Hashimoto’s Thyroiditis

Hashimoto’s thyroiditis is named after Dr Hakaru Hashimoto, who first described the condition in 1912.[1] It is part of the spectrum of autoimmune disease and the most common cause of goitrous hypothyroidism in non-iodine-deficient areas. However, there is also an atrophic form of autoimmune thyroiditis (Ord’s thyroiditis) which is more common in Europe.

Pathogenesis

In this condition, typically there is aggressive destruction of thyroid cells by various cell- and antibody-mediated immune processes (in contrast to the stimulatory effect seen in Graves’ disease). It is not yet understood why this occurs. The major environmental triggers of autoimmune thyroid disease include iodine, medications, infection, smoking and possibly stress.[2]

- Antibodies binding to and blocking the thyroid-stimulating hormone (TSH) receptor have been described and may contribute to further impairment in thyroid function.
- The result is inadequate thyroid hormone production and secretion, although, initially both preformed thyroxine (T4) and triiodothyronine (T3) may 'leak' into the circulation from damaged cells.
- The goitrous form (rather than atrophic) is associated with HLA-DR5.
- Twin studies indicate that there is about 70% genetic contribution to autoimmune thyroid disease.[3]

Epidemiology

- The true incidence of Hashimoto’s thyroiditis is unknown but is approximately the same as Graves’ disease - 0.3-1.5 cases per 1,000 population per year. It is probably underdiagnosed and its frequency seems to be increasing.
- The disease is 15-20 times as frequent in women as in men.
- It occurs especially during the decades from ages 30 to 50, but may be seen in any age group, including children.[4, 5]
- In children, the most common age at presentation is adolescence but the disease may occur at any time, rarely even in children under 1 year of age.[6]

Presentation

- The thyroid gland may enlarge rapidly:
  - Occasionally it is associated with dyspnoea or dysphagia from pressure on structures in the neck, or with mild pain and tenderness.
  - Rarely, pain is persistent and unresponsive to analgesics and requires medical therapy or surgery.
  - The goitre of Hashimoto’s thyroiditis may remain unchanged for decades but usually it gradually increases in size.
  - Occasionally the course is marked by symptoms of mild thyrotoxicosis, especially during the early phase of the disease.

- Symptoms and signs of hypothyroidism may be present when first seen, or commonly develop over a period of several years. These may include:[7]
  - Fatigue, constipation, dry skin and weight gain.
  - Cold intolerance.
  - Slowed movement and loss of energy.
  - Decreased sweating.
  - Mild nerve deafness.
  - Peripheral neuropathy.
  - Menstrual irregularities (typically menorrhagia).
  - Depression, dementia and memory loss.
  - Hair loss from an autoimmune process.

- Eventually, thyroid atrophy and myxoedema may occur.

Investigations

Hashimoto’s thyroiditis is based on clinical findings in combination with histological appearance. The thyroid gland shows diffuse lymphocytic and plasma cell infiltration with formation of lymphoid follicles from follicular hyperplasia and damage to the follicular basement membrane. Atrophy of the thyroid parenchyma is usually evident. Thyroid autoantibodies may also be seen.

- TSH levels; this is a sensitive test of thyroid function.[8] Levels are usually raised in hypothyroidism due to Hashimoto’s thyroiditis (but also in primary hypothyroidism of any cause).
- Thyroid autoantibodies - anti-thyroid peroxidase (anti-TPO) and also anti-thyroglobulin (anti-Tg) antibodies.
- Thyroid ultrasound - usually not necessary in diagnosing Hashimoto’s thyroiditis but it is useful in assessing thyroid size, echotexture and, most importantly, the presence of thyroid nodules.
Radioactive iodine uptake and scan are used to classify a nodule as hot or cold. A cold thyroid nodule would indicate a higher risk for malignancy and would need a fine-needle aspiration biopsy.

Other studies are only performed to evaluate complications of primary hypothyroidism when indicated - eg, dyslipidaemia.

**Associations**[9]

Hashimoto's thyroiditis and hypothyroidism are associated with other autoimmune conditions:

- Addison's disease.
- Diabetes mellitus.
- Hypogonadism.
- Hypoparathyroidism.
- Pernicious anaemia.
- Alopecia areata, totalis and universalis.
- Chronic active hepatitis.\[^{10}\]
- Polymyalgia rheumatica and giant cell arteritis.
- Primary biliary cirrhosis.
- Rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus.
- Systemic sclerosis (scleroderma).
- Vitiligo.\[^{11}\]

Although chronic inflammation, leading to neoplastic transformation, is a well-established clinical phenomenon, the link between Hashimoto's thyroiditis and thyroid cancer remains controversial. There have been reports of patients with Hashimoto's thyroiditis being three times more likely to have thyroid cancer.\[^{12}\]

**Management**

See also the separate article on Hypothyroidism.

**Pharmacological**

- Thyroid hormone replacement - orally administered levothyroxine sodium, usually for life.
- The dose should be titrated to the individual patient's needs. The aim is to restore a clinically and biochemically euthyroid state.
- Patients who are older than 50 years (and younger patients with cardiac disease) should be started on a low dose of 25 micrograms (0.025 mg) per day. Their clinical and biochemical state is then re-examined after 6-8 weeks.
### Surgical Indications for surgery include:

- A large goitre with obstructive symptoms - eg, dysphagia or stridor.
- Presence of a malignant nodule.
- Presence of a lymphoma diagnosed on fine-needle aspiration.
- Cosmetic reasons for unsightly, large goitres.

### Complications

- Over-replacement with thyroxine causing accelerated bone loss or increased heart rate.
- Hyperlipidaemia and consequences, if untreated.\[^{[13]}\]
- Hashimoto's encephalopathy.\[^{[14]}\]
- Myxoedema coma (due to extreme hypothyroidism). Untreated, this has a poor prognosis and a high mortality rate (around 60%).

### Prognosis

With early diagnosis and levothyroxine replacement therapy, the prognosis is excellent and patients may achieve normal thyroid levels. However, normal levels do not always equate with normal functioning.

### Further reading & references

- Hashimoto Thyroiditis; Online Mendelian Inheritance in Man (OMIM)\[^{[14]}\]
- UK Guidelines for the Use of Thyroid Function Tests; British Thyroid Association (2006).

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