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A young woman with fluctuating hypo- and hyperthyroidism

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A 30-year-old woman presented for the first time in August 1990 with signs and symptoms of hypothyroidism: weight gain, fatigue, and muscle aches. She had a small goitre, but no ophthalmopathy or dermopathy. She was a non-smoker and mother of two (last childbirth 2 years previously). There was no history of thyroid disease or drug consumption. Thyroid function tests confirmed the diagnosis of primary hypothyroidism: thyroid-stimulating hormone (TSH) 74 mU/l (reference range 0.4–5 mU/l), free thyroxine (FT₄) 2.4 nmol/l (9–24). Thyroid microsomal antibody (TMA) and antithyroglobulin antibody were positive (one in 256 000 and 1600, respectively). Replacement therapy with thyroxine was started (100 µg daily). Over the next 6 months her dose requirement for thyroxine was reduced to 50 µg daily and the drug was stopped altogether one year after the initial diagnosis while she remained clinically and biochemically euthyroid. In July 1997, she developed symptoms and signs of thyrotoxicosis: weight loss, palpitations, and increased sweating. The diagnosis of thyrotoxicosis was confirmed (TSH undetectable, tri-iodothyronine (T₃) 2.5 nmol/l (0.7–2.1), and FT₄ 29 nmol/l). No treatment was given. While on follow-up over the next 2 months her symptoms subsided and she gained weight; thyroid function confirmed hypothyroidism (TSH 84 mU/l, FT₄ 8.8 nmol/l). In November 1997, although symptomatically she remained well, thyroid function tests showed thyrotoxicosis (TSH undetectable, FT₄ 30 nmol/l) but she has remained euthyroid on follow-up. Her TMA titre remains the same.

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Figure Fluctuation of thyroid function during the follow-up period.

Questions

- 1 What is the diagnosis?
- 2 Why is the thyroid function fluctuating?
- 3 How would you treat this patient?

Answers

QUESTION 1

Autoimmune thyroid disease with fluctuating hypo- and hyperthyroidism.

QUESTION 2

The fluctuations are due to the presence of blocking and stimulating antibodies.

QUESTION 3

There are three possible ways of treating such a patient. The patient must be fully informed about the nature and likelihood outcome of each treatment option:

- following up with serial checks of thyroid function and treatment according to the severity and nature of the thyroid dysfunction
- blocking–replacement therapy with thyroxine and carbimazole or propylthiouracil
- radioiodine treatment with appropriate follow-up.

Discussion

Fluctuating thyroid function can be defined as a spontaneous shift of functional thyroid state from hyperthyroidism to hypothyroidism or *vice versa*. In autoimmune thyroid disease, thyroid function can fluctuate. Thyroid-stimulating immunoglobulin (measured by the capacity of serum immunoglobulin to stimulate cAMP production in cultured human thyroid cells) stimulates the thyroid gland while blocking antibodies (measured by the degree of inhibition of TSH-stimulated cAMP production of cultured human thyroid cells by serum immunoglobulin) do the opposite. At a particular point, it is the balance between the two antibodies that decides the functional thyroid state. Although not common, similar cases have been reported for hyperthyroidism to hypothyroidism¹ and *vice versa*.^{2,3} The end point of all reported cases was hypothyroidism, either spontaneously or as a result of treatment, but our patient remained in a euthyroid state without intervention.

Thyrotoxicosis factitia should be considered in the differential diagnosis. Clinically, the presence of goitre, ophthalmopathy or dermopathy is against the diagnosis. In thyrotoxicosis factitia, radioactive iodine uptake of the

thyroid gland will be negligible, and serum thyroglobulin and antithyroid antibodies will be undetectable. Also, on biochemical testing, serum T₃ is likely to be normal or low with high serum thyroxine and suppressed TSH. The presence of goitre, high serum T₃ and high titre of antibodies clearly argue against such a diagnosis in our patient.

The next question is whether or not we can predict such fluctuating behaviour of the thyroid gland. No clear answer is available. Progressive destruction of the thyroid gland or production of TSH receptor blocking antibodies may be responsible for the development of a hypothyroid state in patients with Graves' hyperthyroidism.⁴ One can assume that blocking antibody plays a greater role than structural damage of the gland in such cases, otherwise the chance of development of a hyperthyroid phase would be very low. On the other hand, hypothyroid patients with radioiodine uptake are likely to remit,⁵ in contrast to those with normal or low uptake. Finally, there may be some yet unidentified factors other than stimulating and blocking antibodies, which are responsible for such fluctuations. It is interesting to note that the very high level of serum TSH at diagnosis and follow-up did not predict the outcome in our patient. Thus, a very high TSH or a very low FT₄ does not necessarily mean the patient will have permanent hypothyroidism.

We believe that radioactive iodine is the best way to treat the hyperthyroid phase, with subsequent observation. Our patient's hyperthyroid phase was short lasting and of less magnitude but such a treatment option will be considered in future, if necessary. In the hypothyroid stage, the only option remains replacement with thyroxine to keep the patient euthyroid. Surgery is an alternative option in the hyperthyroid patient after stabilisation with a blocking–replacement regimen.

Final diagnosis

Autoimmune thyroid disease with fluctuating thyroid function as a result of stimulating and blocking antibodies.

Keywords: hyperthyroidism; hypothyroidism; autoimmune thyroid disorder

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A newborn with watery diarrhoea

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A 35-year-old woman was referred to hospital at 32 weeks gestation because her uterus was large for date. Ultrasound examination done at that time is shown in the figure. At 34 weeks gestation, she gave birth to a baby boy weighing 2.2 kg, who had significant abdominal distension at birth. There was no vomiting. He did not pass meconium but after per rectum examination a large amount of light yellow watery stool was passed, followed by some relief of his abdominal distension. He continued to pass this type of stool. Blood laboratory tests at the age of 2 weeks showed a serum sodium of 131 mmol/l, potassium 3.1 mmol/l, chloride 91 mmol/l and bicarbonate 31 mmol/l. The family had an elder son who had had chronic diarrhoea since birth.

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Figure

Questions

- 1 What does the sonogram show?
- 2 What is the most likely diagnosis?
- 3 How can the diagnosis be confirmed?