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PITUITARY GLAND INSUFFICIENCY (HYPOPITUITARISM)

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Annotation. The syndrome of endocrine pituitary insufficiency is characterized by a complete or partial cessation of hormone production by the anterior and posterior lobes of the pituitary gland. In isolated hypopituitarism, there is a disruption in the production of one of the pituitary tropic hormones: ACTH, STH, LH, FSH, TSH. Total hypopituitarism (panhypopituitarism) occurs when the production of all tropic hormones in the pituitary gland stops. In interstitial-pituitary insufficiency, there is a disruption in the secretion of all tropic hormones, which is combined with a deficiency of vasopressin (diabetes insipidus).
Keywords:endocrine insufficiency syndrome, pituitary gland, hypothalamus, hypopituitarism.

ETIOLOGY AND PATHOGENESIS. Simmonds was the first to link the clinical manifestations of hypopituitarism with postpartum necrosis of the anterior pituitary gland, accompanied by cachexia and senile involution of organs and tissues. However, a decrease in the production of pituitary tropic hormones is observed not only in postpartum necrosis of this gland, but also in various pathological conditions, as well as in damage to the hypothalamic nuclei, and partial or complete necrosis of the anterior pituitary gland is not always accompanied by cachexia. Sheehan's syndrome (postpartum hypopituitarism) is an acute ischemic necrosis of the pituitary gland caused by spasm of the pituitary vessels that occurs after childbirth with severe bleeding and decreased blood pressure. According to statistics, pituitary damage of varying degrees develops in 32% of women who have suffered bleeding and vascular collapse during childbirth. Clinical manifestations of hypopituitarism develop only in cases where 75-90% of the adenohypophysis tissue is destroyed. The development of pituitary insufficiency is caused by: hormonally active and inactive pituitary adenomas; infiltrative processes (autoimmune lymphocytic hypophysitis, granulomatosis); postpartum pituitary necrosis or Sheehan's syndrome, which occurs during bleeding during childbirth; consequences of surgical or radiation interventions in the pituitary gland; pituitary infarctions; metastases to the pituitary gland or pituitary stalk; injuries, infections, hemochromatosis, vascular disorders; rare causes of hypopituitarism (diabetic angiopathy and sickle cell anemia). When at least 75% of all pituitary tissue is destroyed, hypopituitarism develops, in which pituitary tropic hormones are insufficiently produced, hypothyroidism and adrenal insufficiency develop. Hypopituitarism is conventionally divided into primary and secondary. Primary hypopituitarism develops due to the absence or destruction of secretory cells of the pituitary gland, and secondary hypopituitarism is caused by a deficiency of stimulating effects on the secretion of pituitary hormones: disruption of vascular and/or neural connections with the brain at the level of the pituitary stalk; hypothalamus or extrahypothalamic areas of the central nervous system. The most common cause of panhypopituitarism are pituitary tumors (active and inactive), as well as irradiation of the hypothalamic-pituitary region and surgical hypophysectomy. Pituitary insufficiency often develops after hemorrhage (pituitary apoplexy). The most common causes of hypopituitarism in women are: childbirth complicated by eclampsia in the last months of pregnancy, sepsis, thromboembolism, massive blood loss; repeated and frequent

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pregnancies and childbirth leading to pituitary gland strain; abortion; autoimmune lymphocytic hypophysitis (in women with severe toxicosis in the second half of pregnancy). In this case, other autoimmune processes are often detected. One of the signs of hypopituitarism is a violation of the menstrual cycle due to the loss of LH and FSH secretion. With the appearance of other tumors (somatotropinomas, corticotropinomas, thyrotropinomas, prolactinomas (secreting STH, ACTH, TSH,prolactin)) the menstrual cycle is also disrupted, which is caused by a violation of the impulse secretion of gonadotropin-releasing hormone. The function of the neurohypophysis is also disrupted, which is accompanied by the development of diabetes insipidus or panhypopituitarism.

CLINICAL PICTURE

The clinical picture depends on the extent of destruction of the anterior pituitary gland. In most cases, the somatotropic and gonadotropic functions of the pituitary gland are the first to decrease, followed by thyrotropic and adrenocorticotropic insufficiency. In some cases, one of the first symptoms of hypopituitarism is progressive weight loss, which in severe cases can reach 30 kg. Weight loss is usually uniform, a decrease in the volume of internal organs and muscle atrophy are noted. The skin of patients is wrinkled, thinned, pale yellowish in color, and dirty lemon pigmentation appears on the natural folds of the skin and face. The nipples and skin in the perineum are depigmented. Amenorrhea occurs due to ovarian failure. The internal and external genitalia and mammary glands atrophy. In men, secondary sexual characteristics disappear, testosterone levels decrease, the internal and external genitalia atrophy, and oligozoospermia sets in. One of the important symptoms of hypopituitarism is the disappearance of hair in the armpits and pubis. Early graying, decalcification of bones, atrophy of the lower jaw, decay and loss of teeth are observed. Edema is usually absent. Sweating and secretion of the sebaceous glands weaken. The phenomena of marasmus and senile involution increase. There is a sharp general weakness, apathy, adynamia up to complete immobility, orthostatic collapse and coma. Body temperature decreases. Death occurs without specific treatment. One of the first signs of hypopituitarism leading to the development of hypothyroidism is the loss of the thyroid-stimulating function of the pituitary gland. Chilliness, drowsiness, lethargy, adynamia, decreased mental and physical activity are noted. Blood pressure decreases, heart sounds become muffled. Atony of the gastrointestinal tract and constipation develop. When the disease develops after childbirth, amenorrhea and agalactia are observed. Loss of the gonadotropic function of the pituitary gland is accompanied by a violation of the menstrual function and leads to amenorrhea. In rare cases of erased and protracted course of the disease, the menstrual cycle is disrupted, but persists. In such cases, pregnancy is possible. Reduction of internal organs, genital and mammary glands is due to a violation of the function of somatotropin and a decrease in the production of somatotropic hormone by the pituitary gland. With insufficient production of adrenocorticotropic hormone by the pituitary gland, adrenal insufficiency develops. Hypopituitarism develops with hypothalamic insufficiency, in which there is a violation of the menstrual cycle up to amenorrhea. In typical cases, diagnosis of hypothalamic-pituitary insufficiency does not cause difficulties. The appearance of hypopituitarism with the development of insufficiency of the thyroid and sex glands, as well as the adrenal glands after complicated childbirth or in connection with other reasons indicated above, may indicate hypopituitarism syndrome.In severe forms of hypothalamic-pituitary insufficiency (Simmonds' disease), atrophy of muscles, skin, subcutaneous tissue, weight loss, hair loss, osteoporosis, hypotension, hypothermia, apathy, and mental dementia predominate. Blood tests show normo- or hypochromic anemia in most patients, while some have leukopenia and eosinophilia with lymphocytosis, low blood glucose levels, and a flattened glycemic curve. There is a decrease in the

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levels of peripheral endocrine gland hormones (T4, testosterone, estradiol, daily excretion of free cortisol in the urine) with a decrease in the levels of ACTH, thyrotropin, STH, gonadotropic hormones (LH and FSH), and prolactin. The concentration of corticosteroids is also reduced. In order to clarify the reserves of pituitary hormones, stimulating tests with releasing hormones (Thyroliberin, gonadotropin-releasing hormone) are prescribed. Mineralocorticoid secretion does not decrease in secondary hypocorticism, since the production of the latter is regulated independently of the effects of ACTH. In addition to the fascicular and reticular zones, with prolonged ACTH deficiency, the glomerular zone of the adrenal cortex may undergo atrophy, which is accompanied by a decrease in the plasma level of aldosterone and an increase in the activity of renin in the blood plasma. To diagnose secondary hypocorticism, tests with metyrapone, synacthen and insulin hypoglycemia are performed.

DIFFERENTIAL DIAGNOSIS

A number of diseases accompanied by weight loss (malignant tumors, tuberculosis, enterocolitis, porphyria, etc.) must be differentiated from profound atrophy combined with hypothalamic-pituitary insufficiency. Secondary sexual characteristics may be preserved in extreme cases of exhaustion, which is an outcome of the disease, not its dominant manifestation. In this case, the presence of anemia provides grounds for differential diagnosis with blood diseases. In clinical practice, it is necessary to differentiate pituitary cachexia from exhaustion that has developed against the background of nervous anorexia due to the girl's desire to lose weight and forced refusal of food. Refusal of food, sometimes alternating with bouts of bulimia, is accompanied by disruption or disappearance of menstruation, the genitals gradually atrophy, functional symptoms of endocrine insufficiency appear, occurring even before the development of severe exhaustion. Physical, intellectual, and sometimes creative activity are preserved. In case of severe anemia, differential diagnostics with blood diseases should be performed. In case of hypothalamic-pituitary insufficiency, hypoglycemic conditions can simulate organic hyperinsulinism (insulinoma). Patients with hypothalamic-pituitary insufficiency are prone to hypertrichosis. The level of pituitary tropic hormones can be normal, elevated or decreased. This is the functional nature of insufficient hormone production in nervous anorexia. Stimulation tests show their normal release. A combination of insufficiency of several endocrine glands is observed in autoimmune polyglandular syndromes. In this case, primary insufficiency of the endocrine glands and a high level of pituitary tropic hormones are observed.

Treatment of hypothalamic-pituitary insufficiency is aimed at eliminating hormonal deficiency and, if possible, eliminating the cause that led to the development of hypopituitarism. In the presence of a tumor or cyst that leads to the development of destructive processes, surgical treatment or radiation therapy is performed. When conducting hormone replacement therapy, it is necessary to compensate for adrenal insufficiency first. If you start treating hypothyroidism before compensating for adrenal insufficiency, acute adrenal insufficiency may develop. In secondary hypopituitarism, there is no need to prescribe mineralocorticoids (9α-fluorocortisol, Cortineff), since the secretion of the latter is regulated independently of ACTH. Thyroid hormone preparations are prescribed to regulate thyroid insufficiency. Treatment begins with L-thyroxine at a daily dose of 25 mcg, followed by an increase in the dose of the drug. In order not to worsen the condition of the cardiovascular system, elderly patients begin treatment with a dose of 12.5 mcg. In case of impaired somatotropic function of the pituitary gland with a decrease in the function of the hypothalamic-pituitary system, growth hormone is prescribed. To diagnose total somatotropic insufficiency, stimulation tests (insulin, clonidine) are

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carried out, against which the level of growth hormone increases. Euthyroidism is a necessary condition for conducting stimulation tests. An important study in the diagnosis of somatotropic insufficiency is the determination of IGF-1, as well as somatomedin-binding protein-3. First of all, the corresponding study should be prescribed to patients with somatotropic insufficiency. The simplest and most informative study is the determination of the level of IGF-1 (somatomedin C) in the blood. A decrease in the level of the latter suggests stimulating tests with insulin, clonidine, arginine, somatoliberin. In case of insufficiency of the sex glands and atrophic processes in the genitals, patients with hypothalamic-pituitary insufficiency are prescribed hormone replacement therapy with combined oral contraceptives (Zhanin, Belara, Diane-35, Lindinet, Novinet, etc.). If necessary, fertility is restored with drugs that stimulate ovulation (Menopur). Men with hypopituitarism are prescribed androgenic drugs (Androgel, Nebido, etc.). In case of hypopituitar coma, treatment is carried out in the same way as in case of acute adrenal insufficiency.

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