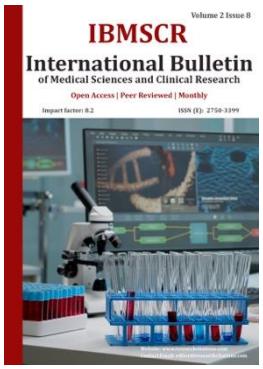

ITSENKO-CUSHING'S DISEASE

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Annotation: Cushing's syndrome is a pathological condition of the body characterized by the effect of excessive amounts of the hormone cortisol produced by the adrenal glands. The main cause of the disease is a violation of the regulatory mechanisms responsible for the functioning of the hypothalamic-pituitary-adrenal system.,

Key words: adenoma, intoxication, striae, osteoporosis, hirsutism, climacteric bend, encephalitis, meningitis, arachnoencephalitis.

A primary degenerative disease of the subcortical and pedunculated structures (hypothalamus, thalamus and reticular formation), with subsequent involvement of the pituitary and adrenal cortex. The disease most often occurs in women aged 20-40.

Historical information: the disease was first described in 1924 by the Russian neurologist N.M. Itsenko, and in 1932 the American neurosurgeon Cushing proved that the cause of the disease is basophilic adenoma of the anterior pituitary gland.

ETIOLOGY:

1) adenoma of the anterior pituitary gland
2) head injuries
3) mental injuries
4) infectious diseases, especially neuroinfections (encephalitis, meningitis, arachnoencephalitis)
5) intoxications
6) pregnancy
7) childbirth
8) menopause
9) idiopathic

PATHOGENESIS: The pathogenesis of the disease is associated with a violation of the regulatory mechanisms that control the hypothalamic-pituitary-adrenal system. These changes occur in the serotonin and dopamine receptors in the CNS. In healthy people, serotonin increases the activity of the corticotropin-releasing hormone (CRH)-ACTH-cortisol system, while dopamine decreases it. In Itsenko-Cushing's disease, the inhibitory effect of dopamine mediators on this system is weakened. As a result, the main pathogenetic factor of the disease, ACTH, is increased The increased production of ACTH enhances the function of the nodal and various zones of the adrenal cortex. In this disease, the sensitivity of the hypothalamic-pituitary system to corticosteroids is impaired, as a result of which the amount of cortisol increases along with ACTH. As a result of increased function of the nodal zone, the amount of glucocorticosteroids increases, which leads to hypertension, osteoporosis, wide lines on the skin (striae), obesity, decreased resistance to infections, and impaired carbohydrate metabolism, which leads to steroid diabetes. As a result of increased function of

the various zones, it leads to hyperproduction of androgenic steroids. As a result, the function of the ovaries is impaired, hypertrichosis develops.

CLASSIFICATION:

1) Depending on the form of Itsenko-Cushing's disease:

A) mild form - in which the symptoms of the disease are poorly expressed, the menstrual cycle is sometimes preserved, osteoporosis is not observed

B) moderately severe form - all symptoms of the disease are expressed, but complications are not observed

C) severe form - all symptoms of the disease are expressed, as well as complications: muscle atrophy and muscle weakness developing as a result of hypokalemia, pathological bone fractures, pulmonary and heart failure, hypertensive kidney, severe mental disorders.

2) Depending on the course of Itsenko-Cushing's disease:

A) progressive - in this case, the course of the disease develops rapidly over several months

B) torpid - the course of the disease develops slowly over several years.

CLINICAL: The disease often develops gradually. Patients complain of general weakness, headache, back and limb pain, menstrual cycle disorders, decreased libido and potency, changes in appearance and facial color, obesity, male-like hair growth in women, drowsiness, apathy, and impaired thinking. Objective: fat deposition is visible on the face (moon face), chest, abdomen, neck, 7th cervical vertebra ("climacteric bend"), limbs become thin. The skin is dry, scaly, marbled in color, prone to the development of furuncles. Wide, drawn, dystrophic lines (striae) of a reddish-purple color are visible on the abdomen, shoulders, mammary glands, and inner surfaces of the thighs. There is a tendency to hemorrhage under the skin. In women, male-like hair growth (hirsutism) and hair loss on the head are observed, while in men, feminization and reduced hair growth on the face are observed. Bone system: Bone fractures and deformations of varying intensity and duration are observed. The pain reaction to bone injuries is not the same, sometimes the patient may not feel pain even with very many bone fractures. Osteoporosis is observed in the bones of the spine, skull, ribs, heels, and fingers. The reason for this is that when glucocorticosteroids are produced in large quantities, protein is deposited in the bone, which in turn disrupts the deposition of calcium salts in the bone. If Itsenko-Cushing's disease occurs at a young age, growth retardation occurs as a result of osteoporosis.

Cardiovascular system: Tachycardia, leftward shift of the heart borders, systolic murmur at the apex, accentuation of the 2nd tone over the aorta, increased systolic and diastolic blood pressure, increased venous pressure. Arterial hypertension and metabolic disorders in the heart muscle lead to chronic heart failure. This is due to the increased production of glucocorticoids, increased pressure in the large circle of blood circulation, which leads to left ventricular hypertrophy and relative coronary insufficiency. On the ECG, a left-sided pattern, a decrease in the T wave, a prolongation of the Q-T interval, and a decrease in the S-T segment are observed.

Respiratory system: As a result of increased cortisol production, antibody production decreases, resulting in a decrease in the body's reactivity, leading to the development of bronchitis, pneumonia, and tuberculosis. Digestive system: Gallstones, pain in the iliac region, chronic hyperacid gastritis, and in some cases gastroduodenal ulcers ("steroid ulcers")

develop. Sometimes bleeding from the gastrointestinal tract is observed. The antitoxic, synthetic, galactose-fixing, and cholesterol-esterifying functions of the liver are impaired.

Urinary system: Cellular filtration and renal blood flow are reduced. Due to excessive production of glucocorticoids, immunobiological processes are disturbed, and the body's resistance to infections decreases. As a result, conditions are created for the development of infections in the urinary tract. Due to overproduction of glucocorticoids

stones form, resulting in skeletal decalcification and decreased citric acid excretion. As a result of this hypercalciuria urinary stones (urolithiasis) develop. Urine, lymph, and blood flow are disturbed, which creates a factor for the development of infections in the kidneys. Pyelonephritis and urinary stones occur. When the blood pressure is high for a long time, nephrosclerosis, then kidney failure and even uremia develop. As a result of kidney damage, the renin-angiotensin system activates and increases arterial hypertension.

Neuromuscular system and psyche: there are 2 types of syndrome:

1) Amyotrophic syndrome (steroid myopathy) - in this case, muscle wasting and atrophy in the proximal parts of the limbs are observed, muscle strength decreases.

2) Pain syndrome - in which the pain is so strong that even the movement of patients is limited. Pain usually occurs in the lower back and limbs. The cause of the pain is the compression of the spinal cord due to the overproduction of glucocorticoids. Neurosthenic from mental disorders

asthenodynamic, depressive, epileptic and hypochondriac-synestopathic syndromes are in the first place. Patients have decreased memory, thinking, intelligence, decreased emotional response to external impressions, and suicidal thoughts.

Endocrine system: impotence in men, dys- or amenorrhea in women, decreased libido. Atrophy of the uterus, ovaries and mammary glands is observed. The decrease in the activity of the gonads is associated with a decrease in the secretion of the gonadotropic hormones FSH and LH. If the disease occurs at a young age, there is a decrease in the production of STG and gonadotropin hormones, growth arrest and retardation of sexual development is observed.

Laboratory changes: Blood-hyperhemoglobinemia, erythrocytosis, neutrophilia

leukocytosis, eosinopenia and lymphocytopenia. In the active stage of the disease, fibrinogen concentration increases, along with hyperheparinemia, blood fibrinolytic activity decreases and hemorrhagic complications occur. Hypercholesterolemia, hypoalbuminemia, hyperglobulinemia, hypernatremia, hyperchloremia,

hypokalemia, hypophosphothemia, hypokalemia, osteoporosis, hyperglycemia, glucosuria (steroid diabetes). Blood plasma levels of ACTH, cortisol, 17-OX, and renin were increased. Protein, erythrocytes, hyaline and granular cylinders appear in the urine. Urinary 17-OCS and cortisol levels were increased.

X-ray diagnosis: On the craniogram, osteoporosis of the skull, osteoporosis of the spine ("fish spine"). Adrenal gland pneumosuprarenography reveals their hyperplasia.

Diagnostic tests:

1) Metapyrone test - 750 mg of metapyrone is administered orally every six hours for 2 days. On the 2nd day, urine is collected to determine the amount of 17-OXS in the urine. The essence of the test is that metapyrone selectively affects the enzyme 1-hydroxylase in the adrenal cortex, as a result of which it disrupts the biosynthesis of cortisol, aldosterone, and corticosterone. A decrease in the amount of cortisol in the blood leads to an increase in ACTH secretion by a feedback mechanism, which in turn increases the secretion of 17-oxy-1-

deoxycorticosterone from the adrenal gland, which does not inhibit the secretion of ACTH from the pituitary gland, but is excreted in the urine in the form of 17-OXS. In Itsenko-Cushing's disease, due to the activity of the hypothalamic-pituitary system, the amount of 17-OX excreted in the urine after taking metapyrone increases by 2-3 times, while in Cushing's syndrome it remains unchanged.

2) Dexamethasone test - based on a decrease in endogenous ACTH production due to the feedback mechanism. Liddell's large test is used: when dexamethasone is given every six hours for 2 days, the amount of 17-OX excreted in the urine decreases by 50% in Itsenko-Cushing's disease. In Itsenko-Cushing's syndrome, it remains unchanged.

DIFFERENTIAL DIAGNOSTICS:

1) With Itsenko-Cushing's syndrome - this occurs in 2 different cases:

a) with a hormonally active tumor of the adrenal cortex (glucosteroma), a roentgenogram shows a tumor in one adrenal gland and hyperplasia in the other, its course is rapid, osteoporosis is poorly expressed, hirsutism is highly developed. Metapirone and dexamethasone tests are negative.

b) ectopic ACTH syndrome - metastasis to the adrenal gland of tumors of other organs that produce biologically active ACTH or ACTH-like products (bronchogenic cancer, lung, parathyroid gland, stomach, esophagus, mediastinum, gallbladder, liver, thyroid gland, pancreas, uterus, ovary, etc.) - this is more common in men, the course is poor, the basal level of ACTH in the blood serum is very high (above 200 ng/l), the level of corticosteroids in plasma and urine is high, the tests are negative

2) Puberty with hypothalamic syndrome - a disease accompanied by obesity in adolescents, the course is good, physical and sexual development is accelerated, in boys bilateral gynecomastia, narrow pale-red lines (striae) on the skin, blood pressure and carbohydrate Metabolism is unstable, the size of the adrenal glands is unchanged, the size of the ovaries is increased, their shape is changed. Liddell's small test is positive: when dexamethasone is administered orally at a dose of 0.5 mg every 6 hours for 2 days, the amount of 17-OX excreted in the urine decreases (less than 3 mg per day). Calcification of the dura mater and hyperostosis of the bones of the skull are observed.

With obesity - the skin color is normal, subcutaneous fat is evenly distributed, hormonal indicators are normal.

TREATMENT: The main goal of treatment is to normalize hypothalamic function, secretion of ACTH and corticosteroids, metabolism.

1) Diet: Patients are limited to table salt

2) Etiotropic: radiation therapy: X-ray therapy, gamma therapy and proton therapy are used. In this case, light is directed from three or four areas: two temples, forehead and crown. The dose of light is given in a progressive system (25-35-50-75 rads with an interval of 1-2 days, then 85 rads every day). The total dose is 2000-4000 rads. If radiation therapy is ineffective or there are no contraindications, the tumor is surgically removed.

3) Pathogenetic - the goal is to block the function of the pituitary gland. For this, parlodel 5-7.5 mg / day, cyproheptadine (peritol, deseril) 25 mg / day or reserpine 2 mg / day. Of the listed drugs, parlodel is considered the most effective. This drug stimulates dopamine structures in the MNS and increases the sensitivity of the hypothalamic-pituitary system to corticosteroids. The secretion of ACTH and cortisol decreases. Parlodel is prescribed at a dose of 5-7.5 mg per day, then reduced to 1 mg. The course of treatment

should be at least 8 months. Other drugs that block ACTH secretion: reserpine and serotonin antagonists cyproheptadine (which reduce corticotropin-releasing hormone secretion) are prescribed as a complex drug therapy. If the effect of Parlodel is insufficient, the adrenal cortex function blockers chloditan, metapyrone, aminoglutethimide, trilostane are prescribed together with it. Chloditan selectively affects the adrenal cortex, causes atrophy and degeneration of the cells of the reticular and zona reticularis, inhibits the secretion of glucocorticoids and androgens, and reduces the response of the adrenal gland to ACTH. The initial dose is 3-4 g per day, then it can be increased to 6-10 g, the course dose is 180-200 g. Treatment is carried out under the control of serum ACTH and corticosteroids, urinary 17-OX. At the same time, hypothalamic-pituitary system and adrenal cortex are simultaneously treated with chlorditant.

X-ray therapy is performed to the hypothalamic-pituitary area. In moderate and severe Itsenko-Cushing's disease, combined therapy is also performed: unilateral adrenalectomy, irradiation of the hypothalamic-pituitary system, and treatment with chlorditan. To ensure a good postoperative period, patients are given adrenal blockers before surgery. Severe Itsenko-Cushing's disease

In Itsenko-Cushing's disease, bilateral adrenalectomy is performed and adrenal cortex tissues are autotransplanted into the subcutaneous tissue, in some cases, bilateral total adrenalectomies are performed, in which case glucocorticoids are administered in a maintenance dose.

Symptomatic: Calcium preparations for osteoporosis, antihypertensive drugs for hypertension are administered intravenously.

CONCLUSION: Itsenko-Cushing syndrome is accompanied by obesity and skin changes, and can also cause high blood pressure, osteoporosis, and steroid diabetes. In this article, we discuss why the syndrome occurs and how to treat it.

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