Thyroid-Stimulating Hormone

TSH is a glycoprotein secreted from the thyrotroph cells of the anterior pituitary. It is composed of alpha and beta subunits. Its release is regulated by TRH (stimulatory) and somatostatin (inhibitory). In addition, it is subject to the negative feedback of thyroid hormones released from the thyroid gland.

Evaluation

Assessment of the pituitary-thyroid axis requires checking levels of TSH as well as thyroid hormones released by the thyroid gland (i.e., thyroxine [T_4] and triiodothyronine [T_3]). Dynamic testing using TRH is no longer available.

Deficiency of TSH

Definition and Epidemiology

Deficiency of TSH leads to secondary hypothyroidism: The diminished secretion of TSH from the pituitary provides inadequate stimulation to the thyroid gland for thyroid hormone release. The estimated prevalence of TSH deficiency is about 1 in 80,000 to 120,000 individuals.

Pathology

Hypopituitarism due to encroachment of a tumor on the normal pituitary can cause deficiency of one or more pituitary hormones. Radiation treatment of the pituitary gland can also cause hypopituitarism over time.

Clinical Presentation

The usual signs and symptoms of hypothyroidism are weight gain, fatigue, cold intolerance, and constipation. If the condition is caused by an underlying sellar tumor, symptoms of mass effect may also be present, depending on the size of the tumor.

Diagnosis and Differential Diagnosis

Secondary hypothyroidism is characterized by low levels of free T_4 along with low or inappropriately normal TSH. The differential diagnosis includes euthyroid sick syndrome, which is often seen in the setting of an acute illness. This syndrome does not require any intervention, and the laboratory results normalize on repeat testing after resolution of the acute illness.

Treatment and Prognosis

Management focuses on replacement of the thyroid hormones, as in primary hypothyroidism. However, measurement of free T_4, rather than TSH, is used as a guide to adjust therapy. Underlying adrenal insufficiency should always be excluded and treated before treatment of secondary hypothyroidism to avoid precipitating an adrenal crisis.

TSH-Secreting Pituitary Tumors

Definition and Epidemiology

TSH-secreting pituitary tumors are rare and are characterized by inappropriate release of TSH that is refractory to the negative feedback mechanism of the thyroid hormones released by the thyroid gland. The prevalence of TSH-secreting pituitary adenomas is 1 to 2 cases per million in the general population.

Pathology

The pathogenesis of TSH-secreting pituitary tumors is unknown.

Clinical Presentation

The most common age of presentation is in the early fifth decade, and there is no gender bias. Presenting symptoms can be the result of a mass effect of the tumor or, most commonly, there are symptoms and signs of hyperthyroidism, including weight loss, tremors, heat intolerance, and diarrhea. Diffuse goiter is observed in up to 80% of patients. Many times, these tumors are initially misdiagnosed as primary hyperthyroidism and patients are mistakenly treated with radioactive iodine. Sometimes, the TSH produced by these tumors is biologically inactive and the tumors are diagnosed as an incidental finding on imaging studies.

Diagnosis and Differential Diagnosis

The diagnosis is made in the setting of elevated or inappropriately normal TSH along with elevated levels of thyroid hormones (free and total T_4 and T_3). The differential diagnosis includes genetic resistance to thyroid hormone and euthyroid hyperthyroxinemia, which is characterized by normal TSH, high total T_4, normal free T_4, and elevated thyroxine-binding globulin levels. Imaging studies (MRI) should be done only after biochemical confirmation because of the high incidence of incidental pituitary tumors.

Treatment and Prognosis

Surgery (transsphenoidal resection) is the first-line treatment and should be performed by an experienced neurosurgeon. Radiotherapy can be used if surgery is declined or contraindicated. Medical therapy with somatostatin analogues (e.g., octreotide, lantreotide) may also be used for persistent hyperthyroidism after surgery. Most patients do well and achieve control of symptoms of thyrotoxicosis as well as reduction in tumor burden.

ADRENOCORTICOTROPIC HORMONE

ACTH is a 39-amino-acid peptide hormone that is formed from a precursor molecule, pro-opiomelanocortin (POMC) and is synthesized and secreted by corticotrophs in the anterior pituitary. It is stimulated by hypothalamic corticotropin-releasing hormone (CRH). ACTH, in turn, stimulates release of glucocorticoids and androgens from the adrenal cortex.

ACTH Deficiency

Definition and Pathology

ACTH deficiency causes secondary adrenal insufficiency leading to decreased cortisol and adrenal androgens. Aldosterone secretion from the adrenal glands is not impaired because it is maintained via the renin-angiotensin axis. ACTH deficiency can result from a large pituitary tumor impinging on the normal pituitary. Secondary or tertiary adrenal insufficiency is most commonly iatrogenic, caused by the use of steroids for other disease processes.