

Severe Hypothyroidism in the Elderly

Matthew Kim, MD, Assistant Professor of Medicine/Associate Physician, Brigham and Women's Hospital, Boston, MA

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CLINICAL RECOGNITION

Elderly patients with severe hypothyroidism often present with variable symptoms that may be masked or potentiated by co-morbid conditions. Characteristic symptoms may include fatigue, weight gain, cold intolerance, hoarseness, constipation, and myalgias. Neurologic symptoms may include ataxia, depression, and mental status changes ranging from mild confusion to overt dementia. Clinical findings that may raise suspicion of thyroid hormone deficiency include hypothermia, bradycardia, goitrous enlargement of the thyroid, cool dry skin, myxedema, delayed relaxation of deep tendon reflexes, a pericardial or abdominal effusion, hyponatremia, and hypercholesterolemia.

DIAGNOSIS AND DIFFERENTIAL

Autoimmune (Hashimoto's) thyroiditis with destruction of functioning tissue is the most common endogenous

cause of hypothyroidism in elderly patients. Checkpoint inhibitors that are used to treat a variety of malignancies can induce a rapidly progressing form of autoimmune thyroiditis. Unrecognized or untreated cases can progress to a state of pronounced thyroid hormone deficiency over weeks to months. Administration of radioactive iodine to treat hyperthyroidism ascribed to Graves' disease usually causes permanent hypothyroidism. Surgery performed to remove thyroid cancer or an enlarged multinodular goiter inevitably leads to overt hypothyroidism. External beam radiation used to treat lymphoid malignancies and head and neck cancer can lead to rapid or delayed development of hypothyroidism. Pituitary dysfunction that inhibits secretion of TSH may be caused by growth of a mass in the sella turcica or may develop as a complication of surgery performed to remove a tumor.

Table 1: Causes of Hypothyroidism in the Elderly**Primary hypothyroidism**

Autoimmune (Hashimoto's) thyroiditis
Amiodarone induced hypothyroidism
Lithium induced hypothyroidism
Post-ablative hypothyroidism
Post-surgical hypothyroidism
Radiation-induced hypothyroidism
Thyroiditis induced by checkpoint inhibitors, tyrosine kinase inhibitors, interferon alpha, or CAMPATH

Central hypothyroidism

Pituitary or hypothalamic dysfunction

Decreased absorption of levothyroxine

Celiac disease
Drugs: iron sulfate, bile acid resins, sucralfate, calcium

Accelerated metabolism of thyroid hormone

Increased deiodinase activity (consumptive hypothyroidism)
Drugs: phenytoin, phenobarbital, carbamazepine, rifampin

DIAGNOSTIC TESTS NEEDED AND SUGGESTED

Laboratory tests that demonstrate an elevated TSH level in tandem with a low free or total T4 level confirm a diagnosis of primary hypothyroidism. Commonly used drugs including ASA and phenytoin lower total T4 levels and may cause interference with FT4 assays. Anti-thyroid peroxidase and anti-thyroglobulin antibody levels may be checked to confirm the presence of autoimmune thyroiditis, but this usually isn't necessary as it is the presumptive diagnosis in patients who haven't been treated with other predisposing therapies. A low free or total T4 level detected in tandem with a low or inappropriately normal TSH level may raise suspicion of central hypothyroidism. This may prompt further biochemical evaluation of other pituitary hormones and anatomic imaging of the pituitary and hypothalamus. Serious illness in the elderly is often accompanied by the non-thyroidal illness (euthyroid sick) syndrome that presents with a normal or low total T4 level, a low total T3 level, and an inappropriately low or normal TSH level. Recognition of this syndrome requires exclusion of other causes of hypothyroidism or pituitary

dysfunction. Appropriate treatment of this condition is controversial. Subclinical hypothyroidism, with a normal range freeT4 level and elevated TSH level is not infrequent in elderly patients, and if due to autoimmune thyroiditis, often progresses to overt hypothyroidism.

THERAPY

Levothyroxine (T4) is the principal thyroid hormone preparation used to treat hypothyroidism. Regimens that include liothyronine (T3) have not been shown to be any more efficacious and run the risk of triggering atrial arrhythmias in susceptible individuals. Most adults require a full replacement dose of 1.6 mcg per kilogram of body weight. The major concern in elderly patients with known or suspected cardiovascular disease is to avoid exacerbating underlying conditions. In these circumstances levothyroxine should be started at a low dose of 12.5-25 mcg daily. If this dose does not provoke ischemic symptoms or an atrial arrhythmia, it can be increased in 25 mcg increment at 4-week intervals. Patients who develop hypothyroidism after treatment of hyperthyroidism can

be treated with full replacement doses from the outset. Agents that may block absorption of levothyroxine include iron sulfate, bile acid resins, sucralfate, and supplemental forms of calcium. Doses should be separated from ingestion of these agents by at least 4 hours. Higher than anticipated doses may be required in patients treated with other agents that increase metabolism of levothyroxine including phenytoin, phenobarbital, carbamazepine, and rifampin.

Appropriate treatment of subclinical hypothyroidism is open to debate. Some clinicians feel that treatment is indicated with any confirmed and unexplained elevation of TSH above normal but most clinicians do not initiate replacement therapy in elderly patients until the TSH level is > 10uU/ml on several occasions.

FOLLOW-UP

When treating primary hypothyroidism, a TSH level should be checked 6 weeks after starting a dose or 4 weeks after changing a dose of levothyroxine. Doses should be adjusted to maintain a TSH level within the reference range. Maintenance of a slightly elevated TSH level may be acceptable in cases where treatment to a full replacement dose triggers ischemic

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symptoms or atrial arrhythmias. When treating central hypothyroidism, doses should be adjusted to maintain a free T4 level in the upper half of the reference range. The TSH level is unreliable in this setting and should not be used to guide treatment.

GUIDELINES

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