Addison´s Disease

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Addison's disease is a chronic metabolic disorder of the adrenal gland that occurs from an insufficient production of steroid hormones with manifestations of symptomatic adrenocortical insufficiencies. Addison's disease or primary adrenal insufficiency is thought to occur from a combination of environmental, immunological, and genetics factors, which is distinguish from secondary adrenal insufficiency that is mostly associated with the chronic administration of steroids.

Pathophysiology

Causes of adrenal insufficiency resulting in Addison's disease may stem from adrenal dysgenesis, impaired steroidogenesis, or from a destruction of the gland from internal processes such as an autoimmune reaction. Autoimmune Addison's disease results from an autoreactivity towards the adrenal cortex involving 21-hydroxylase autoantibodies and autoreactive T cells (https://en.wikipedia.org/wiki/Reactive_lymphocyte). A defect in the immune surveillance mechanism causes a deficiency of immune suppressor cells. This deficiency results in a proliferation of immunocytes that are directed against specific antigens within the adrenocortical cells, which leads to a progressive destruction of the gland. However, other causes may include: • Infections such as tuberculosis, human immunodeficiency virus (HIV), or fungal infections • Tumors such as amyliodosis and [1] (https://en.wikipedia.org/wiki/Metastasis%7Cmetastatic) carcinoma (https://en.wikipedia.org/wiki/Carcinoma) • Adrenal hemorrhage, or blood loss • Use of anticoagulants (blood thinners) • Rare X-linked adrenal deficiencies that may cause adrenoleucodystrophy and adrenomyeloneuropathy. Other autoimmune diseases such as Graves' disease, pernicious anemia, type I diabetes, and myasthenia gravis are risk factors for developing Addison's disease

Addison's disease

Genetics

Addison's disease is a rare autoimmune condition that comprises a complex interplay of genetic and environmental factors, resulting in a deficiency of the adrenal cortex hormones that necessitates a lifetime of hormonal replacement therapy. The strongest reported genetic association of autoimmune Addison's disease (AAD) is linked to the class II HLA alleles of the major histocompatibility complex (MHC) involving the HLA-DRB1, DR3-DQ2 and DR4-DQ8 haplotypes. Weaker associations involve the class I region of the MHC, which includes the HLA-B alleles. Other associated loci include the cytotoxic T lymphocyte antigen 4 (CTLA-4), protein tyrosine phosphatase non-receptor type 22 (PTPN22), NALP1, CYP27B1, CIITA, CD226, and PD-L1, and most recently the C-lectin type gene (CLEC16A). Other mutations involve the SF1, DAX, ACTHR, GPX1, NNT, scavenger receptor B1, and mitochondrial mutations; along with x-linked adrenoleucodystrophy and adrenomyeloneuropathy.

Epidemiology

Autoimmune destruction of the adrenal cortex is the most common cause of Addison's disease in the United States, while tuberculosis remains the leading cause of Addison's disease in developing countries. Addison's disease may appear at any age, however, the disease most often occurs in young and middle aged adults between 30 and 60 years old. Autoimmune Addison's disease is more commonly manifested in women as compared to men. There is no reported gender difference in individuals younger than 30 years old. The prevalence rate (https://en.wikipedia.org/wiki/Prevalence_rate) of primary adrenal insufficiency is reported as 93-140 per million, with a reported incidence rate of 4.7- 6.2 per million among Caucasians.

Disease described

Addison's disease is also known as primary adrenal insufficiency that may not manifest until about 90% of the gland is destroyed. These manifestations are primarily associated with mineralocorticoid and glucocorticoid deficiency, along with hyperpigmentation that results from elevated adrenocorticotrophic hormone (ACTH) levels.

Sign and Symptoms

Symptoms of Addison's disease are directly related to hypocortisolism, and hypoaldosteronism. They include:

- Fever
- Weakness
- Fatigue
- Poor tolerance for stress
- Hypoglycemia
- Skin changes such as hyperpigmentation and vitiligo
- Anorexia
- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Weight loss
- Hypotension which may lead to vascular collapse and shock
- Loss of axillary and pubic hair in women
- Disturbances in mood and motivation

Diagnosis

Diagnosis of Addison's disease involves identifying a suspected adrenal failure, which is followed by a determination as to whether this failure is a result of an adrenal insufficiency. Measures include:

- Obtaining a thorough history and physical
- Biochemical testing involving
- Serum and urine levels of cortisol and ACTH
- Serum levels of electrolytes
- Sodium
- Potassium
- Glucose
- Serum levels of lymphocyte and eosinophil counts
- Serum aldosterone and dehydroepiandrosterone sulphate (DHEA-S) levels
- CT imaging
- Abdominal X- ray
- A Synacthen (tetracosactide) test

Treatment

The treatment of Addison's disease is contingent on the clinical presentation of the suspected patient. A patient that is not well should receive prompt administration of parenteral steroids and intravenous saline, with concomitant biochemical and diagnostic testing. Long term treatment involves the administration of glucocorticoid and mineralocorticoid therapy that is lifelong. Diet modification is also implicated, along with identifying and correcting any underlying disorders.

Links

- Endocrine Society: https://www.endocrine.org/search?q=addisons
- National Institutes of Health: http://search.nih.gov/search?utf8=%E2%9C%93&affiliate=nih&query=addisons&commit.x=0&commit.y=0

Related Articles

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