ADDISON’S DISEASE

Autoimmune Adrenal Insufficiency

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This articles describe primary adrenal insufficiency or Addison's disease, including its causes, symptoms, diagnosis, and treatment.

Primary Adrenal Insufficiency

Addison's disease is a condition of primary adrenal insufficiency that affects all age groups. This disease is named after the London physician, Thomas Addison who first described patients affected by this disorder in 1855. At the time, the typical Addison's disease patient had adrenal insufficiency caused by infection with Mycobacterium tuberculosis, an organism that causes tuberculosis (TB).

With the introduction of effective treatments for TB, it is now only a rare cause of Addison's disease. Today, the primary cause of Addison's disease is autoimmune destruction of the adrenal glands. Nearly 80 percent of all cases are caused by adrenal cortex autoantibodies that destroy the adrenal cortex, the adrenal gland's outer layer. The adrenal cortex produces about 50 different steroid hormones. The two most important and biologically active of these hormones are cortisol and aldosterone. In classical Addison's disease, the adrenal gland fails to produce adequate amounts of both cortisol and aldosterone.

Cortisol is essential for normal metabolism. Cortisol mobilizes nutrients so that they're available for the body's cells as needed, modifies the immune response to inflammation, stimulates the liver to release glycogen and raise blood sugar levels, and helps control the body's fluid volume. Aldosterone regulates the body's salt and water levels, which, in turn, regulate blood pressure and blood volume.

Signs and Symptoms

Common symptoms of Addison's disease include muscle weakness, apathy, fatigue, loss of appetite, weight loss, nausea, vomiting, diarrhea, abdominal pain, low blood pressure (hypotension) that worsens when standing (orthostatic hypotension), hyperpigmentation or bronzing of skin (this condition is known as melasma suprenale), diminished ability to conserve sodium and excrete water, depression, irritability, salt craving, low blood sugar (hypoglycemia), tetany (muscle spasm caused by high phosphorus levels), diminished attention span, numbness of the extremities due to excess potassium (hyperkalemia), and in complete blood counts, an elevated eosinophil count is noted. Because most androgens in the female are produced in the adrenal cortex, females with Addison's disease may have decreased genital and underarm hair.
Addisonian Crisis

In its extreme form, Addison's disease can progress to a potentially fatal condition known as an Addisonian crisis. The most common cause is stopping corticosteroid therapy without first tapering the dose. Other causes in cluded stress, infection, and other conditions that increase the body's need for cortisol. Symptoms of Addisonian crisis include brown coating on tongue and teeth due to iron released from blood cell destruction; sudden sharp leg pain, lower back or abdomen; nausea and vomiting resulting in dehydration, severe hypotension, unconsciousness, and severe hypoglycemia.

Causes

Besides autoimmunity, Addison's disease has other causes. These include interferon treatment for hepatitis C infection, metastatic cancers, which are cancers that originate in other tissues, primarily breast cancer, and spread to other organs, conditions of amyloidosis or sarcoidosis, treatment or surgery for pituitary or hypothalamic cancers, fungal infections (Histoplasmosis, Candididasis, Coccidiomycosis and others), viral infections, especially cytomegalovirus infection in patients infected with the human immunodeficiency virus (HIV), which causes AIDS, and rarely hemorrhage into the adrenal glands in patients with antiphospholipid syndrome or shock.

Addison's disease may also occur in association with other endocrine and non-endocrine autoimmune disorders in conditions involving multiple glands (autoimmune polyglandular or polyendocrine syndromes). And it may rarely be caused in congenital conditions such as adrenal leukodystrophy, a condition that only affects males, and in triple A syndrome.

Diagnosis

Over time, cortisol insufficiency causes the pituitary gland to continuously secrete the hormone ACTH in an effort to correct the problem. As a result cortisol and aldosterone levels are low and ACTH levels are high. In addition, sodium levels are low, and potassium levels are elevated. Tests of dynamic function such as the ACTH stimulation test can be used to determine if cortisol deficiency is due to a damaged adrenal gland or an impaired pituitary response. Blood tests for dynamic adrenal function are described in my article on Adrenal Insufficiency and tests used to determine if the problem is autoimmune are described in my blog on Adrenal Antibodies.

Imaging tests, usually MRI and CT scans, show diminished adrenal gland tissue in patients with Addison's disease. MRI is superior in distinguishing adrenal masses, and CT is superior in showing calcifications related to tuberculosis infection.

Tissue studies vary depending on the type of adrenal gland destruction. In autoimmune Addison's disease, the adrenal glands are characterized by infiltration of lymphocytic white blood cells. Surviving tissue shows atypical cell nuclei due to the prolonged ACTH
stimulation. In patients with adrenal destruction caused by sarcoidosis or malignancy, granulomatous lesions are seen.

**Treatment**

Patients with Addison's disease are treated with synthetic cortisol preparations, such as cortisone (Cortone) or hydrocortisone (Hydrocortone, Cortef) and synthetic preparations of Fludrocortisone (Florinef) in patients with reduced aldosterone levels. Dexamethasone (Decadron, Baldex, and Dexone) may also be used for patients with adrenocorticol deficiency in patients with hypersensitivity to cortisone or who have viral, fungal or tubercular skin infections. Correct dosing of cortisol is accomplished by monitoring urine cortisol levels, and mineral status due to low aldosterone is measured with serum potassium levels and plasma rennin concentrations. Treatment may need to be adjusted during times of stress or infection.

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