



congestive heart failure, and atrial fibrillation resistant to standard therapy.

Eye signs associated with Graves disease may also occur as a nonspecific manifestation of hyperthyroidism from any cause (e.g., thyroid stare). In Graves' disease, a specific inflammatory infiltrate of the orbital tissues leads to periorbital edema, conjunctival congestion and swelling, proptosis, extraocular muscle weakness, or optic nerve damage with visual impairment (E-Fig. 63-4).

Pretibial myxedema (thyroid dermopathy) (E-Fig. 63-5) occurs in 2% to 3% of patients with Graves' disease and results in a thickening of the skin over the lower tibia without pitting. Onycholysis, characterized by separation of the fingernails from their beds, often occurs in patients with Graves' disease. Thyroid acropachy, or clubbing, may also occur.

Diagnosis

Elevated total or free T_4 or T_3 (or both) and a suppressed TSH confirm the clinical diagnosis of thyrotoxicosis. Thyroid-stimulating immunoglobulin is usually elevated, and its measurement may be useful in patients with eye signs who do not have other characteristic clinical features. Increased uptake of ^{123}I differentiates Graves' disease from early subacute or Hashimoto's thyroiditis, in which uptake is low in the presence of hyperthyroidism. Magnetic resonance imaging or ultrasonography of the orbit usually shows orbital muscle enlargement, whether or not clinical signs of ophthalmopathy are observed.

Treatment

Three treatment modalities are used to control the hyperthyroidism of Graves' disease: antithyroid drugs, radioactive iodine therapy, and surgery.

Antithyroid Drugs

The thiocarbamide drugs propylthiouracil, methimazole, and carbimazole block thyroid hormone synthesis by inhibiting thyroid peroxidase. Propylthiouracil also partially inhibits peripheral conversion of T_4 to T_3 . Medical therapy is usually administered for a prolonged period (1 to 3 years), with the dose gradually reduced until spontaneous remission occurs. One approach is to gradually decrease the dose while maintaining T_4 and T_3 in the normal range. After cessation of medication, 40% to 60% of patients remain in remission. Those who experience relapse can either resume therapy with thiocarbamide drugs or undergo definitive surgery or radioactive iodine treatment. Side effects of the thiocarbamide regimen include pruritus and rash (in about 5% of patients), elevated liver function enzymes, cholestatic jaundice, acute arthralgias, and, rarely, agranulocytosis (<0.5% of patients).

Methimazole is less toxic to the liver than propylthiouracil and has now become the preferred medical treatment for hyperthyroidism. Patients must be instructed to discontinue the medication and consult a physician if they develop fever or sore throat, because those symptoms may indicate agranulocytosis. At the onset of treatment during the acute phase of thyrotoxicosis, β -adrenergic receptor blockers are used to help alleviate tachycardia, hypertension, and atrial fibrillation. As the thyroid

hormone levels return to normal, the treatment with β -blockers is tapered.

Radioactive Iodine

In terms of cost, efficacy, ease, and short-term side effects, radioactive iodine has a better benefit profile than either surgery or antithyroid drugs; however, 80% to 90% of patients become hypothyroid after radiotherapy and require lifelong thyroid hormone replacement. ^{131}I is often the treatment of choice in adults with Graves' disease. It is contraindicated in women who are pregnant, but it does not increase the risk of birth defects in offspring conceived after ^{131}I therapy. Patients with severe thyrotoxicosis, very large glands, or underlying heart disease should be rendered euthyroid with antithyroid medication before receiving radioactive iodine, because ^{131}I treatment can cause a release of preformed thyroid hormone from the thyroid gland that could precipitate cardiac arrhythmias and exacerbate symptoms of thyrotoxicosis.

After administration of radioactive iodine, the thyroid gland shrinks; patients become euthyroid and later hypothyroid over a period of 6 weeks to 3 months. Serum free T_4 and TSH levels should be monitored, and replacement with levothyroxine should be instituted when hypothyroidism occurs. Hypothyroidism always occurs after surgical total thyroidectomy, frequently after subtotal thyroidectomy or administration of radioactive iodine, and in a smaller percentage of patients after antithyroid medication; therefore, lifelong monitoring of all patients with Graves' disease is mandated.

Surgery

Either subtotal or total thyroidectomy is the treatment of choice for patients with very large glands and obstructive symptoms, those with multinodular glands, and sometimes in those who desire pregnancy within the next year. It is essential that the surgeon be experienced in thyroid surgery. Preoperatively, patients receive 6 weeks of treatment with antithyroid drugs to ensure that they are euthyroid at the time of surgery. Two weeks before surgery, oral saturated solution of potassium iodide is administered daily to decrease the vascularity of the gland. Permanent hypoparathyroidism and recurrent laryngeal nerve palsy occur postoperatively in fewer than 2% of patients.

Graves' orbitopathy can be treated with glucocorticoids, orbital radiotherapy, or surgery. It was recently found that selenium is effective for Graves' orbitopathy.

Toxic Adenoma

Solitary toxic nodules, which are usually benign, occur more frequently in older patients. The clinical manifestations are those of thyrotoxicosis. Physical examination shows a distinct solitary nodule. Laboratory investigation shows suppressed TSH and significantly elevated T_3 levels, often with only moderately elevated T_4 . Thyroid scan shows a hot nodule in the affected lobe with partial or complete suppression of the unaffected lobe. Solitary toxic nodules are usually treated with radioactive iodine. Euthyroidism results if the unaffected lobe has suppressed uptake on a thyroid scan, and often hypothyroidism occurs if the unaffected lobe does not have suppressed uptake. For large nodules, unilateral lobectomy after the administration