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CUSHING'S DISEASE, COURSE AND PROGNOSIS OF THE DISEASE

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Abstract
Cushing's disease is a neuroendocrine disorder caused by hyperproduction of adrenocorticotropic hormone (ACTH) of pituitary genesis, which leads to secondary hyperplasia of the adrenal cortex and excessive secretion of cortisol. This article discusses the etiology and pathogenesis of the disease, differentiation of Cushing's disease from Cushing's syndrome , the main clinical manifestations, methods of laboratory and instrumental diagnostics. The article is intended for endocrinologists, neurologists, surgeons, as well as specialists in the field of internal medicine and general practice.

Keywords: Cushing 's disease, hypercorticism, ACTH, cortisol, pituitary gland, pituitary adenoma, adrenal glands, adrenal cortex hyperplasia.

Introduction

Cushing's disease is a neuroendocrine disorder caused by hyperproduction of adrenocorticotropic hormone (ACTH) of pituitary origin, which leads to secondary hyperplasia of the adrenal cortex and excessive synthesis of cortisol. Unlike Cushing's disease, Cushing's syndrome includes a set of pathological conditions characterized by chronic hypercorticism, regardless of its etiological origin (pituitary, adrenal or iatrogenic genesis).

Historical Background

The first clinical description of this nosology was presented by the American neurosurgeon Harvey Cushing in 1912, when he linked excessive secretion of cortisol with hyperproduction of ACTH by adenomatous changes in the pituitary gland. Subsequently, the clinical and pathophysiological aspects of the disease were clarified, which made it possible to differentiate Cushing's disease as a pituitary-dependent variant of hypercorticism from other forms of Cushing's syndrome.

Etiology and pathogenesis. Differentiation of Cushing's disease and Cushing's syndrome

- Cushing's disease is caused by hypersecretion of ACTH of pituitary etiology (usually due to pituitary corticotropin), which induces hyperplasia of the adrenal cortex and hyperproduction of cortisol.
- Cushing's syndrome includes all forms of hypercortisolism, including:
  - ACTH-dependent hypercorticism (Cushing’s disease, ectopic production of ACTH or corticoliberin).
  - ACTH-independent hypercorticism (adrenal adenomas, carcinomas, primary macronodular hyperplasia).

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- Iatrogenic hypercorticism resulting from long-term exogenous glucocorticosteroid therapy.

Pathogenetic Mechanisms

- ACTH-dependent hypercorticism (Cushing's disease) is formed as a result of hypersecretion of ACTH by the pituitary gland, which leads to hypertrophy and hyperplasia of the adrenal cortex with subsequent hyperproduction of cortisol.
- Ectopic ACTH syndrome is characterized by the secretion of ACTH outside the pituitary gland (for example, in neuroendocrine tumors of the lungs, thymus).
- ACTH-independent hypercorticism is caused by autonomous hyperfunction of the adrenal tissue.

Clinical Picture

Main Symptoms

- Metabolic disorders : hyperglycemia, steroid diabetes mellitus, insulin resistance .
- Dyslipidemia : abdominal obesity, fat deposition in the face (“moon face”), supraclavicular and cervical areas (“fat hump”).
- Skin changes : thinning of the dermis, purple striae , increased vascular fragility, tendency to hematomas.
- Muscle and bone changes : proximal myopathy, osteoporosis, spontaneous fractures.
- Cardiovascular disorders : arterial hypertension, increased risk of cardiovascular events.
- Neuropsychiatric disorders : depression, cognitive impairment, psychosis.
- Reproductive dysfunctions : oligomenorrhea , amenorrhea in women, hypogonadism in men.

Peculiarities of symptoms depending on age

- In children - growth retardation, obesity without elongation of limbs, premature sexual development.
- In adults – systemic metabolic disorders, cardiometabolic complications.
- In the elderly - pronounced osteoporosis, sarcopenia , high risk of fractures.

Diagnostics. Laboratory methods

- Daily excretion of free cortisol in urine (increased level).
- Dexamethasone test (low-dose and high-dose) to assess cortisol suppression .
- Determination of cortisol in saliva (nighttime cortisol levels are elevated).
- Determination of ACTH concentration (allows to differentiate between ACTH-dependent and ACTH-independent forms).

Instrumental Methods

- MRI of the pituitary gland – detection of pituitary microadenoma (up to 6 mm) or macroadenoma .
- CT scan of the adrenal glands – detection of adenomatous or tumor formations.
- PET-CT with ^18F-fluorodeoxyglucose – diagnostics of ectopic ACTH production.

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Treatment. Pharmacotherapy

- Steroidogenesis inhibitors (metyrapone , ketoconazole , mitotane).
- Drugs that reduce ACTH secretion (pasireotide).
- Symptomatic therapy (antihypertensive drugs, correction of diabetes mellitus).

Surgical Treatment

- Transsphenoidal Adenomectomy is the treatment of choice for Cushing's disease .
- Adrenalectomy is indicated for ACTH-independent hypercorticism .

Radiation therapy. Used in cases of recurrent or inoperable Cushing's disease .

Prognosis and complications. Complications if left untreated

- Cardiovascular complications (coronary heart disease, myocardial infarction).
- Osteoporosis and pathological fractures.
- Decompensated diabetes mellitus.
- High mortality rate in malignant cases of the disease.

Prognosis After Treatment

- If the surgical intervention is successful, the outcome is favorable.
- In cases of resistant hypercortisolism, lifelong cortisol control is possible.

Prevention

Cushing's Syndrome

- Minimization of glucocorticosteroid dosages , their gradual withdrawal.
- Monitoring pituitary-adrenal axis function in patients receiving long-term steroid therapy.

Recommendations for patients at risk of hypercortisolism

- Regular monitoring of cortisol and ACTH levels.
- Maintaining normal weight, reducing metabolic risks.
- Monitoring blood pressure and glycemia.

Conclusions

Thus, Cushing's disease and syndrome require a comprehensive approach to diagnosis, treatment and long-term monitoring. **Disease Cushing's disease** is a severe neuroendocrine disorder caused by hyperproduction of adrenocorticotropic hormone (ACTH) of pituitary origin, which leads to secondary hyperplasia of the adrenal cortex and excessive secretion of cortisol. **Clinical manifestations of Cushing's disease** include carbohydrate and lipid metabolism disorders, arterial hypertension, osteoporosis, muscle weakness, skin changes, psychoemotional disorders, which significantly worsens the quality of life of patients and increases the risk of cardiovascular catastrophes. **Diagnostics disease** is based on laboratory tests to detect hypercorticism (determination of cortisol in daily urine, night cortisol in saliva, dexamethasone test), as well as instrumental visualization methods (MRI of the pituitary gland, CT of the adrenal glands). **The main by method treatment** is surgical removal of the pituitary adenoma (transsphenoidal adenomectomy), which in most cases leads to remission of the disease. In cases where surgery is

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not possible, pharmacotherapy (steroidogenesis inhibitors, ACTH antagonists), radiation therapy or bilateral adrenalectomy are used. **Untimely treatment or The absence of therapy** leads to the progression of hypercorticism and the development of serious complications such as diabetes, osteoporosis, hypertension, cardiovascular diseases, which significantly reduces the duration and quality of life of patients.

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