Transient Hypothyroidism Associated with Increased Anti-microsomal Antibodies

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Synopsis

An unusual case of transient hypothyroidism during the course of chronic thyroiditis was reported. A 25 years old female noticed the remarkable enlargement of thyroid gland 3 months after parturition and was developed to be hypothyroidism with decreased blood thyroid hormone and increased serum TSH. The patient recovered to be euthyroid spontaneously in association with the decrement of goiter size. Anti-thyroid microsomal antibody increased concomitantly with hypothyroid period and decreased parallel with the recovery of thyroid function. The ratio of TSH potency estimated by bioassay to that by immunoassay changed during the course. Possible etiologic factors of this transient changes were discussed.

Idiopathic primary hypothyroidism in adults is considered to be the end result or the severely advanced stage of autoimmune thyroiditis (Smart and Owen 1961; Doniach and Roitt, 1969; Bastenie et al., 1972). Therefore it is generally agreed that spontaneous hypothyroidism should be treated with thyroid hormones as long as life, except the cases of transient hypothyroidism associated with subacute thyroiditis (Volpé et al., 1958). As far as we concerned, no detailed report is available on transient hypothyroidism during the course of chronic thyroiditis.

This paper describes such an unusual case which we recently observed and discusses the possible etiologic factors of this interesting changes.

Materials and Methods

PBI was measured by the method of Crowley and Jensen (1965). T₃ resin sponge uptake (RT₃U) was measured using commercially available kits (Triosorb, Dainabot Radioisotope Laboratories, Tokyo). The immunological and biological activities of serum TSH were measured by double antibody radioimmunoassay (Odell et al., 1968) and by Mckenzie's bioassay (Mckenzie, 1958) with minor modifications. Undiluted or diluted sera were used in order to assay within the range of log-dose response relationship. In both assays, human TSH Research Standard A (National Institute for Medical Research, London) was used as common standard. Serum T₃ was measured by radioimmunoassay (Lieblich & Utiger, 1972) using the antibody which was made in our laboratory. Thyroid auto-antibodies to thyroglobulin and microsomes were measured by tanned sheep red cell hemagglutination technique, using commercially available kits, Thyroid test and Microsome test (Fujizoki Pharmaceutical Co. Ltd., Tokyo), respectively. The size of goiter was expressed with the transverse width of thyroid gland and the measurement was performed by one (N.A.) of the author in every time. Each serum sample obtained in 1968 and 1969 was once kept frozen at −20°C, and was assayed later concomitantly in the same assay run for measurements TSH and thyroid autoantibodies.

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Case Report and Results

A 24 years old house wife attended to the outpatient clinic of Osaka University Hospital with the complaint of goiter in March, 1967.

She was born in 1943 with full term uncomplicated delivery and had no history of special diseases in the past. Her first cousin (30 years old female) had a rheumatoid arthritis. The patient had previously consulted a physician in June, 1966, because of the swelling of anterior neck and had been diagnosed as "goiter" followed by no treatment.

In March 1967, she was pregnant at 4 months of gestational age and had diffusely enlarged soft goiter with second grade according to the classification of Shichijo (Shichijo, 1953) (estimated weight was about 40 grams).

Thyroid function was normal for pregnancy with BMR +7%, PBI 8.2 µg/100 ml, RT₃U 24%. She was diagnosed as "simple goiter" and was followed up without any treatment. She miscarried a baby spontaneously at 7 months of gestation, but got pregnancy again and delivered a healthy baby with full term uncomplicated delivery in June, 1968.

In September of 1968 (3 months after parturition), she had the remarkable enlargement of goiter with second grade according to the classification of Shichijo (Shichijo, 1953) (estimated weight was about 40 grams).

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In September of 1968 (3 months after parturition), she had the remarkable enlargement of goiter and attended to our clinic again. Around this time, she noticed easy fatiguability and the tendency to constipation, but had neither fever, neck pain, cold-intolerance, hair loss nor joint pain.

On physical examination, the patient's general condition was found to be well and her height was 153 cm, body weight 55 kg. The thyroid gland was enlarged diffusely, four-five times the normal size. The consistence of gland was elastic soft, except the upper pole of both lobes which were lobular and elastic firm. No definite nodules, tenderness or bruit were observed. No cervical lymphnode was palpable. Blood pressure and skin was normal. No ophthalmopathy was observed. Edema of legs was not present and the deep tenden reflex was almost normal.

Routine blood counts, urinalysis and liver function were normal. The red blood cell sedimentation rate was 14 mm after 1 hr and 38 mm after 2 hr. Serum total protein was 8.9 g/100 ml. On the electrophoresis of serum protein albumin was 69.8%, α₁-globulin 2.3%, α₂-globulin 7.0%, β-globulin 6.2%, and γ-globulin 14.7%. On thyroid function, PBI was 2.0 µg/100 ml (normal 3.0–8.0); RT₃U (Triosorb) 21% (normal 24–38%). Serum TSH measured by radioimmunoassay and bioassay was 200 µU/ml and 1,400 µU/ml, respectively. Anti-thyroglobulin and -microsomal antibodies by the method of tanned red cells were 1 : 10⁵ and 1 : 10⁶, respectively.

Although the first clinical impression was euthyroid, laboratory data led to the diagnosis of primary hypothyroidism. The diagnosis was confirmed by low serum T₃, 74 ng/100 ml on 5th of October and 77 ng/100 ml on 2nd of November, 1968 (normal T₃ value 90–190 ng/100 ml). She stopped breast-feeding and changed to artificial feeding, because of insufficient lactation in October. Then the ¹³¹I thyroid uptake was examined in order to clarify the etiology of this goitrous hypothyroidism. Twenty four hours uptake was found to be 79.5% in December. During this period, her body weight increased once up to 57 kg and then quickly decreased to 53 kg in accordance with decrement of the size of goiter as shown in Figure 1. Without any treatment, thyroid hormone level in blood was increased and ¹³¹I thyroid uptake was decreased to euthyroid range in January of 1969 as shown in Figure 2. Concomitant with hypothyroid period, a transient increase of serum TSH was clearly demonstrated by both bioassay and immunoassay (Figure 3). The ratio of TSH potency
Fig. 1. Clinical course of patient with transient hypothyroidism. Size of thyroid gland (---) and body weight (-----) were serially measured.

Fig. 2. Changes of thyroid function in the clinical course of the patient with transient hypothyroidism.
Fig. 3. Changes of serum TSH in the clinical course of the patient with transient hypothyroidism. Bio.=biological activity, Immuno.=immunological activity.

estimated by bioassay to that by immunoassay was higher in the serum obtained at earlier period than that at later period of hypothyroid stage (Table 1).

Anti-thyroglobulin hemagglutination antibodies (TGHA) were unchanged in 1968 (Figure 4) and slightly decreased in February and March of 1969. On the contrary, anti-microsomal hemagglutination antibodies (MCHA) were increased in association with the development of hypothyroidism.

During the recovering period of hypothyroidism, the patient did take none of drugs and the possibility of thyroid hormone ingestion was completely excluded by the careful detailed question to the patient. After spontaneous recovery, her clinical course was further followed up without any treatment by our clinic and she was uneventful until May of 1969.

After that, the patient was lost to follow-up by us. In April, 1970, she first noticed the generalized joint pain and diagnosed as rheumatoid arthritis by a house physician.
Table 1. Serum TSH measured by immunoassay and bioassay

<table>
<thead>
<tr>
<th>Date of Sample</th>
<th>Immunoassay (μU/ml)</th>
<th>Bioassay (μU/ml)</th>
<th>B/I Ratio***</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Assay I</td>
<td>Assay II‡</td>
</tr>
<tr>
<td>9-14-68</td>
<td>200</td>
<td>1,400</td>
<td>ND**</td>
</tr>
<tr>
<td>10-5-68</td>
<td>600</td>
<td>1,420</td>
<td>1,200</td>
</tr>
<tr>
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<td>1,440</td>
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<tr>
<td>4-26-69</td>
<td>3.5</td>
<td>&lt;200</td>
<td>ND</td>
</tr>
</tbody>
</table>

Each sample obtained at different date was concomitantly assayed in the same assay run.
* Diluted serum (1 : 3 dilution) was assayed and calculated the original activity.
** Not done.
*** The data of assay I were used as biological activity.

The treatment with betamethasone (2.0–0.5 mg/day) for joint pain was started in February, 1971 and intermittently continued until January of 1974. The patient was recalled for the thyroid evaluation and revealed to be euthyroid with firm small goiter. Thyroid antibodies were remarkably reduced (Figure 1–3). Thyroid function tests, performed after the discontinuance of glucocorticoid medication (six years after transient hypothyroidism) remains within normal limit.

Discussion

Spontaneous transient hypothyroidism has been observed in subacute thyroiditis (Volpé et al., 1958). However, there is little information about transient hypothyroidism during the course of chronic thyroiditis. The possibility of subacute thyroiditis in this case could be ruled out. Patient had neither neck pain nor fever. The red blood cell sedimentation rate was not elevated. Thyroid 131I uptake and autoantibodies were high. Goiter had been exist before the onset of hypothyroidism. The possibility of genetic defect in thyroid hormone synthesis could also be excluded. Because of the high titer of antithyroid antibodies, it is apparent that the patient had chronic thyroiditis. Biopsy was not performed to avoid the influence of artificial damage to natural course of the disease.

There is no doubt that patient was hypothyroid state in September-November, 1968. The high 131I uptake in some patients with hypothyroidism due to chronic thyroiditis has been well documented (Skillern et al., 1956; El Kabir et al., 1963; Greenberg et al., 1970). In our case, high 131I uptake seems to be due to the stimulation by TSH. The changes of uptake, serum TSH concentration and goiter size were well correlated each other in the course of the disease. This may indicate the important role of TSH on goiter formation in vivo, though the inflammatory factor may also be attributable in this case.

The ratio of biological to immunological activity of TSH in this patient is within the range of 1.4~8.9 which had been reported in usual hypothyroidism (Miyai et al., 1969). However, the ratio was changed during the course. The several possibilities, such as immunological serum factor, should be considered, but the exact reason of this change is not known.

It is striking that microsomal antibodies, not thyroglobulin antibodies, increased concomitantly with the development of hypothyroidism. Cytotoxic factor has been reported to correlate well to the microsomal antibodies which were measured by complement fixation and immunofluorescent tech-
techniques (Forbes et al., 1962; Irvine, 1962). If it is assumed that hypothyroidism of this patient is the result of immunological phenomenon, the measurement of microsomal antibodies may be more valuable than that of thyroglobulin antibodies to examine the clinical course.

The importance is to clarify the etiologic factor of this transient changes. It has been reported that the patient with chronic thyroiditis had enhanced susceptibility to iodide myxedema (Braverman et al., 1971). The possibility of the inductive effect of iodide in this case is unlikely, since the patient had high $^{131}$I uptake and remarkably low PBI. Skillern et al. (1956) reported that six patients noted enlargement of thyroid gland at one to three months after delivery in their observed thirty-three women with struma lymphomatosa. They speculated that the stress of pregnancy is one of the precipitating factors of struma lymphomatosa. We speculate that pregnancy and delivery may have the important etiologic role in this transient phenomenon.

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References


