Transitory subclinical and permanent hypothyroidism in the course of subacute thyroiditis (de Quervain)

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Abstract. Sixty-two patients affected with subacute thyroiditis (SAT) were followed for a mean period of 14 months (range 1—40), by monitoring thyroid hormone levels in basal condition, pituitary TSH reserve, antimicrosomal antibodies (MsAb), and antithyroglobulin (TgAb) levels, in order to study the natural course of the disease and to characterize its intermediate phase. In the first phase the mean serum iodothyronine levels were within normal limits, nevertheless elevated T3 and T4 levels were detected in 34 (54%) and 20 (32%) patients, respectively. The next phase was characterized by normal serum iodothyronine levels; TRH stimulation test, however, showed a significant increase of pituitary TSH reserve in 35 (56%) patients. All parameters reverted gradually towards normal in all but 3 patients, who showed overt permanent hypothyroidism. TgAb and MsAb were positive in the early stage in 15 (24%) and 40 (64%) patients, respectively, disappearing at the end of the follow-up period in all but one patient; this particular patient belonged to the group of 3 patients affected with permanent hypothyroidism. Our data indicate that the onset of SAT is characterized by transient hyperthyroidism and that transient subclinical hypothyroidism characterizes the next phase. TRH stimulation test is required for the diagnosis of the latter and for the identification of the few who develop permanent hypothyroidism.

Although the natural course of subacute thyroiditis is sufficiently well known (Czerniak & Harell-Steinberg 1957; Volpé 1979) the incidence of subclinical, or latent, hypothyroidism in the intermediate phase is not established in that it varies, depending on the authors, from 16 to 25%. In addition, its onset, duration and reversibility have not been sufficiently defined (Bastenie & Ermans 1972; Yeo et al. 1980; Fragu et al. 1982). Furthermore, very scanty data exist on the incidence of permanent hypothyroidism (Greene 1971; Volpé 1979; Tikkanen & Lamberg 1982).

In order to better characterize the transitory subclinical and permanent hypothyroidism of SAT, we studied the natural course of the disease in 62 patients.

Materials and Methods

Patients

Sixty-two patients, 1 man and 61 women, aged 12—57 years (mean 35 ± 11 years) affected with SAT, were observed at the Thyroid Center of the University of Rome, between 1975 and 1982. The interval of time between the onset of the first clinical signs of the disease and the clinical examination varied from 1 to 15 days. The patients were followed for a maximum of 40 months, with a mean period of observation of 14 months. They all had a characteristic history of SAT: the diagnosis was made on the basis of typical features, accelerated sedimentation rate and low thyroid uptake of radioactive iodine. In 13 patients giant-cells were present in the cytological specimens and an abundance of lymphoid cells.

From clinical findings and echographic features, in 14 patients the disease involved the whole thyroid, in 20 the lesion was localized in a single nodule, and in 28 in more than one nodule. No hormonal therapy was given to the patients; a 30 day course of acetylsalicylic acid (0.6—0.9 g every 4—6 h) was started in all subjects when first seen. At the end of this period, all the patients but 12, who required additional therapeutic treatment due to relapse, showed improvement of the symptomatology.
Methods

Total serum T₄, T₃, and TSH were measured by radio-immunoassay technique using commercial test-kits (Biodata, S.p.A., Milan, Italy); their normal range was respectively 58–138 nmol/l, 1.4–3.3 nmol/l and 0.5–4.5 mU/l. The thyrotropin releasing hormone (TRH) stimulation test was performed by administering an iv bolus of 200 µg of synthetic TRH and measuring serum TSH at time zero and every 10 min for 1 h. The normal mean maximal TSH value is ≤ 23.0 mU/l. Antithyroglobulin (TgAb) and antimicrosomal antibodies (MsAb) were tested with tanned red blood cell haemagglutination test (Wellcome Ltd., Beckenham, UK). Values of 1:40 for the former and 1:100 for the latter were considered positive. Statistical analysis was performed by means of Student’s t-test for paired and unpaired data.

Results

In the whole study group of 62 patients, the mean T₃, T₄ and TSH values did not significantly differ from those of normal subjects, during the entire study period. Nevertheless, examining the individual values, it was possible to identify early in the course of the disease (less than 30 days from the first observation) a group of hyperthyroid patients:

34 of them (54% of the total) with T₃ values of 3.5–7.5 nmol/l (mean 4.5 ± 1.3) and 20 (32% of the total) with T₄ values of 138–237.5 nmol/l (mean 180 ± 49.3). Table 1 summarizes the clinical findings of these patients. Two months after the beginning of SAT, it was possible to identify a group of 6 patients (9.6% of the total) with a TSH level ≥ 6 mU/l.

Fig. 1 shows the ΔTSH value after TRH stimulation. There is a statistically significant (P < 0.05) increase of ΔTSH 2 months after the beginning of the symptomatology, when compared to the test performed during the other study periods.

TgAb antibodies were present in 15 patients (24%), 5 of them being positive in the early stage and 10 later in the course of the disease. At the end of the follow-up period, all the patients but one were negative for TgAb antibodies.

MsAb antibodies were present in 40 patients (64%); they appeared between the second and the fourth month and disappeared in all but one patient 36 months after the beginning of the disease.

Table 1.
Clinical findings in 34 patients with features of hyperthyroidism.

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/male</td>
<td>34/0</td>
</tr>
<tr>
<td>Painful thyroid</td>
<td>34</td>
</tr>
<tr>
<td>Localized/whole thyroid involvement</td>
<td>30/4</td>
</tr>
<tr>
<td>Diffused/localized defect in thyroid ¹³¹I scan</td>
<td>22/12</td>
</tr>
<tr>
<td>Echographic features:</td>
<td></td>
</tr>
<tr>
<td>non-homogeneous/liquid</td>
<td>33/1</td>
</tr>
<tr>
<td>Total serum T₄ ≥ 138 nmol/l</td>
<td>20/34</td>
</tr>
<tr>
<td>Total serum T₃ ≥ 3.3 nmol/l</td>
<td>34/34</td>
</tr>
<tr>
<td>Total serum T₃ ≥ 3.3 nmol/l + total serum T₄ ≥ 138 nmol/l</td>
<td>20/34</td>
</tr>
<tr>
<td>TSH response to TRH ≤ 3 mU/l</td>
<td>33/34</td>
</tr>
<tr>
<td>TSH response to TRH ≤ 23 mU/l</td>
<td>1/34</td>
</tr>
</tbody>
</table>
At the end of the follow-up period, 59 patients were both clinically and hormonally euthyroid; the remaining 3 presented overt hypothyroidism on the basis of clinical findings and laboratory data (TSH > 20 mU/l). In one of these 3 subjects, MsAb was positive at the titre of 1:1600 and TgAb at the titre of 1:80.

Discussion

Our results confirm the previously reported (Weihl et al. 1977; Yoshida et al. 1982) high incidence of hyperthyroidism during the early stage of SAT: in fact, 54% of the patients showed, within the first month from onset, iodothyronine levels in the hyperthyroid range. This phase is characterized by values that are higher for T₃ than for T₄, possibly as a consequence of the preferential secretion of T₃ by the injured gland (Izumi & Larsen 1978). Our results indicate that the clinical evaluation and the T₃ determination is more useful than T₄ for the detection of the early phase of SAT. In this regard it is necessary to point out that, in our series of patients, the TSH response to TRH was unexpectedly positive. However, the quite large standard deviation, that reflects the important scatter of values in each individual case, suggests that some of the patients were already in the next phase. In this series of patients the first phase is followed, 1 month later, by an unusually high incidence (56%) of subclinical hypothyroidism. This condition is defined by absence of clinical findings typical of hypothyroidism, by normal serum T₃ and T₄, and by a TSH level in the normal, or slightly elevated range. However, the TRH stimulation test demonstrates an exaggerated TSH response, indicative of the increased hypophysal TSH reserve, necessary for the maintenance of the eumetabolic state. None of the patients showed any clinical sign of hypometabolism, and T₄ and T₃ values were within the normal limit, with only 6 patients showing a TSH level between 4 and 8 mU/l. Furthermore, the study of the hypophysal reserve after TRH allowed identifying a much greater percentage of subclinical hypothyroid patients. In fact, 35 patients out of 62 (56%) showed, 2 months after onset of the disease, an exaggerated increase in the TSH response. This latent hypothyroid condition is transient, reverting to normal 6 months after the beginning of the disease. The incidence of the latent hypothyroidism of this phase is similar to that of the transient hyperthyroidism of the first phase, with the latter usually considered a typical finding during the natural course of SAT (Saito et al. 1974; Yoshida et al. 1982).

The detection of the patients in this phase is important because the 3 patients who developed a permanent hypothyroidism after a follow-up period of 36 months belong to this group.

The transient subclinical hypothyroidism was associated with a high incidence (64%) of positivity for MsAb, TgAb being less frequently (24%) detected. Like the subclinical hypometabolic condition, the positivity of the immunological markers also appears to be transient, with only one patient still mildly MsAb and TgAb positive at the end of the follow-up period. However, the positivity of the immunological markers does not seem to be related in this series of patients to the development of permanent hypothyroidism, since only one patient, out of the 3 who developed permanent hypothyroidism, was MsAb and TgAb positive. The evolution of SAT towards permanent hypothyroidism occurs, according to other investigators (Volpé et al. 1967; Bastenie & Ermans 1972; Tikkanen & Lamberg 1982), in about 5% of patients and could be the result of both degenerative processes evolving progressively into fibrosis, and the consequence of autoimmune processes.

In conclusion, in our series of patients, the natural course of SAT is characterized by a 54% incidence of transient hyperthyroidism, during the first phase, followed by a 56% and 5% incidence of transitory subclinical and permanent hypothyroidism, respectively. The basal TSH determination is inadequate to diagnose the former, because it detects only one tenth of the affected subjects. The TRH stimulation test, on the contrary, represents the most appropriate diagnostic tool to ascertain this latent condition, since it allows the identification of those patients who can develop severe and permanent hypothyroidism.

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References


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