Hyperthyroidism

Thyrotoxicosis

The term thyrotoxicosis is retained because hyperthyroidism, i.e. symptoms due to a raised level of circulating thyroid hormones, is not responsible for all manifestations of the disease.

Clinical types are:

- Diffuse toxic goitre (Graves' disease);
- Toxic nodular goitre;
- Toxic nodule;
- Hyperthyroidism due to rarer causes.

Diffuse toxic goitre (Graves' disease)

A. A diffuse vascular goitre appearing at the same time as the hyperthyroidism,
B. The goitre in primary thyrotoxicosis is diffuse and vascular, it may be large or small, firm or soft, and a thrill and a bruit may be present.
C. The onset is abrupt, but remissions and exacerbations are not infrequent.
D. Usually in the younger woman and frequently associated with eye signs.
E. The syndrome is that of primary thyrotoxicosis.
F. The whole of the functioning thyroid tissue is involved, and the hypertrophy and hyperplasia are due to abnormal thyroid-stimulating antibodies (TsAb).
G. . Manifestations of thyrotoxicosis not due to hyperthyroidism per Se, e.g. orbital proptosis, ophthalmoplegia and pretibial myxoedema, may occur in primary thyrotoxicosis.

Toxic nodular goitre

A. A simple nodular goitre is present for a long time before the hyperthyroidism, (The onset is insidious)
B. Usually in the middle-aged or elderly
C. Very infrequently associated with eye signs.
D. Hyperthyroidism is usually more severe than in secondary thyrotoxicosis but cardiac failure is rare.
E. The syndrome is that of secondary thyrotoxicosis.
F. In many cases of toxic nodular goitre, the nodules are inactive, and it is the internodular thyroid tissue that is overactive. However, in some toxic nodular goitres, one or more nodules are overactive and here the

hyperthyroidism is due to autonomous thyroid tissue as in a toxic adenoma.

Toxic nodule

This is a solitary overactive nodule, which may be part of a generalised nodularity or a true toxic adenoma. It is autonomous and its hypertrophy and hyperplasia are not due to TsAb. Because TSH secretion is suppressed by the high level of circulating thyroid hormones, the normal thyroid tissue surrounding the nodule is itself suppressed and inactive.

Histology in hyperthyroidism

The normal thyroid gland consists of acini lined by flattened cuboidal epithelium and filled with homogeneous colloid. In hyperthyroidism there is hyperplasia of acini, which are lined by high columnar epithelium. Many of them are empty and others contain vacuolated colloid.

Clinical features

The symptoms are:

• Tiredness;

• Emotional lability;

•Heat intolerance;

• Weight loss;

• Excessive appetite;

•Palpitations.

The signs of thyrotoxicosis are:

• Tachycardia;

• Hot, moist palms;

• Exophthalmos;

•lid lag/retraction;

•Agitation;

•Thyroid goitre and bruit.

Symptomatology

Thyrotoxicosis is eight times commoner in females than in males. It may occur at any age. The most significant symptoms are loss of weight in spite of a good appetite, a recent preference for cold, and palpitations. The most significant signs are the excitability of the patient, the presence of a goitre, exophthalmos, and tachycardia or cardiac arrhythmia.

The goitre in primary thyrotoxicosis is diffuse and vascular, it may be large or small, firm or soft, and a thrill and a bruit may be present. The onset is abrupt, but remissions and exacerbations are not infrequent. Hyperthyroidism is usually more severethan in secondary thyrotoxicosis but cardiac failure is rare. Manifestations of thyrotoxicosis not due to hyperthyroidism per Se, e.g. orbital proptosis, ophthalmoplegia and pretibial myxoedema, may occur in primary thyrotoxicosis.

In secondary thyrotoxicosis the goitre is nodular. The onset is insidious and may present with cardiac failure or atrial fibrillation. It is characteristic that the hyperthyroidism is not severe. Eye signs other than lid lag and lid spasm (due to hyperthyroidism) are very rare.

Cardiac rhythm

A fast heart rate, which persists during sleep, is characteristic. Cardiac arrhythmias are superimposed on the sinus tachycardia as the disease progresses, and they are commoner in older patients with thyrotoxicosis because of the prevalence of coincidental heart disease. Stages of development of thyrotoxic arrhythmias are:

• Multiple extrasystoles;

• Paroxysmal atrial tachycardia;

• Paroxysmal atrial fibrillation;

• Persistent atrial fibrillation, not responsive to digoxin.

Myopathy

Weakness of the proximal limb muscles is commonly found if looked for. Severe muscular weakness (thyrotoxic myopathy) resembling myasthenia gravis occurs occasionally. Recovery proceeds as hyperthyroidism is controlled.

Eye signs

Some degree of exophthalmos is common. It may be unilateral.

- ✓ True exophthalmos is a proptosis of the eye, caused by infiltration of the retrobulbar tissues with fluid and round cells,
- ✓ Retraction or spasm of the upper eyelid. (Lid spasm occurs because the levator palpebrae superioris muscle is partly innervated by sympathetic fibres.) This results in widening of the palpebral fissure so that the sclera may be seen clearly above the upper margin of the iris and cornea (above the 'limbus').Spasm and retraction usually disappear when the hyperthyroidism is controlled. They may be improved by 3-adrenergic blocking drugs, e.g. guanethidine eye drops.
- ✓ Oedema of the eyelids, conjunctival injection and chemosis are aggravated by compression of the ophthalmic veins.
- ✓ Weakness of the extraocular muscles, particularly the elevators (inferior oblique), results in diplopia. In severe cases, papilloedema and corneal ulceration occur. When severe and progressive, it is known as malignant exophthalmos and the eye may be destroyed.
- ✓ Graves' ophthalmopathy is an autoimmune disease in which there are antibody-mediated effects on the ocular muscles.
- ✓ Exophthalmos tends to improve with time. Sleeping propped up and lateral tarsorrhaphy will help to protect the eye but will not prevent progression. Hypothyroidism increases proptosis by a few millimetres and should be avoided.
- ✓ Improvement has been reported with massive doses of prednisone. Intraorbital injection of steroids is dangerous because of the venous congestion, and total thyroid ablation has not proved effective. When the eye is in danger, orbital decompression may be required (see Dysthyroid exophthalmos).
- ✓ Pretibial myxoedema is a thickening of the skin by a mucin-like deposit, nearly always associated with true exophthalmos, past or present hyperthyroidism, and high levels of TsAb.

Diagnosis of thyrotoxicosis

Most cases are readily diagnosed clinically. Difficulty is most likely to arise in the differentiation of mild hyperthyroidism from an anxiety state when a goitre is present. In these cases, the thyroid status is determined by the diagnostic tests described earlier. A TRH test is rarely indicated.

T3 thyrotoxicosis is diagnosed by estimating the free T3. It should be suspected if the clinical picture is suggestive but routine tests of thyroid function are within the normal range. A thyroid scan is essential in the diagnosis of an autonomous toxic nodule.

Thyrotoxicosis should always be considered in:

• Children with a growth spurt, behaviour problems or myopathy;

• Tachycardia or arrhythmia in the elderly;

• Unexplained diarrhoea;

• Unexplained loss of weight.

Principles of treatment of thyrotoxicosis

Antithyroid drugs

Those in common use are carbimazole and propylthiouracil. Beta-adrenergic blockers, such as propranolol and nadolol, may also be used. Iodides, once thought to reduce the vascularity of the thyroid, should only be used as immediate preoperative preparation in the 10 days before surgery. Antithyroid drugs are used to restore the patient to a euthyroid state and to maintain this for a prolonged period in the hope that a permanent remission will occur, i.e. that production of TsAb will diminish or cease. It should be noted that antithyroid drugs cannot cure a toxic nodule. The overactive thyroid tissue is autonomous and recurrence of the hyperthyroidism is certain when the drug is discontinued.

Advantages

No surgery and no use of radioactive materials.

Disadvantages

•Treatment is prolonged and the failure rate after a course of 1.5—2 years is at least 50 per cent.

•It is impossible to predict which patient is likely to go into a remission.

•Some goitres enlarge and become very vascular during treatment —even if thyroxine is given at the same time. This is probably due to TsAb stimulation during the prolonged course of treatment and not a direct effect of the drug.

•Very rarely, there is a dangerous drug reaction, e.g. agranulocytosis or aplastic anaemia. In the event of agranulocytosis, the patient should be instructed to discontinue treatment, if a sore throat develops, until the white cell count has been checked.

Initially, 10 mg of carbimazole4 is given three or four times a day, and there is a latent interval of 7—14 days before any clinical improvement is apparent. It is most important to maintain a high concentration of the drug throughout the 24 hours by spacing the doses at 8- or 6-hourly intervals. When the patient becomes euthyroid, a maintenance dose of 5 mg two or three times a day is given for another 12—18 months. Thyroxin (0.1 mg daily) is given in conjunction with anti-thyroid drugs, there is less danger of producing iatrogenic thyroid insufficiency or an increase in the size of the goitre (‘block and replacement treatment’).

Surgery

In diffuse toxic goitre and toxic nodular goitre with overactive internodular tissue, surgery cures by reducing the mass of overactive tissue. Cure is probable if the thyroid tissue can be reduced below a critical mass. This may result in a reduction of TsAb or it may be that circulating TsAb, however high its level, can only produce limited hypertrophy and hyperplasia when the mass of thyroid tissue is small. In the autonomous toxic nodule, and in toxic nodular goitre with overactive autonomous toxic nodules, surgery cures by removing all of the overactive thyroid tissue: this allows the suppressed normal tissue to function again.

Advantages

The goitre is removed, the cure is rapid and the cure rate is high if surgery has been adequate.

Disadvantages

•Recurrence of thyrotoxicosis occurs in approximately 5 per cent of cases.

•Every operation carries a morbidity but with suitable preparation and an experienced surgeon the mortality is negligible.

•Postoperative thyroid insufficiency occurs in 20—45 per cent of cases.

•Long-term follow-up is highly desirable as the few patients who develop recurrence may do so at any time in the future.

•Parathvroid insufficiency: this should he permanent in less than 0.5 per cent.

Radioiodine

Radioiodine destroys thyroid cells and, as in thyroidectomy, reduces the mass of functioning thyroid tissue to below a critical level.

Advantages

No surgery and no prolonged drug therapy.

Disadvantages

•Isotope facilities must be available.

•There is a high and progressive incidence of thyroid insufficiency which may reach 75—80 per cent after 10 years. This is due to sublethal damage to those cells not actually destroyed by the initial treatment and this eventually causes failure of cellular reproduction.

•Indefinite follow-up is essential.

The dose of radioiodine varies between 300 and 600 MBq. Response is slow, but a substantial improvement is to be expected in 8—12 weeks. Accurate dosage is difficult and, should there be no clinical improvement after 12 weeks, a further dose is given. Two or more doses are necessary in 20—3 0 per cent of cases.

Choice of therapeutic agent

Each case must be considered individually.

Guiding principles depend on:

- Type of toxic goitre;
- Age;
- The facilities available;
- Personality;
- Intelligence;
- Wishes of the individual patient;
- Business or family commitments and
- Any other coexistent medical or surgical condition.

Diffuse toxic goitre

Over 45: radioiodine. Under 45: surgery for the large goitre, antithyroid drugs for the small goitre. As mentioned above, radioiodine is being increasingly used in younger patients, particularly when their families are complete.

Large goitres are uncomfortable and remission with antithyroid drugs is less likely than in the small goitre.

Toxic nodular goitre

Surgery: Toxic nodular goitre does not respond as well or as rapidly to radioiodine or antithyroid drugs as does a diffuse toxic goitre, and the goitre itself is often large and uncomfortable and enlarges still further with antithyroid drugs.

Toxic nodule

Surgery or radioiodine. Resection is easy, certain and without morbidity. Radioiodine is a good alternative over the age of 45 because the suppressed thyroid tissue does not take up iodine and there is thus no risk of delayed thyroid insufficiency.

Hyperthyroidism due to other causes

- **Thyrotoxicosis factitia**. Hyperthyroidism may he induced by taking thyroxine, but only if the dosage exceeds the normal requirements of 0.15—0.25 mg a day.
- **Jod-Basedow thyrotoxicosis**. Large doses of iodide given to a hyperplastic endemic goitre which is iodine avid may produce temporary hyperthyroidism, and very occasionally persistent hyperthyroidism.
- **In sub acute or acute forms of autoimmune thyroiditis or of de Quervain's thyroiditis**, mild hyperthyroidism may occur in the early stages due to liberation of thyroid hormones from damaged tissue.
- **A large mass of secondary carcinoma** will rarely produce sufficient hormone to induce mild hyperthyroidism.
- **Neonatal thyrotoxicosis** occurs in babies born to hyperthyroid mothers or to euthyroid mothers who have had thyrotoxicosis. High TsAb titres are present in both mother and child because TsAb can cross the placental barrier. The hyperthyroidism gradually subsides after 3—4 weeks' time as the TsAb titres fall in the baby's serum.