. The mean duration of therapy was 3.8 years (range 0.5–20).

Forty-two healthy individuals matched with respect to sex and age (mean age 50.2 years, range 22–61) were studied for comparison.

Blood samples were taken in the morning for analysis of total thyroxine (T_4), free thyroxine (FT_4), total triiodothyronine (T_3) free triiodothyronine (FT_3), reverse triiodothyronine (rT_3) as well as thyroid-stimulating hormone (TSH). T_4, FT_4, T_3, FT_3, and TSH were analysed by the Department of Nuclear Medicine, Rigshospital, Copenhagen according to radioimmunological routine techniques, and rT_3 was analysed at Medicinsk Laboratorium, Copenhagen, by similar principle. This laboratory also determined thyroid-stimulating immunoglobulins (TSI) of the scleroderma patients by a radioreceptor assay (14).

Statistical analysis was carried out by Student's *t*-test.

RESULTS

Table I shows results of analyses of thyroid hormones in scleroderma patients in comparison with matched controls. T_4 was not changed, but T_3 was significantly increased ($p<0.01$). FT_4 and FT_3 were both decreased ($p<0.01$ and $p<0.001$) while TSH was increased ($p<0.01$). The rT_3 was not changed. Normal ranges as given by the laboratories are also included in the table.

TSI of scleroderma patients (mean 1.148 arbitrary units, SD 0.204 was within normal range (0.41–1.24 arbitrary units), however, in the upper third of this.

DISCUSSION

Thyroxine and to a lesser extent triiodothyronine are produced in the thyroid. In peripheral tissues thyroxine is mainly deiodinated to triiodothyronine, which is the metabolically more active hormone (Fig. 1). In numerous conditions with affection of the general condition the peripheral deionidation follows the foetal pattern with increased formation of

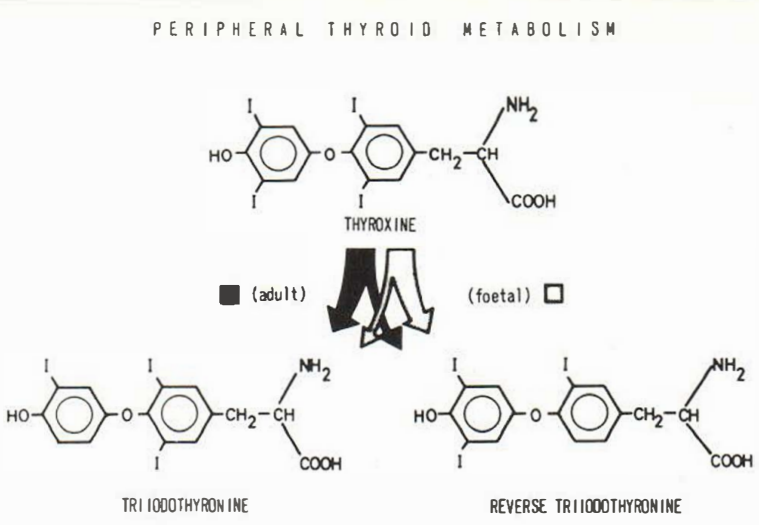

Fig. 1. Peripheral metabolism of thyroid hormones in adult and foetal life. During diseases affecting the general condition the deiodination changes in the direction of a foetal metabolism with increased formation of reverse triiodothyronine.

rT_3, which is metabolically inactive, leading to decreased concentration of FT_3 in the blood (15, 16). In severe affection of the general condition the hypophyseal stimulation of the thyroid as represented by TSH may be depressed resulting in decreased concentration of FT_4 in addition to decreased FT_3 (17, 18, 19, 20).

The main findings of the present study were decreased free thyroid hormones including FT_4 and FT_3 in combintion with increased TSH. This pattern is well known and characteristic for a myxoedema state. The increase in T_3 but not in T_4 was probably attributable to binding to abnormal serum proteins in scleroderma known frequently to influence concentrations of total thyroid hormones. TSI was normal as this immunoglobulin is in true myxoedema in contrast to elevated concentrations in hyperthyroidism (21).

Normal concentration of rT_3 indicated a normal peripheral metabolism of thyroid hormones in scleroderma. As mentioned, increased concentration of TSH is not typical in severely affected general condition despite decreased concentrations of thyroid hormones in the blood. The slight myxoedema state of scleroderma was, probably, secondary to minor glandular affection with slight insufficiency and compensatory increase in hypophyseal incretion of TSH.

Decreases of FT_4 and FT_3, and the increase in TSH were quantitatively small with mean values within normal ranges in accordance with the study of Schwarz, Schell & Hornstein (11). Thus, it is questionable whether the mild but definite myxoedematous state of scleroderma patients is of any clinical consequence. The characteristic myxoedematous alteration of skin afflicted with scleroderma mentioned initially seems mainly to have a local causation linked to the pathological process of connective tissue formation.

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