SEVERE THYROTOXICOSIS IN THE ELDERLY

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Updated May 31, 2022

CLINICAL RECOGNITION

Thyrotoxicosis in the elderly may elude detection by manifesting only fatigue, weakness, and relative apathy. More commonly it presents with any of a range of symptoms including fatigue, weight loss, heat intolerance, palpitations, weakness, insomnia, irritability, confusion, and agitation. Clinical findings that may raise suspicion include tachycardia, proptosis, goitrous enlargement of the thyroid, palpable thyroid nodules, warm moist skin, brisk deep tendon reflexes, and a resting tremor. A newly detected atrial arrhythmia may be the first manifestation identified.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Endogenous thyrotoxicosis may be caused by disorders that increase thyroid hormone production in functional thyroid tissue, or by disorders associated with inflammation of the thyroid that cause leakage of preformed thyroid hormone. The distinction between these classifications helps to dictate treatment. Increased thyroid hormone production may be caused by autoimmune stimulation of the thyroid, or by the growth of autonomously functioning nodules or neoplasms. Checkpoint inhibitors that are used to treat a range of malignancies can induce a rapidly progressing form of autoimmune thyroiditis associated with transient thyrotoxicosis. In patients treated with thyroid hormone preparations, ingestion of excessive doses may lead to severe thyrotoxicosis. Rarely thyrotoxicosis is induced during therapeutic administration of interferon alpha or CAMPATH. Finally, tyrosine kinase inhibitors can also induce hyperthyroidism.

Table 1. Causes of Thyrotoxicosis in Elderly
Increased thyroid hormone production
Graves' disease
Toxic multinodular goiter
Toxic adenoma
Type 1 amiodarone-induced thyrotoxicosis
Metastatic thyroid cancer
Inflammation with leakage of thyroid hormone
Subacute thyroiditis
Autoimmune (Hashimoto's) thyroiditis
Type 2 amiodarone-induced thyrotoxicosis
Ingestion of exogenous thyroid hormone
Iatrogenic thyrotoxicosis
TSH-secreting pituitary adenoma

DIAGNOSTIC TESTS NEEDED AND SUGGESTED

Suspected thyrotoxicosis may be confirmed when lab tests reveal a suppressed TSH level in tandem with an elevated free or total T4 level. A total T3 level should also be checked, as it is often disproportionately elevated in cases of untreated Graves' disease. In patients who aren't taking amiodarone and haven't been recently exposed to iodinated contrast, a thyroid uptake study can distinguish increased production of thyroid hormone (marked by increased uptake), from inflammation with leakage of thyroid hormone (marked by decreased uptake). Thyroid scan images that reveal the distribution of increased uptake can help to distinguish Graves' disease from toxic nodular disorders. In cases that demonstrate decreased uptake, an elevated ESR or CRP may reflect subacute thyroiditis, while elevated anti-thyroid peroxidase or anti-thyroglobulin antibody levels may reflect autoimmune thyroiditis. The absence of either of these findings may raise suspicion of iatrogenic thyrotoxicosis.

A suppressed TSH level with "normal" T4 and T3 levels indicates subclinical hyperthyroidism. This problem is common in elderly individuals with multinodular goiter or "hot" nodules. Long standing subclinical hyperthyroidism is associated with atrial arrhythmias, and for this reason, if confirmed and persistent, is often treated in the same manner as overt hyperthyroidism.

THERAPY

Severe thyrotoxicosis may induce or exacerbate atrial arrhythmias, ischemia, congestive heart failure or diabetes mellitus, problems requiring urgent diagnosis and therapy. Coincident anemia should be recognized. If tolerated, and in the absence of CHF, beta blockers may help to ameliorate some symptoms in patients presenting with thyrotoxicosis. Since administration of beta-blockers to patients with severe thyrotoxicosis has rarely been associated with vascular collapse, a reduced dose may be administered initially. In cases of severe hyperthyroidism ascribed to Graves' disease, a toxic multinodular goiter, or a toxic adenoma, antithyroid drugs are usually administered as first line treatment. Methimazole is the usual agent of choice. Relatively high doses (20-40 mg daily) may be needed at the outset. Once adequate control of hyperthyroidism has been achieved, definitive therapy with radioactive iodine ablation or thyroid surgery may be considered. Patients who demonstrate an allergy or adverse side effects when taking antithyroid drugs may need to proceed directly to treatment with radioactive iodine ablation. Consideration should be given to the possibility of triggering increased thyrotoxicosis as a result of radioactive iodine treatment with adverse effects on cardiovascular disease. Pre-treatment with antithyroid drugs, repeated partial dose radioactive iodine therapy, or post-treatment with beta blockers or saturated solution of potassium iodide (at least 10 mg daily) may be considered. Thyroid surgery may be indicated in cases where substernal enlargement of a toxic multinodular goiter has caused significant compressive symptoms, and in cases with any suggestion of a thyroid malignancy. Temporizing treatment with high doses of NSAIDs or prednisone may help to relieve discomfort associated with the onset of subacute thyroiditis.

Table 2. Treatment
Beta blockers Propranolol: 10-30 mg tid-qid, or 60-120 mg ER daily Atenolol: 25-100 mg daily Metoprolol: 25-50 mg bid, or 50-100 mg ER daily
Antithyroid drugs Methimazole: 10-60 mg daily Propylthiouracil: 50-150 mg bid-tid
Radioactive iodine
Thyroid surgery
Iodide Saturated solution of potassium iodide: 1 drop bid
Antinflammatory agents Ibuprofen 400-800 mg tid Prednisone 10-40 mg daily

FOLLOW-UP

Serial profiles of thyroid function tests including TSH, free or total T4, and total T3 levels should be followed at regular 2-4 week intervals when treating and monitoring thyrotoxic disorders. In cases of treated hyperthyroidism, suppression of the TSH level may persist for several weeks after thyroid hormone levels have been brought under control. Treatment of post-ablative or post-surgical hypothyroidism with levothyroxine should be considered once T4 and T3 levels drop to low normal or subnormal ranges.

GUIDELINES

2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, Walter MA.
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