Two Cases of Hashimoto’s Thyroiditis with Transient Hypothyroidism

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Two cases of Hashimoto’s thyroiditis are presented: a woman who suffered twice from transient hypothyroidism (Case 1), and a woman with polycystic ovary syndrome who had transient hypothyroidism which was inferred to have been caused by exacerbation of Hashimoto’s disease (Case 2). In both cases, fluctuation in titers of both anti-thyroglobulin (TGHA) and anti-microsomal antibodies (MCHA) was observed. Although an increased serum thyroid stimulating hormone (TSH) concentration in Case 2 was associated with the increased titer of MCHA, this was not true of Case 1. Measurement of serum iodine concentration in Case 1 disclosed no correlation between serum TSH and iodine concentrations, suggesting that episodes of hypothyroidism in this patient are not due to iodine-induced hypothyroidism. The transient hypothyroidism in Case 2 was considered to be due to fluctuations in immune mechanism(s), but the reason in Case 1 was not clear in the present study.

Key words: chronic thyroiditis, PCO, anti-thyroglobulin antibodies, anti-microsomal antibodies, serum iodine, immune mechanism

Introduction

Thyroid function of Hashimoto’s disease has been generally thought to change gradually from euthyroidism to hypothyroidism. Thus, hypothyroidism due to Hashimoto’s thyroiditis has been regarded as an irreversible disorder requiring life-long thyroid replacement therapy. Recently, however, cases of Hashimoto’s thyroiditis with spontaneous remission (1-8), and normalization of thyroid function after restriction of iodine intake (9-11) has been reported. Furthermore, transient hypothyroidism in post-partum women thought to have Hashimoto’s disease (12, 13) has been reported. These reports suggest that impairment of the thyroid function due to Hashimoto’s disease may not be unidirectional.

We report here two cases of Hashimoto’s thyroiditis, a woman who suffered twice from transient hypothyroidism (Case 1), and a woman with polycystic ovary syndrome (Case 2) who had transient hypothyroidism. In order to clarify the underlying mechanism(s) of transient hypothyroidism in these cases, serial measurements of serum titers of anti-thyroid antibodies and serum iodine concentrations were performed.

Materials and Methods

Serum concentrations of triiodothyronine (T₃) and thyroxine (T₄) were measured by double antibody radioimmunoassay (RIA) kits (Eiken kit T₃ and T₄, Eiken, Tokyo). Normal ranges of T₃ and T₄ were 90-210 ng/dl and 4.5-13.0 μg/dl, respectively. Serum free T₃ (FT₃) and free T₄ (FT₄) concentrations were measured by analogue method RIA kits (Amerlex FT₃ and FT₄, Amersham International, Tokyo). Normal ranges of FT₃ and FT₄ were 2.7-5.9 pg/ml and 0.78-2.11 ng/dl, respectively. Serum thyrotropin (TSH) concentration in Case 1 was measured by a double antibody method RIA kit (Daichi Isotope Co., Tokyo, normal range: 2-10 μU/ml) and that in Case 2 was measured by an immunoradiometric assay kit (Spac TSH, Daiichi Isotope Co., Tokyo, normal range: 0.2-3.9 μU/ml). Anti-thyroglobulin (TGHA) and anti-microsomal antibodies (MCHA) were tested by the tanned-red blood cell hemagglutination method (Microsome test and Thyroid test, Fujizoki, Tokyo). Titers of anti-thyroglobulin (anti-Tg) antibodies were also measured by a commercially available RIA kit (Anti-Tg RIA, Eiken, Tokyo, normal...
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Case Reports

Case 1

A 23-yr-old woman visited a general hospital on April 16, 1983 with the chief complaint of swelling in her neck. She noticed excessive sweating and a slight weight gain, but did not have palpitation or finger tremor. She was a single woman and had no history of pregnancy. Her thyroid gland was found to be diffusely enlarged, rubbery hard with a smooth surface. Each lobe was of a dove egg size. Her patellar jerk was weak, and the relaxation phase of her Achilles’ jerk was slightly delayed. Thyroid function tests on April 16 were as follows: T3, 160 ng/dl; T4, 3.7 µg/dl; TSH, 81 µU/ml; MCHA, 1:80²; TGHA, 1:10²; basal metabolic rate (BMR), -9%. Twenty-four hour thyroidal ¹³¹I uptake rate done on June 18 was 78.9%. Without any medication, normalization of serum T4 (7.9 µg/dl) and TSH (7 µU/ml) were observed 2 months later. Serum T3 level had been increased to 220 ng/dl, and decreased to 134 ng/dl 2 wk later. She was referred to our outpatient clinic on June 18, 1983. Routine laboratory tests were unremarkable. On thyroid function test, she had normal serum thyroid hormone levels ($T_3$, 134 ng/dl; $T_4$, 6.0 µg/dl), with an elevated basal TSH level (14.9 µU/ml), suggesting subclinical hypothyroidism. MCHA and TGHA were 1:80² and 1:10², respectively. Twenty-four hour thyroidal ¹³¹I revealed an increased uptake (59.1%) on July 10. Thyroidal ¹³¹I scintigram was homogeneous. Serum TRAb level was 24.0%. Serum TSAb and TSBAb activities on July 18, 1983 were lower than 0.3 µU/ml and 20%, respectively, which was positive for TSBAb. In order to confirm the diagnosis of Hashimoto's thyroiditis, fine needle biopsy of the thyroid gland was performed on July 16, 1983. Histological examination revealed marked fibrosis and remarkable lymphocyte and plasma cell infiltration, which are compatible with the findings of Hashimoto’s disease.

The clinical course of the patient is summarized in Fig. 1. Serum levels of $T_3$, $T_4$, FT4 and TSH were almost within the normal range and the size of her thyroid gland gradually decreased. However, in April 1986, serum levels of $T_3$, $T_4$, and FT4 decreased to 69 ng/dl, 2.6 µg/dl, and 0.28 ng/dl, respectively. The serum level of TSH rose again to 65 µU/ml, followed by spontaneous normalization. The size of her thyroid gland did not change at the second episode of hypothyroidism. There was no clinical picture suggesting hypothyroidism. The titers of MCHA, TGHA, and TRAb did not change during the observation period. Since we were informed that she had taken in an excessive amount of seaweed just before the second episode of hypothyroidism, serum iodine concentrations was measured. Serum iodine concentration in April, 1986, when she had the second episode of hypothyroidism, was 126 ng/ml. Serum iodine concentration in May 1984, when her thyroid function tests had been normalized was 190 ng/ml. On June 10, 1986, when the thyroid function tests normalized again, perchlorate discharge test was done. The release rate of ¹²³I was -11.3%, a negative result.

Case 2

A 24-yr-old female was admitted to our hospital in June 1986 for evaluation of hypertrichosis and oligomenorrhea (three menstruation periods per yr), which persisted until 18 yr of age. Hormonal examination revealed elevation of both basal (31.8 mIU/ml) and peak values (179 mIU/ml) of plasma LH after LH-RH load with normal basal (12.5 mIU/ml) and peak (19.5 mIU/ml) values of plasma FSH. Serum testosterone concentration was elevated at 70.8 ng/ml. Polycystic change of her bilateral ovaries had been demonstrated by computed tomography. From the above findings a diagnosis of polycystic ovary syndrome was made and was accordingly
treated with clomiphene in the outpatient clinic. In June 1988, she consulted our hospital with complaints of fatigue and swelling of the anterior neck. She denied any preceding symptoms suggesting hyperthyroidism, such as excessive sweating and finger tremor. She denied ingestion of iodine-containing medicine nor excessive intake of seaweed.

On physical examination, her ht was 153 cm, wt 46 kg, blood pressure 120/76 mmHg and pulse 84/min and regular. She had diffusely enlarged thyroid gland which was rubbery hard with smooth surface. She complained slight tenderness in the anterior neck. The size of each lobe of her thyroid was almost equal to walnut. Superficial neck lymph nodes were not palpable. Her chest, heart and abdomen were unremarkable. Her deep tendon reflex was normal and the relaxation phase of her Achilles’ jerk was also normal. Her skin was not dry.

The results of routine laboratory tests, including blood chemistry, ECG, and chest X-ray were unremarkable. She had a normal erythrocyte sedimentation rate (3 mm/h) and her CRP was negative. Thyroid function tests were as follows: T3, 84 ng/dl; T4, 2.8 µg/dl; FT3, 2.3 pg/ml; FT4, 0.34 ng/dl; TSH, 142.0 µU/ml. Titer of MCHA was 1:3202, whereas titer of TGHA was negative. Titer of TRAb was -1.3%, and BMR was -1.0%. A diagnosis of primary hypothyroidism due to Hashimoto’s disease was made.

99mTc scintigram of the thyroid, performed on June 22, 1988, showed a low accumulation of 99mTc to the upper pole of the left lobe. Her clinical course is summarized in Fig. 2. Although physical findings of hypothyroidism such as dry skin and slow relaxation time of patellar jerk were absent, levothyroxine sodium (25 µg/day) was prescribed from July 5, 1988. During the treatment, she complained of palpitation, oversweating and finger tremor. The dose of levothyroxine sodium was decreased to 12.5 µg/day. Despite the decreased dosage level of supplemental T4, the thyrotoxic complaints persisted so the T4 supplement was discontinued on August 16, 1988. After replacement treatment of levothyroxine sodium, serum levels of FT3 and FT4 were elevated to the level of normal range, which was associated with a simultaneous decline of serum TSH, being 0.9 µU/ml on Feb. 9, 1989. The titer of MCHA which had been elevated to 1:3202, decreased. Although the serum TRAb value showed a negative value, -32.1% on Nov. 8, the test for anti-TSH antibodies was negative with the antibodies. The size of her thyroid gland became smaller and was almost not palpable in January 1989. Her fatigability persisted even after normalization of thyroid function.

Discussion

Both cases had transient hypothyroidism which spontaneously resolved. A diagnosis of Hashimoto’s thyroiditis was made in both cases based on histopathologic as well as serologic examinations. The reason for excessive
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sweating with an elevated TSH concentration in Case 1 is difficult to explain, however the low serum T₄ level supports the diagnosis of primary hypothyroidism. It is well known that the clinical course of subacute thyroiditis and silent thyroiditis have a hypothyroid period following the hyperthyroid state. Neither of the two present cases had an increased serum CRP or an accelerated erythrocyte sedimentation rate. In addition, neither of the two cases experienced thyrotoxic symptoms prior to episodes of hypothyroidism. Therefore, it is unlikely that they had subacute thyroiditis or silent thyroiditis.

Rallison et al reported that resolution of thyroiditis occurred in 29 of 62 patients with juvenile chronic thyroiditis, suggesting that the complete recovery from thyroiditis could occur spontaneously in children (5). Yamamoto and Sakamoto reported a 24-yr-old woman who spontaneously recovered from hypothyroidism due to chronic thyroiditis, which was not associated with pregnancy (1). Since then, cases of spontaneous remission of hypothyroidism due to chronic thyroiditis, which are not associated with pregnancy (12, 13), have been reported (2–4, 16). According to these reports (1–4), the size of the enlarged thyroid gland decreased in almost all cases when the spontaneous remission of hypothyroidism occurred. The changes in the titers of serum anti-microsomal and anti-thyroglobulin antibodies before and after normalization of thyroid function vary from case to case. This was true in the present two cases. The size of the thyroid gland in both cases decreased when the remission of thyroid function occurred. Titers of serum anti-microsomal antibodies fluctuated in both cases. In Case 1, the second episode of elevated TSH concentration was associated with an increased titer of the antibody, however, the highest titers of the antibody were not associated with the increased TSH level (Fig. 1). Increased titers of TRAb with blocking activity (TSBAb), which is reported to be present in 4% of goitrous hypothyroidism (17) was found in serum from Case 1. Although serum TSBAb activity was not measured, TRAb values did not change during the second episode of hypothyroidism. Thus, the possibility of TSBAb-induced hypothyroidism in Case 1 is unlikely. In Case 2, the highest titers of the anti-microsomal antibodies were associated with the increase in TSH concentration (Fig. 2), suggesting that the fluctuations in immune function were responsible for her hypothyroidism.

Braverman et al (1970) reported that hypothyroidism is induced by an increased iodine intake in euthyroid patients with Hashimoto’s disease (9). Later, it was reported that approximately half of the patients with primary hypothyroidism restored thyroid function by dietary iodine restriction alone (10, 11). In Case 1, the second episode of hypothyroidism occurred when excess iodine was ingested, however, the time when her serum iodine concentration was highest did not exactly coincide with the second episode of hypothyroidism. Perchlorate
discharge test in Case 1 was negative. In addition, the histopathologic finding of marked fibrosis of the thyroid gland is contrary to the clinical features of iodine-induced reversible hypothyroidism (11). Although we were unable to measure the serum iodine concentration in Case 2, she denied an excessive intake of seaweed and iodine containing foods. Therefore the possibility of iodine-induced hypothyroidism in Case 2 is unlikely.

Since sporadic hypothyroidism due to Hashimoto’s thyroiditis can be reversible, it is important to be cautious in the life-long supplementation of thyroid hormone in such patients.

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References