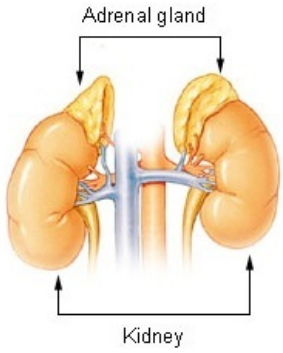
Adrenal crisis

Adrenal crisis (Addisonian, saline) is a state of acute insufficiency of the adrenal cortex. It can manifest itself from the beginning, or it can appear at any time during the course of chronic insufficiency. It is a very treacherous condition that can quickly endanger the life of the patient (especially children). If the cause of the deficit is damage to the adrenal glands, we speak of primary adrenal insufficiency (Addison's disease), in case of ACTH or CRH (*corticotropin releasing hormone*) deficiency, we speak of secondary insufficiency.

Etiology



adrenal glands

Congenital

- **Congenital hypopituitarism**',
- **enzyme defects** in the biosynthesis of cortisol and aldosterone*: congenital adrenal hyperplasia/hypoplasia (CAH)*,
- **metabolic causes**: adrenoleukodystrophy, M. Wolmann (= acid lipase deficiency), hereditary resistance to ACTH.

Obtained

- Autoimmune adrenalitis, autoimmune polyglandular syndromes;
- infection: tuberculosis, histoplasmosis, AIDS, sepsis;
- amyloidosis;
- sarcoidosis;
- radiation;
- Waterhouse-Friderichsen syndrome (most often in meningococcal sepsis);
- birth trauma in a newborn;
- **damage to the hypothalamus and pituitary gland**': tumors, injuries, infections, bleeding, autoimmunity, radiation;
- **iatrogenic** - sudden discontinuation of corticoid therapy.

Pathogenesis

Chronic adrenal insufficiency occurs when more than 90% of adrenal function is damaged. In primary chronic adrenal insufficiency, low plasma cortisol levels stimulate the synthesis of CRH and thus ACTH and MSH (melanocyte-stimulating hormone). The diagnosis is confirmed by the finding of a low cortisol level together with a high serum ACTH level and an insufficient response of cortisol secretion in the intravenous ACTH stimulation test (Synacthen test). Confirmation of an autoimmune mechanism damaging the adrenal glands is based on the finding of circulating anti-adrenal autoantibodies. Autopsies show lymphatic infiltration of the adrenal cortex - adrenalitis. Some patients with autoimmune adrenalitis also have increased titers of autoantibodies against other affected organs as part of the autoimmune polyglandular syndrome.

Chronic insufficiency of the adrenal cortex (adrenal cortex atrophy) can be the result of insufficient trophic stimulation due to insufficient production of CRH in the hypothalamus and/or ACTH in the pituitary gland when the hypothalamo-pituitary system is damaged. Chronic suppression of cells producing CRH in the hypothalamus and ACTH in the pituitary gland can also be caused by long-term administration of corticoids.

Within congenital adrenal insufficiency, we distinguish different forms of CAH syndrome. The most common type – 21-hydroxylase deficiency has two subtypes: the *salt wasting* form (75% of cases), where we find a salt crisis, and the so-called *simple virilizing* form (25% of cases), where we only find varying degrees [[virilization]] without salt disorder.

Clinic

Symptoms of '*acute and chronic insufficiency* are:

- anorexia,
- hunger for salt,
- nausea and vomiting,
- apathy,
- weakness and fatigue,
- dehydration,
- hypotension,
- tachycardia.

Symptoms of **chronic insufficiency** are:

- weight loss,
- diarrhea,

- loss of pubic and axillary hair,
- hyperpigmentation,
- low voltage EKG waveform and small heart on chest x-ray.

An excess of MSH is manifested by hyperpigmentation, mostly on the skin exposed to the sun and on the flexor sides of the knees, elbows and also on the mucous membranes (graphite spots).

It is important for practice that in the context of hypopituitarism with simultaneous hypothyroidism, the metabolism and degradation of cortisol is reduced, and therefore its level in the serum can be normal even with ACTH deficiency. The treatment of hypothyroidism itself will adjust the metabolism of cortisol to normal, its level in the serum will decrease and the adrenal insufficiency will be "unmasked"! It is therefore always necessary to start replacement therapy with hormones of the adrenal cortex in such cases.

Adrenal crisis occurs frequently in children with undiagnosed chronic insufficiency during stressful situations such as trauma, surgery, and more serious infections. The main clinical symptoms of an impending crisis are abdominal pain, fever, nausea and vomiting, weakness, altered mental status, hypotension, hyperkalemia, hypoglycemia with convulsions. '*Unrecognized and untreated, the condition leads to death from circulatory failure or hypoglycemic coma*.

In newborns after a traumatic birth, massive bleeding into the adrenal glands can occur. The hematoma can be palpable ("abdominal mass"), the diagnosis is confirmed by sonography or MRI. Massive adrenal hemorrhage often accompanies sepsis, especially meningococcal (Waterhouse-Friderichsen syndrome), but it can also be caused by other gram-positive microbes.

Acute adrenal crisis can occur in newborns after the 5th day of life, but most often between the 2nd and 4th week of life in congenital adrenal hyperplasia with a concomitant salt disorder (*salt wasting* type). In girls, the diagnosis can be indicated by *malformation of the external genitalia* detected immediately after birth, in boys the genitalia are without major changes. Similarly, a salt crisis also occurs in rare congenital adrenal hypoplasia. A risk to a newborn's life is prevented by the established screening for CAH in the Czech Republic.

Treatment with glucocorticoids

In the treatment of glucocorticoids in doses exceeding replacement doses for longer than 4 weeks, there is already a possibility of insufficiency of the adrenal cortex. Recovery of adrenal cortex function after long-term glucocorticoid treatment requires a longer time. For a period of 6-12 months after discontinuation of this therapy, a reduced secretory reserve must be expected. During this time, it is necessary to cover a two- to three-fold increase in the physiological need by replacing glucocorticoids with surgical interventions and febrile conditions. Adrenal crisis symptoms when long-term treatment with corticoids administered in high doses is discontinued too quickly may occur even in situations of supraphysiological residual doses. Long-term therapy with high-dose glucocorticoids reduces the number and sensitivity of glucocorticoid receptors ("down regulation").

Diagnostics

In the serum we find hyperkalemia, hyponatremia, hypochloremia, hypoglycemia and metabolic acidosis. Patients with a secondary form of insufficiency, i.e. ACTH or CRH deficiency, have preserved mineralocorticoid activity and normal ECT volume. Mild hyponatremia here arises from the retention of free water during the overproduction of ADH, which is a consequence of glucocorticoid deficiency.

We establish a definitive diagnosis based on serum cortisol levels and an ACTH stimulation test: if in children under stressful conditions the serum cortisol level is **less than 550 nmol/l**, it indicates adrenal insufficiency. In critically ill patients, however, it is imperative to perform an ACTH test - Synacthen test. Examination of ACTH at the beginning of the test differentiates primary from secondary forms of adrenal insufficiency.

Sonography or MRI will anatomically show the adrenal glands, if a central cause is suspected, MRI of the CNS is the imaging method of choice. If CAH is suspected, blood must be taken for a more detailed later hormonal analysis (most often detection of 21-hydroxylase deficiency) before starting hormonal treatment. A suitable screening for CAH is the determination of 17-α-hydroxyprogesterone in the serum (we find elevated levels in CAH).

Salt Crisis Therapy

Volume expansion

We administer full solutions (1/1), due to initial volume depletion. Initially, in boluses of 20 ml/kg over 10–20 minutes i.v., we calculate the total need for fluids at about 150–200% of the normal daily requirement. Solutions containing potassium can only be administered after the serum potassium level has been verified (hyperkalemia must be assumed!).

Hydrocortisone

Initially, we administer a bolus of 25–100 mg of hydrocortisone i.v. (which also has weak mineralocorticoid activity), followed by a continuous infusion of 0.8–1 mg/kg/hour. If the diagnosis of adrenal insufficiency is not certain, we can use dexamethasone in a dose of 0.1–0.2 mg/kg (maximum 1 mg for a dose of 12 hours), because it does not

interfere with the determination of cortisol by the immunochemical method. High doses of hydrocortisone should only be given until a stable condition is achieved. Over the course of a few days, we gradually switch to replacement administration at an approximate dose of 10-20 mg/m^2/day divided into 3 daily doses. After. we clearly prefer the hydrocortisone form to the p.o. in the form of dexamethasone, because hydrocortisone does not lead to growth retardation, while dexamethasone does, even in replacement doses. Mineralocorticoid substitution is ensured by the administration of fludrocortisone orally (i.e. also after stabilization of the condition) in a dose for older children of 0.1–0.2 mg/day.

In stressful situations (fever, infection, surgery, trauma) it is necessary to increase the replacement doses, at least 2-3 times. If it is not possible p.o. reception, we give substitution i.v.

Hypoglycemia

Accompanying hypoglycemia is a common finding in children with adrenal crisis. Hypoglycemia itself can be the cause of death. Its treatment does not differ from the standard recommendation for the treatment of hypoglycemia.

Links

Related Articles

- Glucocorticoids
- Mineralocorticoids
- Adrenogenital syndrome

Resources

- HAVRÁNEK, Jiří: *Adrenal crisis*.