Hashimoto's thyroiditis

Hashimoto's thyroiditis is characterised by destructive lymphoid infiltration of the thyroid, ultimately leading to a varying degree of fibrosis and thyroid enlargement. There is an increased risk of thyroid lymphoma, although this is exceedingly rare. Some authorities reserve the term 'Hashimoto's thyroiditis' for the condition of patients with positive antithyroid peroxidase autoantibodies and a firm goitre who may or may not be hypothyroid, and use the term 'spontaneous atrophic hypothyroidism' for the condition of hypothyroid patients without a goitre in whom TSH receptor-blocking antibodies may be more important than antithyroid peroxidase antibodies. However, these syndromes can both be considered as variants of the same underlying disease process.

Hashimoto's thyroiditis increases in incidence with age and affects approximately 3.5 per 1000 women and 0.8 per 1000 men each year. Many present with a small or moderately sized diffuse goitre, which is characteristically firm or rubbery in consistency. Around 25% of patients are hypothyroid at presentation. In the remainder, serum T4 is normal and TSH normal or raised, but these patients are at risk of developing overt hypothyroidism in future years. Antithyroid peroxidase antibodies are present in the serum in more than 90% of patients with Hashimoto's thyroiditis. In those under the age of 20 years, antinuclear factor (ANF) may also be positive.

Levothyroxine therapy is indicated as treatment for hypothyroidism and also to shrink an associated goiter. In this context, the dose of levothyroxine should be sufficient to suppress serum TSH to low but detectable levels.

Transient thyroiditis

Subacute (de Quervain's) thyroiditis

In its classical painful form, subacute thyroiditis is a transient inflammation of the thyroid gland occurring after infection with ***Coxsackie, mumps or adenoviruses***. There is pain in the region of the thyroid that may radiate to the angle of the jaw and the ears, and is made worse by swallowing,

coughing and movement of the neck. The thyroid is usually palpably enlarged and tender.

Systemic upset is common. Affected patients are usually females aged 20–40 years. Painless transient thyroiditis can also occur after viral infection and in patients with underlying autoimmune disease. The condition can also be precipitated by **drugs**, including *interferon-α and lithium*.

Irrespective of the clinical presentation, inflammation in the thyroid gland occurs and is associated with release of colloid and stored thyroid hormones, but also with damage to follicular cells and impaired synthesis of new thyroid hormones. As a result, T4 and T3 levels are raised for 4–6 weeks until the pre-formed colloid is depleted. Thereafter, there is usually a period of hypothyroidism of variable severity before the follicular cells recover and normal thyroid function is restored within 4–6 months (Fig. 18.9). In the thyrotoxic phase, the iodine uptake is low because the damaged follicular cells are unable to trap iodine and because TSH secretion is suppressed. Low-titre thyroid autoantibodies appear transiently in the serum, and the erythrocyte sedimentation rate (ESR) is usually raised. High-titre autoantibodies suggest an underlying autoimmune pathology and greater risk of recurrence and ultimate progression to hypothyroidism.

The pain and systemic upset usually respond to simple measures such as non-steroidal anti-inflammatory drugs (NSAIDs). Occasionally, however, it may be necessary to prescribe prednisolone 40 mg daily for 3–4 weeks. The thyrotoxicosis is mild and treatment with a β-blocker is usually adequate. Antithyroid drugs are of no benefit because thyroid hormone synthesis is

impaired rather than enhanced. Careful monitoring of thyroid function and symptoms is required so that levothyroxine can be prescribed temporarily in the hypothyroid phase. Care must be taken to identify patients presenting with hypothyroidism who are in the later stages of a transient thyroiditis, since they are unlikely to require life-long levothyroxine therapy (see Fig. 18.6).

Post-partum thyroiditis

In Lec. No.2 Graves disease

Iodine-associated thyroid disease

Iodine deficiency

Iodine is an essential micronutrient and is a key component of T4 and T3. The World Health Organisation (WHO) recommends a daily intake of iodine of 150 μg/day for adult men and women; higher levels are recommended for pregnant women (p. 1279).

Dietary sources of iodine include seafood, dairy products, eggs and grains. Dietary iodine deficiency is a major worldwide public health issue, with an estimated one-third of the world population living in areas of iodine insufficiency. Iodine deficiency is particularly common in Central Africa, South-east Asia and the Western Pacific. It is associated with the development of thyroid nodules and goitre (endemic goitre); the reduced substrate available for thyroid hormone production increases thyroid activity to maximize iodine uptake and recycling, and this acts as a potent stimulus for enlargement of the thyroid and nodule formation. Most affected patients are euthyroid with normal or raised TSH levels, although hypothyroidism can occur with severe iodine deficiency.

Suspected iodine deficiency can be assessed by measuring iodine in urine (either a 24-hour collection or a spot sample). Endemic goitre can be treated by iodine supplementation, and a reduction in nodule and goitre size can be seen, particularly if it is commenced in childhood. Iodine deficiency is not associated with an increased risk of Graves' disease or thyroid cancer, but the high prevalence of nodular autonomy does result in an increased risk of thyrotoxicosis and this risk may be further increased by iodine supplementation. Conversely, iodine supplementation may also increase the prevalence of subclinical hypothyroidism and autoimmune hypothyroidism. These complex effects of iodine supplementation are further discussed below.

In pregnancy, iodine deficiency is associated with impaired brain development, and severe deficiency can cause cretinism. Worldwide, iodine

deficiency is the most common cause of preventable impaired cognitive development in children (p. 1279). The WHO and other international organisations have made reversal of iodine deficiency a priority and have helped organise national supplementation programmes. These have mainly involved the iodisation of table salt, but have also included schemes to administer oral or intramuscular iodised oil to at-risk populations and the addition of iodine to wells supplying water to local communities. These schemes have been extremely effective in reducing the prevalence of iodine deficiency, but lower consumption of table salt has actually led to an increase in iodine deficiency in some developed countries like Australia and New Zealand.

Iodine-induced thyroid dysfunction

Iodine has complex effects on thyroid function. Very high concentrations of iodine inhibit thyroid hormone synthesis and release (known as the Wolff–Chaikoff effect) and this forms the rationale for iodine treatment in thyroid crisis and prior to thyroid surgery for thyrotoxicosis . This is an autoregulatory response to protect the body from the sudden release of large amounts of thyroid hormone in response to the ingestion of a substantial load of iodine. This effect only lasts for about 10 days, after which it is followed by an ‘escape phenomenon’: essentially, the return to normal organification of iodine and thyroid peroxidase action . Therefore, if iodine is given to prepare an individual with Graves’ disease for surgery, the operation must happen within 10–14 days; otherwise, a significant relapse of the thyrotoxicosis could occur.

Iodine deficiency and underlying thyroid disease can both moderate the effects of iodine on thyroid function. In iodine deficient parts of the world, transient thyrotoxicosis may be precipitated by prophylactic iodinisation programmes. In iodine-sufficient areas, thyrotoxicosis can be precipitated by iodine-containing radiographic contrast medium or expectorants in individuals who have underlying thyroid disease predisposing to thyrotoxicosis, such as multinodular goitre or Graves’ disease in remission. Induction of thyrotoxicosis by iodine is called the Jod–Basedow effect. Chronic excess iodine administration can also result in hypothyroidism; this

is, in effect, a failure to escape from the Wolff–Chaikoff effect and usually occurs in the context of prior insult to the thyroid by, for example, autoimmune disease, thyroiditis, lithium, antithyroid drugs or surgery.

Amiodarone

The anti-arrhythmic agent amiodarone has a structure that is analogous to that of T4 and contains huge amounts of iodine; a 200 mg dose contains 75 mg iodine. Amiodarone also has a cytotoxic effect on thyroid follicular cells and inhibits conversion of T4 to T3 (increasing the ratio of T4:T3). Most patients receiving amiodarone have normal thyroid function but up to 20% develop hypothyroidism or thyrotoxicosis, and so thyroid function should be monitored regularly. TSH provides the best indicator of thyroid function. The thyrotoxicosis can be classified as either:

• type I: iodine-induced excess thyroid hormone synthesis in patients with an underlying thyroid disorder, such as nodular goitre or latent Graves' disease (an example of the Jod–Basedow effect).

• type II: thyroiditis due to a direct cytotoxic effect of amiodarone administration.

These patterns can overlap and may be difficult to distinguish clinically, as iodine uptake is low in both. There is no widely accepted management algorithm, although the iodine excess renders the gland resistant to 131I. Antithyroid drugs may be effective in patients with the type I form but are ineffective in type II thyrotoxicosis. Prednisolone is beneficial in the type II form.

A pragmatic approach is to commence combination therapy with an antithyroid drug and glucocorticoid in patients with significant thyrotoxicosis. A rapid response (within 1–2 weeks) usually indicates a type II picture and permits withdrawal of the antithyroid therapy; a slower response suggests a type I picture, in which case antithyroid drugs may be continued and prednisolone withdrawn. Potassium perchlorate can also be used to inhibit iodine trapping in the thyroid. If the cardiac state allows,

amiodarone should be discontinued, but it has a long half-life (50–60 days) and so its effects are long-lasting.

To minimise the risk of type I thyrotoxicosis, thyroid function should be measured in all patients prior to commencement of amiodarone therapy, and amiodarone should be avoided if TSH is suppressed.

Hypothyroidism should be treated with levothyroxine, which can be given while amiodarone is continued.