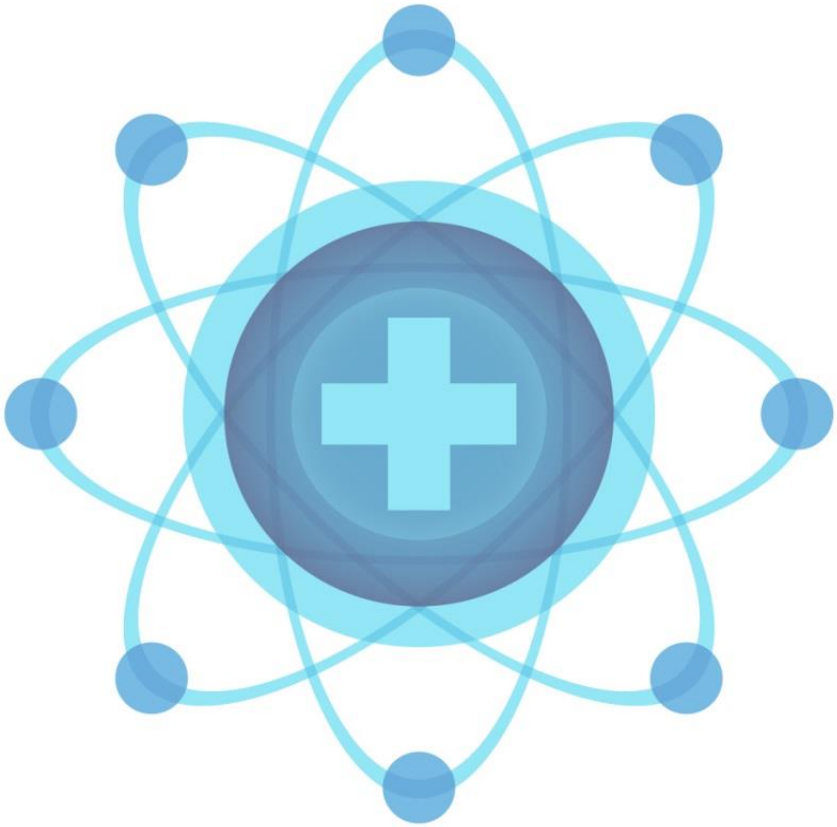

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Carbon metal disorders in cushing syndrome

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Abstract: The article analyzes the specificity of carbohydrate metabolism in Cushing's syndrome from a scientific point of view. Thus, the article draws conclusions about carbohydrate metabolism in Cushing's syndrome.

Keywords: Cushing's syndrome, steroid diabetes mellitus, hyperglycemia, carbohydrate metabolism, hypercortisolism.

The relevance of studying carbohydrate metabolism in patients with Itsenko-Cushing's disease is explained by the frequent occurrence of glucose metabolism disorders, on the one hand, and difficulties in the selection of antihyperglycemic therapy in these categories of patients, on the other. The effectiveness of the treatment of hyperglycemia in such patients may be reduced due to the difficulty of achieving remission / cure of the underlying disease, as well as due to the use of specific therapy that promotes the development of hyperglycemia. Recently, there has been growing interest in studies aimed at studying the role of the incretin system in the pathogenesis of secondary hyperglycemia associated with neuroendocrine diseases[1]. 1

Itsenko-Cushing's disease (BIK) is a severely symptomatic disease of hypothalamic-pituitary genesis, occurring with a clinical picture of hypercortisolism, caused by the presence of a pituitary tumor (85%) or pituitary hyperplasia and characterized by increased secretion of adrenocorticotropic hormone (ACTH) and an increase in adrenocorticotropic hormone (ACTH).

Epidemiology

This is the most common cause of endogenous Itsenko-Cushing syndrome (about 68%). The disease is more common in women than in men. Women are more likely to get sick between the ages of 20 and 40, there is an addiction to pregnancy and childbirth, as well as from brain injuries and neuroinfections (in particular, herpes infection). In adolescents, the disease often begins during puberty [2].

In childhood and old age, Itsenko-Cushing's disease is rarely diagnosed.

Classification

There are several degrees of severity of NIK:

- mild form (moderately severe symptoms of the disease);
- moderate form (pronounced symptoms in the absence of complications);
- severe form (severe symptoms in combination with complications, including cardiopulmonary failure, steroid diabetes,

progressive myopathy, pathological fractures, severe mental disorders).

ticism is distinguished by a rapidly progressive (3-6 months) and torpid course of the disease (> one year). There are four main reasons for the state of excess glucocorticoids of any origin:

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1. Exogenous glucocorticoids. Cushing's syndrome develops over time in patients who receive glucocorticoids for inflammatory or autoimmune diseases (including bronchial asthma, rheumatoid arthritis, systemic lupus erythematosus, skin diseases).
2. Pituitary Cushing's syndrome. This pathology, called Itsenko-Cushing's disease, develops with benign pituitary adenomas, which secrete excess ACTH.
3. Ectopic ACTH products. Of the two variants of ectopic production, ACTH of the first type is caused by malignant tumors, most often of the lungs. Patients have clear signs
metastatic tumor: weight loss, hypertension, hypokalemia, and hyperpigmentation. The second variety is due to slowly growing
tumors referred to as carcinoids. Patients with ACTH-producing carcinoid tumors may have the same clinical symptoms.
phenomena and biochemical shifts, as well as patients with pituitary disease Itsenko-Cushing. Thus, the differential diagnosis between a pituitary tumor and a carcinoid tumor in a patient with Cushing's syndrome is difficult [3]

4. Adrenal causes of Cushing's syndrome. Both benign and malignant adrenal tumors can produce excess glucocorticoids and be accompanied by Cushing's syndrome. Benign adrenal adenomas are clinically similar to other varieties of this syndrome; hirsutism, however, is absent, as the tumor only secretes cocortisol and not androgens. Malignant adrenal carcinomas with manifestations of Cushing's syndrome are usually large tumors in the abdominal cavity and have poor

forecast [4].

Etiology and pathogenesis

The reason for the BIK has not been precisely established. Most of the patients are diagnosed with a pituitary adenoma, which, according to modern concepts, is the cause of the disease. In recent years, using the methods of molecular biology, the pathogenesis of pituitary adenomas, and corticotropin in particular, has been clarified. It has been shown that most of these adenomas are monoclonal, as evidenced by the presence of the same gene mutations in adenoma cells. A potential mechanism for the development of corticotropin may be spontaneous mutation of the receptors of the corticotropin-releasing hormone (CRH) or vasopressin genes. In the absence of obvious signs of a pituitary adenoma, we can talk about damage or dysfunction of higher structures, for example, the limbic region [5].

Clinical signs and symptoms

Cortisol and other glucocorticoids have multifaceted effects as physiological regulators. They increase glucose production, inhibit protein synthesis and increase protein breakdown, stimulate lipolysis and affect immunological and inflammatory processes. Glucocorticoids contribute to the maintenance of blood pressure and largely determine the body's response to stress.

The production of cortisol by the adrenal glands is stimulated by ACTH. The secretion of ACTH, in turn, depends on the CRH produced in the hypothalamus

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and vasopressin. Cortisol, acting on the pituitary gland, hypothalamus, suppresses the production of ACTH and CRH. In normal (non-stress) conditions, the products of cor-

tizole is carried out in accordance with certain biological rhythms: with a higher activity in the morning and a lower activity late in the morning.

black. Under stressful conditions, the secretion of CRH, ACTH and cortisol increases, and biological rhythms are disrupted. Since cortisol levels can vary widely throughout the day and increase in a certain way under stress, it can be difficult to distinguish between normal and impaired secretion of this hormone.Many biochemical tests are used to diagnose pathological hypercortisolemia, but

none of them is absolutely reliable. Therefore, the examination of a patient with suspected NIK is often difficult and can give conflicting results [6].

The clinical picture of NIK is caused by excessive secretion of corticosteroids, and primarily corticosteroids. Characterized by the defeat of almost all organs and systems with the development of a symptom complex inherent in hypercortisolism [7].

Dysplastic obesity (the earliest and most common symptom). Characterized by the redistribution of subcutaneous adipose tissue (cushingoid type of obesity) with the deposition of fat in the shoulder girdle, supraclavicular spaces, above the cervical vertebrae ("climacteric hump") and on the abdomen with relatively thin limbs. The face becomes round (moon-shaped), the cheeks become purple-red (matronism) [8].

Trophic changes in the skin. The skin is thinned, dry, with a tendency to hyperkeratosis, purple-cyanotic color. Stretch stripes (striae) of red-violet color appear on the hips, chest, shoulders, abdomen, due to increased protein catabolism and thinning of the skin. Characterized by the formation of hematomas of minor injuries due to increased fragility of capillaries and thinning of the skin, hyperpigmentation of the skin in places of friction (neck, elbow joints, armpits) due to increased secretion of ACTH. Often women have hirsutism (mustache, beard, sideburns), breast hypertrichosis.

Secondary hypogonadism (early symptom). In women, the menstrual cycle is disrupted in the form of opsomenorrhea and amenorrhea, which leads to primary or secondary infertility. In men, potency decreases and gynecomastia often develops. At puberty, boys have underdevelopment of the testicles and penis, and girls have underdevelopment of the mammary glands and primary amenorrhea. These changes are accompanied by a decrease in plasma gonadotropins, testosterone and estrogens [9].

Arterial hypertension (AH). Develops in the majority of patients. Subsequently, violations of myocardial metabolism and the appearance of symptoms are possible.

ptomes of heart failure. Signs of left ventricular hypertrophy can often be seen on electrocardiography (ECG).

Myopathy. Muscle hypotrophy affecting the striated and muscular systems, benno of the upper and lower extremities (thinning of the arms and legs), atrophy of the muscles of the anterior abdominal wall with an increase in the abdomen [10].

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Disorders of carbohydrate metabolism. Manifested by impaired glucose tolerance (in 70-80% of patients) or type 2 diabetes mellitus (DM). Diabetes mellitus is characterized by hyperinsulinemia, insulin resistance, lack of tendency to ketoacidosis, and a favorable course (usually, to compensate for carbohydrate metabolism, it is sufficient to prescribe a diet and oral hypoglycemic drugs) [11].

Secondary immunodeficiency. Manifested by pustular (acne) or fungal lesions of the skin and nail plates, trophic ulcers

shins, a long period of healing of postoperative wounds, chronic pyelonephritis. Characteristic is the inhibition of all links of cellular immunity (a decrease in the number of T and B lymphocytes), a decrease in the activity of phagocytes and a decrease in humoral immunity. Vegetative changes

nervous system are pronounced and diverse, they form the syndrome of vegetative dystonia, which manifests itself in emotional and personal

shifts - from mood and sleep disorders to severe psychosis [12].

Changes in the skeletal system. In children and adolescents, early symptoms of hypercortisolism are growth retardation or complete cessation, as well as a delay in skeletal differentiation; there is a difference between passport and bone age of 1–5 years. Steroid osteoporosis with bone demineralization and suppression of protein matrix synthesis at any age is one of the most severe manifestations of hypercortisolism. The severity of the process depends on the degree and duration of hypercortisolism. Frequent symptoms of osteoporosis are pain in the spine, often a decrease in the height of the vertebral bodies and spontaneous fractures of the ribs and vertebrae.

Disorders of carbohydrate metabolism are a frequent symptom of Itsenko-Cushing's disease Patients with this pathology may experience en-

precrinologists, family doctors diagnosed with type 2 diabetes, hypertension, dyslipidemia, osteoporosis. At the same time, the secondary genesis of the clinical symptoms of the disease often remains unrecognized for a long time, which contributes to the progression of the disease and the development of complications. A cohort of patients with Itsenko-Cushing's disease has a high risk of atherosclerotic cardiovascular disease, which can continue despite remission of the disease and normalization of cortisol levels [13].

We have presented the patient's case history, which was observed by primary care specialists for type 2 diabetes and hypertension. A thorough examination of the patient, in which attention was drawn to the rapid weight gain, dysplastic structure, matronism, made it possible to suspect the secondary nature of the disorders and establish the correct diagnosis of Itsenko-Cushing's disease. The performed surgical treatment made it possible to eliminate the clinical manifestations of hypercortisolism, namely, secondary diabetes mellitus, dysplastic obesity, hypertension. We draw the attention of various specialists to the problem of hypercortisolism and the possibility of developing atypical, erased forms of this pathology, without characteristic skin symptoms of the disease. Endogenous hypercortisolism, in our opinion, should be inappropriate in patients control of

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diabetes in combination with hypertension, dysplastic obesity or rapid weight gain. Such patients require a comprehensive endocrinological examination, including a study of cortisol, a small dexamethasone test, an assessment of the content of thyroid-stimulating hormone, lipid profile, as well as the state of bone tissue [14].

Steroid diabetes mellitus is an endocrine pathology that develops as a result of a high content of adrenal cortex hormones in the blood plasma and a violation of carbohydrate metabolism. It is manifested by symptoms of hyperglycemia: rapid fatigue, increased thirst, increased profuse urination, dehydration, increased appetite. Specific diagnosis is based on laboratory detection of hyperglycemia, assessment of the level of steroids and their metabolites (urine, blood). Treatment for steroidal diabetes includes withdrawal or reduction of glucocorticoid dosage, surgery to reduce the production of corticosteroid hormones, and antidiabetic therapy.

Steroid diabetes mellitus (SD) can be triggered by a prolonged increase in the secretion of corticosteroids or by taking them in the form of drugs. In the second case, the disease has a synonymous name - drug diabetes. Initially, it is not associated with the functional state of the pancreas, develops against the background of hormonal treatment and can go away on its own after drug withdrawal. SJS, provoked by an increase in natural hormones, is most often observed in Itsenko-Cushing's disease. In this group of patients, epidemiological indicators reach 10-12%. There is no exact information on the prevalence of SJS in the general population.

Causes

Etiologically, steroidal diabetes mellitus is subdivided into endogenous and exogenous. In the endogenous form, pancreatic dysfunction is caused by primary or secondary hypercortisolism. The reasons for this group include:

Secondary hypercortisolism. Cushing's syndrome occurs when the level of ACTH, a hormone produced by the pituitary gland and regulating the activity of the adrenal glands, rises. The secretion of corticoids increases, there is a high risk of dysfunction of the pancreas.

Adrenal neoplasms. In primary hypercortisolism, corticosteroid production is stimulated by the growing tumor of the adrenal gland. SJS is often diagnosed with corticosteroma, aldosteroma, corticoestroma, androsteroma.

The second variant of the origin of steroidal diabetes is exogenous. The high-risk group includes patients with autoimmune pathologies, chronic renal failure, and arterial hypertension. Diabetes develops with prolonged therapy with drugs that inhibit the secretion of insulin by beta cells in the pancreas. These drugs are glucocorticoids, thiazide diuretics, hormonal contraceptives [15].

The level of incretins can act as a possible marker of specific disorders of carbohydrate metabolism in patients with Itsenko-Cushing's disease and, presumably, can help in the differential diagnosis of steroidal diabetes and type 2 diabetes mellitus. Further research is needed to confirm these assumptions.

Itsenko-Cushing's disease and type 2 diabetes sometimes have a similar clinical picture, which complicates the timely diagnosis of endogenous hypercortisolism. The presence of disorders of carbohydrate metabolism, especially in combination with

other manifestations of this neuroendocrine disease, such as dysplastic obesity, poorly controlled arterial hypertension, etc., dictates the need to exclude its secondary nature. In turn, the achievement of a satisfactory postoperative result in relation to corticotropinoma does not always lead to a regression of the formed complications. The lack of normalization of glycemic parameters, lipid metabolism, and blood pressure puts patients at high risk for the development of cardiovascular complications in the future and dictates the need for careful dynamic monitoring by specialists. To achieve compensation for DM in comorbid patients, it is worth considering therapy with new generation drugs (inhibitors of dipeptidyl peptidase-4, inhibitors of sodium glucose transporter type 2), if necessary, in combination with other drugs.

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