LATE THYROTOXICOSIS COMPLICATING AUTOIMMUNE THYROIDITIS

By

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ABSTRACT

The cases of 2 women who had clinical and biochemical evidence of autoimmune thyroiditis, who progressed to develop hypothyroidism and who then, some years later, developed thyrotoxicosis are described. Possible mechanisms for the production of this unusual clinical course are discussed.

The association of thyrotoxicosis with autoimmune thyroiditis has been recognised and well documented for several years.

Between 67-85% of thyrotoxic patients have been found to have demonstrable thyroid antibodies (Anderson et al. 1967), and there is increasing evidence that in some of these cases the lesion progressed to a more widespread thyroiditis with spontaneous remission of thyrotoxicosis and final hypothyroidism (Doniach & Roitt 1968). The whole process may take a few months or up to 30 years to develop (Doniach et al. 1960). In addition active thyrotoxicosis may coexist with the classical histological picture of lymphadenoid goitre of Hashimoto's type (Anderson et al. 1967; Doniach & Roitt 1968; Doniach et al. 1960; Joplin & Fraser 1959; Buchanan et al. 1961).

However, the development of frank thyrotoxicosis in long standing cases of autoimmune thyroiditis who were initially found to be hypothyroid and required replacement therapy with thyroxine, is a quite unusual clinical course. Two such cases are described in the present paper.

CASE RECORDS

1st Case

Female aged 61 years at the time of initial presentation in 1958 when she...
attended the Thyroid Clinic at Royal Infirmary, Glasgow with a complaint of a goitre of many years' duration; the history of thyroid enlargement, in fact, extending back to her teens. In the previous year a diagnosis of pernicious anaemia had been made at another hospital on the basis of a sternal marrow examination and histamine test meal.

At the time of presentation she was euthyroid and she weighed 82 kg. The thyroid gland generally enlarged (about 60 g) with a firm nodule at the isthmus.

The following relevant investigations were carried out: radioactive $^{131}$I studies: 24 hours uptake $^{131}$I = 56% dose, 48 hour total plasma $^{131}$I = 0.08% dose/litre, plasma 48 hour protein bound $^{131}$I negligible. Intravenous thyroid clearance of $^{131}$I = 96.0 ml/min/1.73 m$^2$ (normal range 15-80), KClO$_4$ discharge test = $^{131}$I uptake blocked but no discharge of $^{131}$I from thyroid. Serum protein: total 7.9 g/100 ml, albumin 3.5 g/100 ml, globulin 4.4 g/100 ml. Thyroid precipitin test strongly positive.

On the basis of these data a diagnosis of Hashimoto's thyroiditis was made and treatment with thyroxine started. She took the thyroxine therapy very irregularly for approximately one year and then stopped.

When reviewed in 1960 she had been off thyroxine for 6 months. Clinically her skin was dry, her weight had increased by 1.5 kg despite dieting. The clinical diagnosis at the time was of hypothyroidism and she was started on sodium thyroxine 0.05 mg daily. 5 months later on 0.1 mg daily she appeared euthyroid and had lost 2.5 kg in weight. Her goitre was unchanged.

At this time she again stopped thyroxine and defaulted from the clinic until 1967 when she presented with a history of loss of 16 kg in weight, marked heat intolerance and increased sweating. The thyroid gland was similar to that when last seen, with a large central nodule. She had atrial fibrillation at 80/min (on digoxin). The clinical diagnosis was of obvious thyrotoxicosis.

The following investigations were performed: 24 hour $^{131}$I uptake = 80% dose, 48 hour total plasma $^{131}$I = 0.37, 48 hour protein bound $^{131}$I = 0.28% dose/litre, protein bound $^{127}$I = 9.2 µg/100 ml. Antibody studies: thyroid precipitin test positive, antithyroglobulin tanned red cell titre 1/256, antibody to thyroid microsomes strongly positive, parietal cell antibody negative.

She was given a therapeutic dose of 15 mCi $^{131}$I in May, 1967. Six months later she had gained 6.5 kg in weight, her goitre had shrunk to approximately 20 g. Clinically she was euthyroid and her PB$^{127}$I was 5.6 µg/100 ml. She has remained euthyroid on follow up to the present (October, 1970).

2nd Case

Female aged 39 years at the time of first visit in 1965. She was complaining of loss of weight, palpitation, tremor, sweating over the last year and had a firm goitre. She had a past history of pulmonary tuberculosis, now inactive, and periods of palpitation and weight loss in the past 10 years, which subsided
spontaneously. She had a background of serious domestic problems, her husband being under psychiatric care after a suicidal attempt.

Her weight was 47 kg and the clinical picture was that of mild thyrotoxicosis or severe anxiety state.

Investigations gave following results:

$^{131}$I uptake at 24 hours = 78% of dose, total plasma $^{131}$I at 48 hours = 0.62% dose/litre, protein bound $^{131}$I = 0.41% dose/litre. Precipitin test negative; tanned red cell agglutination test was positive at 1:4000. She was given no specific antithyroid therapy and three months later the $^{131}$I uptake at 24 hours was 40% of dose, total plasma $^{131}$I at 48 hours = 0.48% dose/litre, and protein bound $^{131}$I at 48 hours = 0.33% dose/litre. Butanol extractable $^{131}$I was 84% of PB$^{131}$I. Serum protein bound $^{127}$I was 3.3 μg/100 ml. Over the next 6 months, with no treatment, the patient’s condition improved, she gained 8 kg in weight and was clinically euthyroid. Her PB$^{127}$I was repeatedly between 2.4 μg/100 ml and 4.4 μg/100 ml, the Triosorb T₃ resin sponge uptake was 29% (normal 25-35%) and the thyroid microsomal antibodies were strongly positive.

The diagnosis was that of Hashimoto’s thyroiditis which perhaps had an initial toxic phase and was now progressing to the stage of hypothyroidism. She was started on treatment with thyroxine 0.2 mg initially, reduced later to 0.1 mg because of palpitation, sweating and nervousness. Treatment was maintained for 3 years and in spite of the above complaints her weight gradually increased to 63 kg and remained steady for 3 years.

At that time she discontinued thyroxine on her practitioner’s advice. She attended the Thyroid Clinic again one year later complaining of tachycardia, sweating, retrosternal pain on exertion, and a loss of 12 kg in weight. Clinically she was now frankly thyrotoxic and investigations were as follows:

$^{131}$I uptake at 24 hours = 84% dose, total $^{131}$I at 48 hours = 0.80% dose/litre, protein bound $^{131}$I at 48 hours = 0.80% dose/litre, uptake after 8 days treatment with triiodothyronine (80 μg/day) was 88%, i.e. there was no suppression, serum PB$^{127}$I was 8.6 μg/100 ml. A dose of 200 mg NaClO₄ intravenously discharged at 25 min 16% of the accumulated $^{131}$I indicating a partial binding defect, compatible with the diagnosis of Hashimoto’s thyroiditis (Gray et al. 1970). Precipitin test negative; tanned red cell agglutination test positive at 1:1000, microsomal antibody strongly positive.

She was treated with 3.5 mCi $^{131}$I and rapidly became euthyroid and has remained so on follow up until the present time.

**DISCUSSION**

The first case reported is of a patient who had a small goitre since adolescence, who was found to have pernicious anaemia and biochemical evidence of auto-
immune thyroiditis in 1958. She was diagnosed as clinically hypothyroid at one point and had replacement therapy which she discontinued on her own initiative. Seven years after stopping thyroxine she presented with frank clinical thyrotoxicosis confirmed by laboratory studies and required treatment with a therapeutic dose of $^{131}$I to restore euthyroidism.

The second patient presented in 1965 with mild thyrotoxicosis, eventually developed spontaneously biochemical evidence of hypothyroidism, had 3 years' treatment with thyroxine and one year after stopping she presented again with frank clinical and laboratory evidence of thyrotoxicosis and was treated by a dose of $^{131}$I.

Since both thyrotoxicosis and autoimmune thyroiditis are known to coexist at times, and to be associated with other diseases of recognised autoimmune origin, such as pernicious anaemia, idiopathic Addison's disease and myasthenia gravis (Anderson et al. 1964, 1967) in different combinations, it is not surprising that at any given point the clinical symptoms of the one or the other condition might be predominant.

The commonly accepted view is that cases of euthyroid autoimmune thyroiditis probably progress to hypothyroidism (Anderson et al. 1967; Doniach & Roitt 1968; Buchanan et al. 1965). However, there are 2 cases reported who initially been shown to have severe focal thyroiditis and who eventually developed and laboratory evidence of thyrotoxicosis (Doniach et al. 1960; Joplin & Fraser 1959). Both of these were submitted to partial thyroidectomy for non-toxic goitre, had histological evidence of thyroiditis of autoimmune type, and became thyrotoxic 10 years later. At no time was there evidence of hypothyroidism.

In the present cases although there is no histological proof of the diagnosis of autoimmune thyroiditis at the time of the first visit, this diagnosis would seem to be firmly established on the basis of the clinical presentation, the alteration in the serum proteins and the presence of strongly positive precipitin test or tanned red cell agglutination test. One possible explanation of the subsequent development of thyrotoxicosis in our first case is that the thyrotoxic state might be due to the stimulation of the central nodule by TSH (Skillern et al. 1956) with later onset of truly autonomous function in the nodule, the function of the rest of the gland being suppressed by the nodule. The patient was found to have a prominent central nodule when thyrotoxic but as no thyroid scan done this remains only a reasonable speculation. Perhaps by analogy with parathyroid disease the development of hypothyroidism followed by hyperfunction of a thyroid nodule under excessive TSH stimulation with subsequent autonomy of the nodule might be termed “tertiary hyperthyroidism”.

Another unusual finding in the first case is that after a high dose of radioactive iodine the patient is still euthyroid 3 years later. Patients with high titre of C.F. antimicrosomal antibodies tend to become hypothyroid spontaneously.
or after surgery (Buchanan et al. 1962; Irvine et al. 1962), although the relationship of antibody titres to the result of $^{131}$I therapy is more conflicting (Blagg 1960; Irvine et al. 1962). The possible functional supression of the rest of the parenchyma by the autonomous adenoma with inhibition of uptake of the therapeutic dose of $^{131}$I could account for this.

The second patient developed thyrotoxic symptoms during her replacement treatment and these persisted after treatment was discontinued. In this case the thyroxine-induced thyrotoxicosis, as described in older papers, should probably be considered (Brochner-Mortensen 1945; Bruun 1945; Lous 1945). However, the clinical entity of autoimmune thyroiditis was not yet well recognised at that time. In reviewing under this light, cases reported as Grave’s disease, induced by thyroid preparation treatment for either myxoedema or simple metabolic obesity, one could characterize at least some of these as cases of autoimmune thyroiditis on the basis of histological picture and high “family predisposition”.

It remains difficult to explain how a thyroid gland, especially if it is already damaged enough to produce hypothyroidism, suddenly becomes overactive while replacement therapy which ought to suppress it completely is given. We have no satisfactory explanation for this phenomenon.

It would therefore seem that the late development of clinical thyrotoxicosis in a euthyroid or even hypothyroid patient with autoimmune thyroiditis can occur occasionally and should be kept in mind when following up such patients.

REFERENCES


Received on June 19th, 1971.