Long Term Treatment of Congenital Hypothyroidism with L-Triiodothyronine: 24 Year Follow-Up

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Abstract

A congenital hypothyroidism complicated by ventricular septal defects which was treated with L-triiodothyronine (L-T3) alone from 1 5/12 to 25 years, is described.

The patient’s growth and development was satisfactory and without side effects. It suggests that L-T3 may be a safe drug for long term treatment of congenital hypothyroidism.

L-triiodothyronine (T3) was originally identified in human plasma by Gross and Pitt-Rivers in 1952 (Gross et al., 1952). Shortly thereafter, it was shown that T3 is approximately 3–4 times as effective in the treatment of hypothyroidism as L-thyroxine (T4) and the turnover of T3 is considerably more rapid than that of T4 (Gross et al., 1952; Lerman et al., 1953).

Fortunately, we have had synthetic T3 since 1959 and it appeared to be reasonable to use T3, with its rapid onset of action on administration and its effects which disappear more rapidly after its discontinuation, for the treatment of congenital hypothyroidism complicated by ventricular septal defects (VSD).

To the best of our knowledge, no report is yet available on the treatment of congenital hypothyroidism with T3 alone for many years. Thus this case seems to be worth reporting here as a rare case.

Case Report

The patient was referred to the Pediatric Endocrinology Clinic of Chiba University Hospital in June 1961, at the age of 1 5/12 years with suspected congenital hypothyroidism. At 6 months, the pediatric cardiologist made a diagnosis of VSD. He was born by vertex presentation at 38 weeks gestation for placenta praevia. Birth weight was 2450 g and the length was 48 cm. He was the second child of healthy, intelligent parents. His parents were not related and his elder brother was normal. There was no family history of thyroid disease. He was a dull, apathetic child. His height was 71.3 cm (−1.6 SD) and his weight was 8.2 kg (−2.3 SD). The skin was dry and sallow. The thyroid gland was not palpable. Systolic murmur was heard at the 3rd and 4th intercostal spaces to the left of the sternum. Umbilical hernia was present. The abdomen was protruding, the liver and spleen were not enlarged. There were no teeth. Neuro-
logic examination results were entirely normal. Severe anemia was present. The serum total cholesterol was elevated. Roentgenogram showed delayed osseous development. There was no ossification center of the hand. His DQ was estimated to be 30.

The results of thyroid function test were as follows. Serum PBI was 3.7 µg/dl (normal 4–8 µg/dl). $^{131}$I-T$_3$ red cell uptake was 6.6 % (normal 9.9–19.2 %). Thyroidal uptake of $^{131}$I sodium iodide was 1.0 % at 24 hours (normal 10–40 %). Ectopic thyroid was not detectable by scintiscanning.

According to these findings, he was diagnosed as congenital hypothyroidism. And thyroid replacement therapy was instituted.

Fig. 1 Results of treatment (patient T. O.)
Clinical Course (Fig. 1)

The initial dose of T₃ was 2.5 µg/day, given in 3 divided doses. This dose was gradually increased while paying attention to the development of side effects. The maintenance dose of 35 µg/day (75 µg/m²/day) was reached on the 16th day. He became more active on the replacement therapy. His development appeared satisfactory, although possibly slow. He walked at 24 months, but spoke only a few words until 3 years of age.

After 1 year of treatment, his height increased by 13 cm and his weight by 4.3 kg, approximately reaching the mean height for Japanese boys as determined by the Japanese Ministry of Health and Welfare. The appearance of the ossification center of the hand was delayed and the first center appeared after 1 year of treatment, after which bone age rapidly approached the chronological age.

Throughout the course of treatment, he remained clinically euthyroid and the ¹³¹I-T₃ red cell uptake and/or ¹³¹I-T₃ resin uptake stayed within the normal range. Serum PBI, however, was below the lower limit of the normal range.

As growth increased, the maintenance dose of T₃ was increased, reaching 100 µg/day at 11 years of age. After the age of 20 years, the dose was reduced to 75 µg/day, which is the dose currently used.

Serum TSH and T₃ were measured when the radioimmunoassay of TSH and T₃ became possible. Serum TSH values consistently stayed within the normal range (normal <2–8 µU/ml). Serum T₃ levels varied between 182–340 ng/dl (normal 98–202 ng/dl). Even after a steady state was achieved, each dose produced a detectable postabsorptive rise in the serum T₃ level. This variation in the T₃ level did not produce symptoms.

At the age of 15 years, the cardiac murmur disappeared, which suggested spontaneous closure of the VSD.

Development of secondary sexual characteristics was normal. Because of the delay in initiating the treatment, the IQ at the age of 4 1/2 years was 75, without further noticeable improvement. At the present time his height is 162.8 cm and his weight, 49.4 kg. His behavior is somewhat slow but he is observed to be serious and obedient in the performance of his work at the bakery.

Recently serum T₄ was measured and found to be below the limit of sensitivity, serum T₃ 200 ng/dl, serum TSH 4.1 µU/ml and serum free T₃ 5.0 pg/ml (normal 2.0–6.0 pg/ml).

Discussion

Treatment of congenital hypothyroidism has traditionally consisted of thyroid hormone in gradually increasing amounts to bring the patient to a euthyroid state slowly, because of the belief that patients with untreated hypothyroidism may have myxedematous hearts and associated high risk of developing cardiac arrhythmias or cardiac failure (Wilkins, 1965).

Although there is need for same caution in the use of T₃ in the initial treatment of congenital hypothyroidism, the use of rapid acting T₃ capable of quickening the induction of the euthyroid state is described (Malvaux, 1981).

With sufficient care, T₃ may be a safe drug for initial and long term treatment of congenital hypothyroidism (Petricciani et al., 1971; Federman et al., 1958).

Even when serum T₃ levels exceeded the upper limit of the normal range, symptoms of hyperthyroidism did not appear, probably because the rise in T₃ was only transient. Serum T₄ levels, essentially non-detectable, may be related to the lack of signs of hyperthyroidism.

Considerable variation in serum T₃ may influence delicate body functions, although
T₃ was apparently free of unfavorable effects on the heart in this case with VSD.

In this case the long term use of T₃ was associated with a clinical course quite indistinguishable from that of patients treated with other thyroid hormone preparations such as desiccated thyroid and T₄ (Niimi and Nakajima, 1977).

T₄ is now generally accepted as the treatment of choice in hypothyroidism, because of its greater reliability. However, our experience presented here suggests the possibility of safe and adequate long term administration of T₃.

References


