Hyperthyroidism

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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)

- Appear at the same time as the hyperthyroidism,
- The appearance is abrupt
- Hyperthyroidism is usually more severe than in secondary thyrotoxicosis but cardiac failure is rare.
- Usually in the younger woman
- Frequently associated with eye signs.
- The syndrome is that of primary thyrotoxicosis.
- The whole of the functioning thyroid tissue is involved, and the hypertrophy and hyperplasia are due to abnormal thyroid-stimulating antibodies (TsAb).

Toxic nodular goitre

- A simple nodular goitre is present for a long time before the hyperthyroidism,
- Usually in the middle-aged or elderly
- Very infrequently associated with eye signs.
- The syndrome is that of secondary thyrotoxicosis.
- 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***.
- The onset is insidious and may present with cardiac failure or atrial fibrillation

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

The normal thyroid gland consists of acini lined by flattened cuboidal epithelium and filled with homogeneous colloid. In hyperthyroidism there is hyperplasia ofacini, 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.

Notes

- Thyrotoxicosis is eight times commoner in females than in males. It may occur at any age.
- 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.
- Manifestations of thyrotoxicosis not due to hyperthyroidism per Se, e.g. orbital proptosis, ophthalmoplegia and pretibial myxoedema.
- In secondary thyrotoxicosis the goitre is nodular.. 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 ,arrhythmias 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. 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
- Varying degree of 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 β-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. 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.
- **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.
- TSH,T3,T4 and thyroid autoantibodies
- 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;
- 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**, 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

1- 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.

2- 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.

3- 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 carbimazole** is given three or four times a day, and there is a latent interval of 7—14 days before any clinical improvement is apparent.

When the patient becomes euthyroid, a maintenance dose of 5 mg two or three times a day is given for another 12—18 months.

If tri-iodothyronine (20 micro gm three to four times daily) or thyroxine (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.
- 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.

There is no convincing evidence that radioiodine has been responsible for genetic damage, leukaemia, damage to the foetus if given inadvertently in early pregnancy, or carcinoma in the adult. In some clinics, radioiodine is given to almost all patients over the age of 25, i.e. when development is complete. 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—30 per cent of cases.

Choice of therapeutic agent

- Each case must be considered individually. Principles on the most satisfactory treatment for a particular toxic goitre at a particular age; these must however be modified according to the facilities available and the personality, intelligence and 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.

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.

Preoperative preparation for thyrotoxic patient

- The patient must be euthyroid at the time of surgery as proved by physical signs e.g. pulse rate and by serial estimation of thyroid function test.
- Preparation is usually done on an out patient basis and rarely hospitalization required.
- ***Carbimazole at a dose of 10 mg tid*** or qid is the drug of choice. When euthyroid state is reached, the dose is reduced to 5 mg tid continuing to the evening of surgery.
- ***Iodine*** may be given in conjuction with carbimazole during the last 10 -14 days prior to surgery to decrease the vascularity of the gland. 10 drops of lugol's iodine three times daily (8 hourly).
- ***Propranolol 40 mg tid*** is used either alone for preparation of mild cases or in conjunction with carbimazole. Propranolol as a beta blocker, it acts on the target organs. However it has no effect on the thyroid gland neither itself nor its hormonal production, thus, hormonal levels remain elevated during treatment with propranolol alone, and some days post operatively, hence it is mandatory to continue the drug (propranolol) for a few days after operation

Post operative complications following thyroidectomy

They include:

1. haemorrhage
2. respiratory obstruction
3. recurrent laryngeal nerve paralysis
4. thyroid insufficiency
5. parathyroid insufficiency
6. thyrotoxic storm (crisis)
7. wound infection
8. hypertrophic or keloid scar
9. stitch granuloma

Haemorrhage

1. ***Tension haematoma*** deep to the cervical fascia is usually due to slipping of ligature on the superior thyroid artery or occasionally from the thyroid remnant or middle thyroid vein.

It maybe necessary to open the layers of the wound not simply the skin stiches to relieve tension before taking the patient to the theater to evacuate the haematoma and secure the bleeding vessel.

1. ***Subcutaneous haematoma*** or collection of serum may form under the skin flaps and should be evacuated or aspirated in the following 72 hr.

Respiratory obstruction

- Most cases due to laryngeal oedema which is mainly due to tension haematoma. Also trauma to the larynx by the anesthetic tube and surgical manipulation are important factors, particularly if the goiter is very vascular and may cause laryngeal oedema without tension haematoma.
- Another cause is recurrent laryngeal nerve paralysis (unilateral or bilateral) especially if associated with laryngeal oedema.
- If releasing tension haematoma do not immediately relieve airway obstruction, the trachea should be intubated at once, which can be left in place for several days.
- Steroids are given to reduce oedema. Tracheostomy is rarely indicated. If so urgent, needle tracheostomy as a temporary measure using 12 G needle (diameter 2-3 mm) is highly satisfactory.

Recurrent laryngeal nerve paralysis

- This may be unilateral or bilateral, transient or permanent.
- Transient paralysis occurs in about 3% of nerves at risk and recovers in 3 weeks to 3 months. Permanent paralysis is extremely rare if the nerve is identified at operation.

Thyroid insufficiency

- This usually occurs within two years and sometimes delayed for 5 years or more. It is often insidious and difficult to recognize.
- The incidence is 20-45% after operations.

The causes of thyroid insufficiency are:

1. *Change in autoimmune response from stimulation to destruction of the thyroid cells.*
2. *There is relation ship between the estimated weight of the thyroid remnant and the development of thyroid failure after subtotal or near total thyroidectomy for grave's disease.*

- Thyroid insufficiency is rare after surgery for toxic adenoma because there is no autoimmune disease present.

Parathyroid insufficiency

It is due to:

1. removal of the parathyroid glands
2. infarction through damage to the parathyroid end artery (more important than the first cause)

The incidence should be less than 0-5% and most cases present dramatically 2-5 days post operatively and very rarely delayed presentation for 2-3 weeks.

Thyrotoxic crisis (storm)

- This is an acute exacerbation of hyperthyroidism. It occurs if a thyrotoxic patient has been inadequately prepared for thyroidectomy.
- This require administration of intravenous fluid, cooling the patient with ice packs, giving O2, diuretics for the heart failure, digoxin for uncontrolled AF, sedation and intravenous hydrocortison.
- Specific treatment is by carbimazole 10-20 mg 6 hourly, lugol's iodine 10 drops 8 hourly by mouth or sodium iodide 1 gm I.V., propranolol 40 mg 6 hourly orally will block the adverse B adrenergic effect. This agent may be given by careful I.V administration (1-2 mg) under precise ECG control.

Wound infection

Subcutaneous or deep cervical abscess should be drained.

Hypertrophic or keloid scar

It occur if the incision overly the sternum. The intradermal injection of corticosteroid should be given at once and repeated monthly if necessary.

Stitch granuloma

This may occur with or without sinus formation and is seen after the use of non absorbable suture material.

Absorbable sutures and ligatures should be used through out the thyroid surgery.

If the skin staples are used, they can be removed in less than 48 hrs because the skin closure is supported by platysma stitch.

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