Chapter 9
Autoimmune Hypothyroidism with Persistent Elevation of TSH

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Objectives

To understand the investigation and treatment of patients with autoimmune hypothyroidism, and to recognize causes of persistent thyroid-stimulating hormone (TSH) elevation despite adequate thyroxine treatment.

Case Presentation

A 39-year-old man presented to his primary care physician in January 2005 with a 4-month history of generalized aches and pains and tiredness. There also appeared to be increased stress in his work and personal life, and a trial of amitriptyline 25 mg/day was commenced. Although his symptoms improved, they did not resolve completely. Blood tests including thyroid function tests were performed and revealed marked hypothyroidism: TSH >150 mU/L, and free thyroxine (FT4) 3.0 pmol/L. He was referred to an endocrinologist and was seen in April 2005. A detailed history revealed a normally fit and active person who had been unable to perform his normal activities in the preceding few months. There was no history of neck swelling or pain. His skin had become very dry but with no pigmentation, he had become constipated, and he had dizziness on standing. There was no family history of thyroid disease but he had a sister and an aunt with type 1 diabetes.

His weight was 70 kg. He had mildly hypothyroid facies but no increase in pigmentation. There was no goiter and no signs of thyroid eye disease. His pulse was 68 in sinus rhythm and his blood pressure was 100/70 with no postural drop. Systematic examination was normal.

Routine blood tests revealed a normal full blood count, thyroid function, renal and liver function, cortisol and glucose. Thyroid peroxidase antibodies were positive. The TSH was >150 mU/L (normal 0.35–4.5), FT4 was 5.4 pmol/L (normal
10.3–21.9), and free triiodothyronine (FT$_3$) was 2.6 pmol/L (normal 3.5–6.5). He was commenced on thyroxine (levothyroxine) 100 µg per day and was advised to take it 30 minutes before breakfast to aid absorption of the medication.

When next seen in early June 2005, his condition was improved although he did not feel “100 percent.” The serum TSH was checked, with a planned review in 3 months. The TSH had improved but was still elevated at 10.8 mU/L. He was contacted by letter and advised to increase the thyroxine to 125 µg per day.

The patient was next reviewed 2 months later. He felt better on thyroxine 125 µg per day, but had only collected his prescription 3 weeks beforehand so it was too early to recheck the TSH. He was encouraged to have a repeat TSH test in 4 weeks, but he did not come in for this investigation until 4 months later. The TSH had improved slightly but was still elevated at 8.43 mU/L with an FT$_4$ of 15.3 pmol/L. His thyroxine dose was increased to 150 µg/day and he was advised of the importance of compliance and attending for blood tests at appropriate times.

He was next seen in January 2006 when he was still feeling tired, particularly over the last 2 months. The TSH remained high at 9.3 mU/L (FT$_4$ 16.2 pmol/L), even on 150 µg of thyroxine per day. When asked about compliance, he insisted that he took the prescribed dose of thyroxine every day, and had only missed three or four doses 3 months ago when he was away on a business trip. No new medications had been introduced that could interfere with thyroxine requirements. The importance of adherence with treatment was once again emphasized, and he was advised to put a 1-week supply of thyroxine in a separate bottle and to take his medication from this bottle. If any tablets were left at the end of the week he should take them all at that time.

He was reviewed again 2 months later. His TSH was once again elevated at 10.0 mU/L on 150 µg of thyroxine. Again he insisted that he was compliant with treatment. Based on a body weight of 70 kg, 150 µg was considered to be more than adequate to normalize his TSH. In view of his previous record of not collecting prescriptions or attending for blood tests on time, and having previously missed tablets, poor compliance was suspected as the cause of his persistently raised TSH. To test this hypothesis, he was asked to come to the hospital for observed administration of thyroxine (1000 µg as single dose once weekly) and measurement of thyroid function, as follows:

Baseline week 1 (immediately before the administration of thyroxine):

- TSH 9.0 mU/L, FT$_4$ 16.6 pmol/L
- Week 2:
  - TSH 10.2 mU/L, FT$_4$ 13.9 pmol/L
- Week 3:
  - TSH 9.5 mU/L, FT$_4$ TSH 14.2 pmol/L
- Week 4:
  - TSH 10.5 mU/L, FT$_4$ 11.8 pmol/L
- Week 5:
  - TSH 9.8 mU/L, FT$_4$ 12.0 pmol/L