A case of untreated chronic goitrous autoimmune thyroiditis with spontaneous fluctuation between different metabolic levels

Jan H. Solem and Helge Svaar

Akershus Central Hospital, University of Oslo, N-1474 Nordbyhagen, Norway

Abstract. Documented thyrotoxicosis developed in a 12 year old girl with chronic autoimmune thyroiditis. During the following 3 years there was a spontaneous progression from hyperthyroidism to hypothyroidism and vice versa fluctuating from one metabolic state to another. The diagnosis of Hashimoto’s thyroiditis was based upon thyroid function tests, elevated titres of antibodies against thyroid constituents, and upon thin-needle biopsy of the enlarged thyroid gland.

Chronic goitrous autoimmune thyroiditis, or Hashimoto’s thyroiditis is a chronic autoimmune disorder of the thyroid gland which is characterized histologically by diffuse lymphocytic infiltration.

Clinically it is clear that chronic autoimmune thyroiditis may masquerade in a variety of clinical presentations (Fisher & Beall 1976).

Endocrine function is normal in most cases during the first months. Later there may be a degree of hyperthyroidism (‘Hashitoxicosis’) or hypothyroidism. Interesting is the transition from hypothyroidism caused by autoimmune thyroiditis to hyperthyroid Graves’ disease as originally described by Gavras & Thomson (1972). Up to now 20 additional cases have been described in whom thyrotoxicosis developed during thyroid hormone therapy in patients with a prolonged course of primary hypothyroidism (Irvine et al. 1979; Guansing et al. 1980; Mäenpää 1983).

It is the purpose of this report to present a case of autoimmune thyroiditis in a 12 year old girl in whom the endocrine function fluctuated between hyper- and hypothyroidism over a 3 year period. During these years no drug treatment was introduced.

Case Report

A girl of 12 years was first admitted to our hospital in March 1980 because her mother a few weeks previously had observed an enlargement of the thyroid gland. There had been no fever, and no complaints of pain. The girl had always enjoyed good health and was very active participating in outdoor sports. When the family physician first was consulted in the middle of February, the laboratory tests strongly supported the diagnosis of hyperthyroidism (Table 1).

On admittance to the hospital 4 weeks later she was clinically borderline hypothyroid. She presented a moderately enlarged non-tender thyroid gland, approximated weight 30 g. It was a typical soft diffuse goitre, no palpable nodules nor cervical lymphnodes and no endocrine ophthalmopathy. The thyroid function tests demonstrated low levels of triiodothyronine (T3) and thyroxine (T4) and increased level of thyrotophin (TSH). During the spring of 1980 close surveillance was kept with the patient, and clinically the patient appeared moderately hypothyroid during April/May.

In July the patient was clinically and biochemically euthyroid. High titres of antibodies against microsomal antigens were measured (Table 1). When she was reviewed in January 1981 the patient still appeared clinically euthyroid, an impression substantiated by thyroid tests as indicated in Table 1.

During spring and summer 1981 she experienced heat intolerance and some fatigue. In August there was bio-
chemical evidence of hyperthyroidism with moderately increased values of T₃ and T₄. The patient was moderately hyperthyroid with tremor and shortened tendon jerks. Due to the intermittent course of the disease no treatment was given.

No symptoms or signs of hypothyroidism had appeared when the patient was reviewed in March 1982. Surprisingly a very low value of T₄ was found, TSH was high and T₃ moderately decreased. During the following months she developed symptoms and signs of hypothyroidism with increasing cold intolerance and chronic fatigue, but specific therapy once again was withheld. Gradually her complaints subsided.

In May 1982 the mother of the patient noted irritability, nervousness and intolerance to heat in her daughter. On examination the patient was restless and tachycardia with tremor. The thyroid tests were compatible with thyrotoxicosis.

The metabolic state was then more or less unchanged for the following 8 months. The values for T₃ and T₄ remained at high levels. There was no decline in the patient's school performance and no treatment was employed. We enjoyed a very good cooperation with the patient and her mother who both very much agreed to 'a wait and see' attitude since the course of the disease had been so fluctuating.

Finally, in January 1983 when still thyrotoxic she was admitted to our hospital for a final check before drug therapy was to be introduced. During the stay she presented the picture of a frank hyperthyroidism. Her goitre was typically diffuse, soft, smooth, and non-tender.

The thyroid tests confirmed the diagnosis of thyrotoxicosis. The microsomal antibody titres were increased. No other organ-specific antibodies (adrenal, pancreas, ovary, gastric-parietal antibodies) nor intrinsic factor antibody could be demonstrated in serum from the patient. Thyrotropin-binding inhibiting immunoglobulins (TBI) were determined and found weakly positive. For the first time isotope studies were carried out. An uptake with ¹³¹I showed an enlarged thyroid gland with even patterns of isotope distribution. The 24 h uptake of ¹³¹I was 89%. These examinations were now supplied with a thin-needle biopsy which revealed a very striking lymphoid infiltration in the gland. The aspiration biopsy was dominated by large amounts of lymphocytes and small groups of thyroid epithelium consistent with the diagnosis of Hashimoto's thyroiditis (Fig. 1).

There was no change in her high metabolic state during January, and in February 1983 therefore the patient was given a therapeutic trial with prednisone orally 15 mg daily for 4 weeks. A moderate decrease of her goitre was observed, but no clear-cut improvement of the laboratory tests. The corticosteroid treatment was therefore concluded and from 1st of March therapy with carbimazole alone was initiated. Six weeks later, in April, she was clinically and biochemically euthyroid and since then she has remained so on a moderate maintenance dose of antithyroid agent.
Large amounts of lymphocytes (L) and small groups of thyroid epithelium (E). H/E $\times$ 400.

Methods

Thyroxine ($T_4$), triiodothyronine ($T_3$) and thyrotrophin (TSH) in serum were analyzed according to standard radioimmunoassay techniques. Antibodies against thyroidal microsomal antigens (MsA) were in 1980 detected by indirect immunofluorescence and in 1981–83 by indirect haemagglutination techniques. Circulating thyroglobulin antibodies (TgA) were detected by haemagglutination techniques (Kornstad & Kornstad 1964), modified according to Cayzer et al. (1978). Thyrotrophin-binding inhibiting immunoglobulins (TBII) were determined by the radioreceptor assay described by Wägar et al. (1982). See Table 1 for normal reference values.

Discussion

The diagnosis of autoimmune thyroiditis in our patient is based upon the persisting antibody titres and upon the cytological examination of the thin-needle biopsy.

The spontaneous course of Hashimoto’s disease is difficult to determine, since most patients receive treatment for this condition. When hypothyroidism is present, it is usually regarded as stable condition. A fluctuating course with long periods of remission may however occur (Doniach et al. 1960; Frey 1981; Riddervold 1983). A few patients with hypothyroidism caused by autoimmune thyroiditis have been subsequently reported to develop hyperthyroidism, although surely this must be a rare sequence. To our knowledge there is one report only of documented thyrotoxicosis in a patient with untreated Hashimoto’s thyroiditis and primary hypothyroidism (Kohut et al. 1982). All other cases of progression from spontaneous hypothyroidism to a hyperthyroid state were observed after initiation of thyroid hormone replacement.
(Irvine et al. 1979; Mäenpää 1983). The reason for the progression in these patients from hypothyroidism to hyperthyroidism is not readily understood. Occurrence of hyperthyroidism after thyroid hormone replacement therapy has been well documented (Dymling & Becker 1967). Thyroxine might possibly precipitate the disease. It is generally accepted that Hashimoto’s goitre is unduly sensitive to the effect of iodine (Volpé 1977).

The course of the disease in our patient is unusual according to a review of the literature (Irvine et al. 1979). Between the age of 12 and 15 years spontaneous progression from hyperthyroidism to hypothyroidism was observed twice, and her metabolic state ended up in a frank thyrotoxicosis which had to be treated with antithyroid agents after 10 months observation. During these 3 years there had been no ingestion of large doses of iodide (Okamura et al. 1978), and no specific treatment was given in the periods of hypothyroidism. In autoimmune thyroiditis there may be an alternation with time in the stimulating immune mechanisms directed at the thyroid. Christy & Morse (1977) have drawn attention to the possibility of the thyrotoxic, the euthyroid and the hypothyroid variant of Graves’ disease. Irvine et al. (1979) have emphasized how spontaneous changes in the subject’s thyroid autoimmune reactions could make possible a change from a hyperthyroid state to a hypothyroid metabolic state and vice versa. The unusual course of the autoimmune thyroiditis in our patient is compatible with such a theory.

Acknowledgments

We wish to thank Bror-Axel Lamberg (University of Helsinki), Per Gaarder (National Institute of Public Health) and Asbjørn Aakvaag (The Hormone and Isotope Laboratory, Aker Hospital) both Oslo, for their kind professional service.

References


Received on July 20th, 1983.