The Changes of Serum Triiodothyronine, Thyroxine and Thyroid Stimulating Hormone in Two Cases of Hypothyroidism with Unusual Complications

TOSHIRO SAKURADA, SHINTARO SAITO, TORU YAMAGUCHI, KATSUMI YOSHIDA, MAKIKO YAMAMOTO, RIKIYA ABE* and KAORU YOSHINAGA

Department of Internal Medicine and Department of Surgery,* Tohoku University School of Medicine, Sendai

SAKURADA, T., SAITO, S., YAMAoucHI, T., YOSHIDA, K., YAMAMOTO, M., ABE, R. and YOSHINAGA, K. The Changes of Serum Triiodothyronine, Thyroxine and Thyroid Stimulating Hormone in Two Cases of Hypothyroidism with Unusual Complications. Tohoku J. exp. Med., 1974, 112 (4), 365-371 — In a case of hypothyroidism with clubbing of fingers and toes, exophthalmos, myxoedema tuberosum and myxoedema pretibiale, serum T₄ value was low, but both values of serum T₃ and TSH were normal and serum LATs was positive. Three months later both values of serum T₄ and T₃ decreased and serum TSH value increased without any treatment. These results show that serum T₄ as well as T₃ might be related to the feedback control of TSH secretion. In a case of Pendred’s syndrome, serum T₄ value was low, values of serum T₃ and BMR were within normal and serum TSH value was high. Normal serum T₃ may have kept this patient in a state of compensatory hypothyroidism. In these patients, administration of 25-50 µg of l-T₃ per day was sufficient to suppress the secretion of serum TSH from thyroid gland completely. ——— triiodothyronine; thyroid stimulating hormone; pretibial myxedema; Pendred’s syndrome

Recently it has been made possible to measure the precise value of serum triiodothyronine (T₃) with a method of radioimmunoassay, and serum T₃ as well as T₄ has been taken into consideration for a feedback control of the secretion of thyroid stimulating hormone (TSH). Two cases of hypothyroidism with unusual complications are reported in the present paper and several problems among serum T₃, thyroxine (T₄) and TSH are discussed.

Case 1: A 7-year-old boy had had a slight difficulty of hearing from childhood. In July 1972, he was noticed of goiter by his family and was admitted to our hospital.

His height was 118.5 cm, and weight 23.2 kg. Pulse rate was 78/min and was regular. Skin was normal. Ocular signs were not observed. The thyroid gland was diffusely enlarged, elastic and soft. Bruit was not heard on the thyroid gland. Tendon reflexes were all normal and no edema was observed.

Serum total protein was 7.5 g/100 ml and serum total cholesterol was 148 mg/100 ml. BMR was -9%. Resin-sponge ¹³¹I-T₃ uptake (Abbott Co.) was 19%.

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Serum T₄ measured by radioimmunoassay (Yamaguchi et al. 1973) was 1.0 μg/100 ml. Serum T₃ measured by radioimmunoassay (Sakurada et al. 1973a) was 162 ng/100 ml. Thyroidal 24-hr ¹³¹I-uptake was 61% and failed to be increased by the intramuscular administration of 10 USP of bovine TSH per day for three days (TSH-test). ¹³¹I accumulated into the thyroid gland was discharged from it by the administration of 1 g of KSCN. Serum TSH measured by double-antibody radioimmunoassay (normal range: below 8 μU/ml) was 240 μU/ml.

Histological features of the thyroid gland obtained by open biopsy showed that the epithelia were low and cuboid, and some of which projected into the follicles (Fig. 1). The follicles were large and filled with an eosinophilic colloid. Pathological diagnosis was struma colloides macrofollicularis nonproliferans.

Fig. 1. Histological appearance of the thyroid gland of Case 1.

Hearing test revealed that the present patient and his elder sister had perceptive deafness.

The result of TSH-test in Case 1 was very interesting. In normal subjects, serum T₃ increased to a maximum and then decreased to the pre-administration level more rapidly than serum T₄ after TSH administration (Sakurada et al. 1973b). In hypothyroidism due to chronic thyroiditis, serum T₃ and T₄ responded very weakly to exogenous TSH (Fig. 2). However in Case 1, serum T₃ was increased to 250 ng/100 ml by TSH test though serum T₄ and ¹³¹I-uptake were unchanged (Fig. 3).

The Case 1 was diagnosed as Pendred’s syndrome with compensated hypothyroidism, and treated with l-T₃. Serum T₃ increased to 400 ng/100 ml by the administration of 50 μg of l-T₃ per day and serum TSH became undetectable (Fig. 4).

**Case 2:** A 58-year-old farmer had noticed swelling on his legs for 20 years
Fig. 2. Changes of the levels of serum $T_3$ and $T_4$ in a patient of hypothyroidism caused by chronic thyroiditis after the injection of TSH.

Fig. 3. Changes of the levels of serum $T_3$ and $T_4$ in Case 1 after the injection of TSH.

and on right shoulder since 10 years ago. He was admitted to the Surgery Department in our hospital in September 1972, because of the enlargement of swelling on his right shoulder. As histological findings of both swellings on his legs and shoulder revealed to be myxedema, he was referred to our clinic. He complained of sensation of cold, fatiguability and constipation.

Pulse rate was 52/min, regular. His face was slightly edematous, eyebrow was scanty, voice was slightly hoarse, skin was dry. Exophthalmos and clubbed fingers and toes were observed. Thyroid gland was not palpable. The Achilles tendon reflex was absent.
Fig. 4. Changes of the levels of serum T₄, T₃ and TSH in Case 1 during the replacement therapy.

Fig. 5. Changes of the levels of serum T₃ and T₄ in Case 2 after the injection of TSH.

ECG showed sinus bradycardia but no low voltage. Serum total cholesterol was 190 mg/100 ml. Serum total protein was 6.6 g/100 ml, of which 12.6% was γ-globulin.

BMR was −10%. Resin sponge ¹³¹I-T₃ uptake was 25%. Serum T₄ and T₃ were 4.8 μg/100 ml and 85 ng/100 ml, respectively. ¹³¹I-uptake was 4% and failed to respond to stimulation by bovine TSH (TSH-test). And both serum T₃ and T₄ gave weak response in TSH-test (Fig. 5). Serum TSH was 2.5 μU/ml. Serum LATS, measured by bioassay method of McKenzie with minor modification (Ochi and DeGroot, 1970), was positive (490±200). The tanned-red-cell hemagglutination test was 1: 5.

Histological appearance of the thyroid gland (Fig. 6) obtained by open biopsy revealed considerable variation in size and shape of the follicles, and the enlarged epithelia. There were variation in the size of the nuclei, marked increase of
Fig. 6. Histological appearance of the thyroid gland of Case 2.

Histologically, pretibial changes were proved to be myxoedema pretibiale and swelling on the right shoulder was myxoedema tuberosum.

As shown in Fig. 7, early in January 1973, BMR became -16% without any treatment and serum T₃ and T₄ decreased to 15 ng/100 ml and 3.3 μg/100 ml, respectively. Serum TSH at this time increased to 125 μU/ml and serum total cholesterol was 310 mg/100 ml.

Late in January, serum TSH further increased to 142 μU/ml and serum T₃ and T₄ increased spontaneously to 125 ng/100 ml and 5.1 μg/100 ml. In February, serum T₃ and T₄ became 142 ng/100 ml and 6.3 μg/100 ml, respectively, and serum TSH decreased to 70 μU/ml, but BMR was still -16%.

After he was treated with 25 μg of l-T₃ per day for 10 days, serum TSH became undetectable, and his complaints and condition of hypothyroidism disappeared.
DISCUSSION

In some clinically euthyroid patients treated previously with $^{131}$I for hyperthyroidism (Sterling et al. 1971) and similar ones with congenital goiter (Bellabarba et al. 1972), serum $T_3$ value is normal or high, serum $T_4$ value is low and serum TSH value is high. In these patients, it is thought that decreased serum $T_4$ increases TSH secretion by feedback control, and elevated TSH increases the secretion of serum $T_3$ from thyroid gland to maintain them euthyroid. On the other hand there are clinically hypothyroid patients, whose serum $T_4$ value is low, serum TSH value is high and serum $T_3$ value is normal (Wahner and Gorman 1971; Lieblich and Utiger 1972).

In Case 1 of Pendred’s syndrome, neither low value of BMR nor dwarfism was observed, and serum $T_4$ decreased, serum TSH increased and serum $T_3$ was normal. So he seemed to be in the state of compensated hypothyroidism. As shown in Fig. 2, there is no response of serum $T_3$ and $T_4$ to the stimulation by exogenous TSH in the patient of hypothyroidism. However, the serum $T_3$ in Case 1 responded better to the TSH stimulation than $T_4$ (Fig. 3). These results might show that there still remained an ability to secrete sufficient $T_3$ to maintain him euthyroid state in spite of the deficiency of hormone synthesis. There has been no other report on Pendred’s syndrome in which above-mentioned changes among $T_3$, $T_4$ and TSH were observed.

In Case 2, there were symptoms of mild hypothyroidism, both BMR and serum $T_4$ values decreased, but interestingly, serum $T_3$ was normal and serum TSH was not increased. Three months after the admission to our clinic, the values of all serum $T_3$, $T_4$ and BMR decreased and the values of serum TSH and total cholesterol were increased. These findings show that not only endogenous serum $T_4$ but also $T_3$ might be related to the feedback control of TSH secretion.

In Case 2, the values of serum $T_3$ and $T_4$ increased to normal with an increase in serum TSH value late in January, indicating that increased serum TSH may stimulate the secretion of serum $T_3$ and $T_4$. As shown in Fig. 5, intramuscular injection of 10 USP of bovine TSH daily for three days had only a weak effect on serum $T_3$ and $T_4$ in Case 2. Thus the endogenous TSH, elevated to as high as 125 $\mu$U/100 ml was a more effective stimulus to secrete the thyroid hormones than the exogenous bovine TSH used here.

In February serum $T_3$ and $T_4$ values in Case 2 became normal and serum TSH value tended to decrease though its value was still high and BMR value remained low. At this time increased serum $T_3$ and $T_4$ might begin to suppress the secretion of serum TSH.

In Case 2, localized myxedema started about 20 years ago, but interrelationship between serum thyroid hormones and serum TSH was kaleidoscopic during the observation period of about four months. Since the myxedema tuberosum on the shoulder had been suspected to be a malignant one and he had received a lymphangiography at the surgery department just before the admission to our
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clinic, the effect of iodide in the contrast medium could not be excluded as a causative factor for these unexpected changes in hormone levels.

From 75 to 100 µg of l-T₃ is reported to be sufficient to suppress the secretion of serum TSH from thyroid gland in hypothyroidism (Cotton et al. 1971). But in the Cases 1 and 2, secretion of serum TSH was suppressed completely by the administration of 25–50 µg of exogenous l-T₃ (Fig. 4 and 7). This may be explained by the remaining ability to secrete T₃ in the present patients.

References