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HYPERPROLACTINEMIA IN SYNDROME EMPTY SELLA TURCICA

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Relevance. *Empty sella turcica syndrome (ESS) is one of the poorly studied problems of neuroendocrinology. The relevance of this problem has increased at present with the widespread use of non-invasive magnetic resonance imaging (MRI) in diagnostics, as well as with the growing number of patients who have undergone radiation, surgery, and combined treatment for pituitary adenoma. The term "ESS syndrome" should be understood as prolapse of the suprasellar cistern into the sella turcica cavity with flattening of the pituitary gland along the bottom and walls of the sella turcica, accompanied by endocrine, neurological, and visual disorders. A distinction is made between primary (idiopathic) and secondary ESS, which occurs after radiation, surgery, and combined treatment of chiasmatic-sellar region diseases. This review will focus mainly on primary ESS syndrome.*

Keywords: *hyperprolactinemia, intrasellar, pneumoencephalography, chiasmatic-sellar region.*

Historical excursion. The PTSS syndrome was first described quite a long time ago. As early as 1875, Key and Retzins noted the existence of a peripituitary, intrasellar subarachnoid space. In 1924, Schaffer proposed an anatomical classification of diaphragm types, which represented either a dense, fully formed vault over the sella cavity, or an underdeveloped vault with a sharply enlarged infundibular opening. In 1935, Hamby reported the discovery of an intrasellar subarachnoid cyst in a child. Of decisive importance for defining PTSS was the work of W. Busch "Morphology of the sella turcica and its relationship with the pituitary gland", which appeared in 1951 [15]. The work was based on the results of a study of autopsy material from 788 people who

died from diseases not associated with pituitary pathology. Based on the observations conducted in 40 (5.5%) individuals, including 34 women, a combination of almost complete absence of the sella turcica diaphragm with flattening of the pituitary gland in the form of a thin layer of tissue at its bottom was found. In this case, the sella seemed empty. Robertson described this phenomenon for the first time in clinical practice, based on pneumoencephalography data. E. Engels [20] reported the possible detection of PTS during contrast myelography. In such cases, the sella turcica was filled with a contrast agent. An analysis of the literature showed that the problem of PTS was devoted to works concerning both the anatomical, radiological, and endocrinological aspects of this disease. In the literature, the term "PTS syndrome" unites various nosological forms regardless of their origin: intrasellar arachnoid diverticulum, intrasellar cyst, primary arachnoid cyst, intrasellar cistern, intrasellar subarachnoid hernia. Common to all nosological forms is the presence of an expanded subarachnoid space in the cavity of the sella turcica. M. Colby and T. Kearns [17] by the term PTS meant the presence of dense non-tumor, cicatricial tissue surrounding the optic chiasm and the sella turcica, formed after operations or radiation therapy for pituitary tumors, accompanied, in addition, by newly occurring visual disturbances. Later, the term PTS began to be used in cases where the sella turcica area was filled with air on the pneumoencephalogram and the patient had a history of previous surgery or irradiation of the pituitary region. S. Weiss and R. Raskind pointed out the need to differentiate between primary [65] (idiopathic) and secondary PTS, which occurs against the background of previous interventions in the hypothalamic-pituitary region [77]. Etiology and pathogenesis To date, a wide range of pathological and physiological factors have been described that are directly or indirectly related to the development of PTS syndrome. They can be conditionally divided into the following groups.

1. Trauma. Damage to the central part of the neuroendocrine system can lead to the development of PTS.
2. Infectious diseases of various origins,particularly severe, ultimately lead to pathological changes in the hypothalamic-pituitary region.
3. Local and general circulatory disorders: bleeding, embolism, necrosis, as well as hypertension and intracranial hypertension.
4. Drug effects: oral contraceptives and dopamine agonists, hormone replacement therapy, radiation therapy, surgery.
5. Tumors. A tumor developing in the hypothalamic-pituitary region can suppress the activity of the pituitary gland and lead to glandular hypofunction, which gives rise to the development of a number of compensatory processes.

6. Heredity factor. The formation of PTS is facilitated by a violation of the elastic structure of the diaphragm of the sella turcica with congenital inferiority of the connective tissue.
7. Recent studies indicate that autoimmune disorders (lymphocytic adenohypophysitis - LA) may play a certain role in the development of PTS.
8. Physiological processes: pregnancy, menopause. The mechanism of PTS formation is based on the anatomical features of the structure of the sella turcica. At the entrance to the sella turcica, the dura mater splits into 2 layers, one of which lines the walls and bottom of the sella, the second closes the entrance to the sella turcica, forming the diaphragm of the sella. In the center of the diaphragm there is an opening for the passage of the stalk (peduncle) of the pituitary gland. Normally, the arachnoid membrane and cerebrospinal fluid do not penetrate into the cavity of the sella turcica. R. Mortara and H. Noreli reported cases of penetration of the chiasmatic cistern and the bottom of the 3rd ventricle into the cavity of the sella turcica [48]. The attachment of the diaphragm and its thickness, the nature of the opening are subject to significant anatomical variations. W. Busch described 3 types of diaphragm [15]: Type 1 - the diaphragm is a connective tissue vault with an opening in the center, allowing only the pituitary stalk to pass through; Type 2 - the diaphragm is not completely closed and contains an opening up to 3 mm in diameter around the pituitary stalk; Type 3 - the diaphragm is a narrow strip (2 mm or less) of dura mater duplication along the periphery of the sella. Insufficiency of the diaphragm leads to the spread of the subarachnoid space into the intrasellar region and to the emergence of the ability of cerebrospinal fluid pulsation to directly affect the pituitary gland, which can lead to its flattening [36] and pressing against the fundus or back. M. Farber et al. [21] have data on the congenital absence of the diaphragm. Congenital underdevelopment of the sella turcica, according to various authors, occurs in 40-50% of cases of pathological anatomical studies [1]. It should be noted that diaphragm insufficiency may not only be congenital, but also develop as a result of physiological processes such as pregnancy and menopause. During pregnancy, the size of the pituitary gland increases approximately twofold, and in women who have given birth to multiples or twins, it can be even larger, not returning to its original size after childbirth.This circumstance explains to some extent the development of primary PTS mainly in women. When taking oral contraceptives, hormone replacement therapy for hypofunction of peripheral endocrine glands, transient hypertrophy of the pituitary gland and stalk occurs with their subsequent involution, which ultimately leads to thinning of the diaphragm and an increase in its opening [38]. The formation of PTS syndrome against the background of congenital [33] or long-term untreated hypothyroidism [49], hypopituitarism gives some authors reason to consider the connection between

hypoplasia and hypofunction of the pituitary gland with the development of this syndrome. Another point of view regarding the mechanism of PTS occurrence has an equal right to exist, associated with the normal existence of a pituitary cistern located under the diaphragm of the sella turcica [20]. In this regard, it can be assumed that primary PTS is formed not as a result of the descent of the suprasellar cisterns into the cavity of the sella turcica, but due to the compensatory expansion of the pituitary cistern and a decrease in the volume of the pituitary gland. In the formation of secondary PTS, the descent of the suprasellar cisterns into the cavity of the sella turcica is possible, since the pituitary cistern is subject to degenerative changes under the influence of the tumor itself, radiation therapy, or is destroyed during surgical removal of the pituitary adenoma. Kaufmann believed that an important factor in the development of PTS is an increase in pulse cerebrospinal fluid pressure due to intracranial hypertension, hypertension, hydrocephalus, and an intracranial tumor. In practice, this means a long-term increase in intracranial pressure and impaired circulation of cerebrospinal fluid (block of the fornix and hydrocephalus), which subsequently leads to an increase in the size of the sella turcica and the formation of primary PTS. However, at present it is difficult to assert that transient or permanent increase in cerebrospinal fluid pressure is required for enlargement of the sella turcica in such cases, since cerebrospinal fluid pressure is already normal with formed PTS [11]. A certain role in the etiology of PTS syndrome belongs to the violation of volumetric ratios between the pituitary gland and the sella turcica. A decrease in the volume of the pituitary gland can be the result of necrosis of the pituitary adenoma [13]. In search of the causes of PTS formation, R. Bjerre conducted studies, as a result of which evidence was obtained that PTS is a consequence of autolysis of a previously existing pituitary adenoma. This theory explains the frequent presence of a hypoplastic pituitary gland, visual field impairment, non-traumatic cerebrospinal rhinorrhea and benign intracranial hypertension in patients with PTS. Thus, according to the author, PTS syndrome is a stage in the spontaneous resolution of a pituitary tumor [63]. J. Montalbay et al. concluded thatthat pituitary apoplexy is an inevitable cause of the development of subsequent panhypopituitarism and PTS [47] Along with all the listed factors, an important role in the pathogenesis of PTS is played by arachnoid cysts that developed as a result of optic-chiasmatic arachnoiditis; infarctions and necrosis of giant granulomas and gummas of the pituitary gland; necrosis and hemorrhage of pituitary adenomas [13]. It is even considered possible that PTS is an evolutionary stage in the development of the syndrome [Lichen’s disease [43]. Some researchers present data on the PTS syndrome that arose as a result of pituitary artery infarction after pulse therapy with prednisolone for systemic lupus erythematosus [37]. Consequently, one cannot exclude from the structure of PTS formation a group of patients taking glucocorticoids for a long time

or in massive doses. It is impossible not to note the fact of the occurrence of PTS syndrome, described by Scandinavian scientists, in a patient with hemorrhagic fever caused by the Puumala virus, the complication of which was the development of nephropathy and PTS with pituitary insufficiency [23]. Apparently, the development of this disease against the background of chronic periorbital vasculitis can be attributed to the same category of causes [29]. Summarizing all of the above, we can conclude that the most important factors for the formation of PTS are diaphragmatic insufficiency and increased cerebrospinal fluid pressure. Other factors are only predisposing. Recent years have been marked by increasing attention to the problems of immunogenesis of diseases, including endocrinopathies [6]. Research in recent years indicates the possible participation of the autoimmune link in the pathogenesis of PTS syndrome. M. Komatsu et al. In an analysis of humoral autoimmunity in patients with primary PTSD, data were obtained confirming the involvement of autoimmune processes in the development of lymphocytic hypophysitis, leading to pituitary atrophy [39]. This study showed that antibodies to corticotrophs and lactotrophs were found in 75 and 47% of cases, respectively, and 44% of patients had antibodies to both types of cells (for comparison: in patients with pituitary adenomas, the frequency of the presence of antibodies to the surface of adenohypophyseal cells is 22%, with diabetes insipidus - 33%, and in patients with other autoimmune diseases and in healthy individuals, antibodies were not found). To substantiate the proposed assumption, we will give the following example. K. Okada and S. Ishikawa report on a 28-year-old woman who developed persistent amenorrhea, fatigue, weakness, and weight loss after childbirth [54]. Laboratory data showed hyperprolactinemia and decreased levels of adrenocorticotropic hormone (ACTH). Serological blood testing showed the presence of antibodies to the superficial cells of the adenohypophysis, and MRI of the brain revealed a picture of PTSD. It is possible that PTSD syndrome and ACTH deficiency are caused by autoimmune destruction of the gland. It has been suggested that PTSD syndrome plays a role in the development of ACTH deficiency.The autoimmune nature of the PTSD phenomenon may be indicated by the fact that this syndrome exists in the father and his two daughters or that one patient has several diseases based on autoimmune disorders (Sjogren’s disease, Hashimoto‘s thyroiditis, PTSD syndrome). LA was first described in 1962 by Goudie and Pinkerton in a woman whose autopsy revealed LA and Hashimoto‘s thyroiditis [57]. The histological picture of LA is as follows: infiltration of the adenohypophysis by lymphocytes, plasma cells, and eosinophils with lymphoid follicles and interstitial fibrosis. Most patients with LA have concomitant autoimmune diseases. A number of authors note the obligatory presence of antibodies to the superficial cells of the adenohypophysis in the blood of such patients. LA is often accompanied by hyperprolactinemia. However, to date, no

correlation has been found between the presence of circulating antibodies to the pituitary gland and the development of pituitary insufficiency [46]. Complaints In most cases, PTSD syndrome occurs in women over 50 years of age and men over 60 years of age, which is probably due to age-related involution of the pituitary gland [22[. The main complaints of patients are usually the following: headaches, dizziness, memory impairment, increased blood pressure (the hypothalamic origin of which is being clarified), changes in vision, thirst, swelling of the face and limbs, changes in sexual function, weight gain, weakness, fatigue, decreased performance. The hypothalamic component can manifest itself in a violation of thermoregulation, most often an increase in body temperature to subfebrile numbers. The most common complaint in PTSD syndrome is headache. It is usually constant, more pronounced in the forehead, has a meningeal character, i.e. occurs as a result of tension of the dura mater. Some researchers believe that PTSD should be suspected in overweight, middle-aged women with daily headaches [16]. More than half of the patients complain of excess body weight [33]. It should be noted that the distribution of subcutaneous fat in PTSD is nonspecific. A case of Cushingoid obesity in a patient without any other clinical and laboratory signs of Itsenko-Cushing disease, whose brain MRI revealed a picture of PTSD, is described [19]. The authors of the article emphasize the importance of searching for the causes of obesity, especially if it is combined with external signs of hypothalamic-pituitary diseases. Rare complaints of patients with PTSD include decreased visual acuity and deterioration of lateral vision; watery nasal discharge diagnosed as cerebrospinal fluid rhinorrhea. Spinal rhinorrhea as a symptom of PTSD was first observed by Ommaya in 1968. Rhinorrhea, which occurs more often during coughing and sneezing, is often the only manifestation of this syndrome, which leads to an incorrect diagnosis of allergic or vasomotor rhinitis and incorrect treatment tactics [26]. The cause of rhinorrhea is the presence of communication between the sella turcica and the oral cavity,which periodically occurs when coughing or sneezing. The resulting connection between the suprasellar subarachnoid space and the sphenoid sinus increases the risk of meningitis. Therefore, it is extremely important to understand the causes of rhinorrhea. Clinical picture Often, PTS syndrome is asymptomatic and is diagnosed by chance during a tomographic examination. Clinical manifestations of PTS syndrome can be conditionally divided into 3 groups.

1. Endocrine disorders. The cause of neuroendocrine disorders in PTS syndrome is considered to be not the compression of the secretory cells of the pituitary gland, but the compression of its stalk and, accordingly, a violation of the hypothalamic control over pituitary functions as a result of a periodically occurring violation of the intake of inhibitory and releasing factors of the hypothalamus. This position is based on the lack of correlation between the degree of compression of the pituitary gland itself and

clinical symptoms and is confirmed by the polymorphism and instability of clinical neuroendocrine disorders. The functional state of the pituitary gland in PTS syndrome changes in half of the patients, and in some cases PTS can be combined with pituitary adenomas [5]. Endocrine disorders in PTS syndrome can manifest themselves as changes in the tropic functions of the pituitary gland without clinical symptoms. PTS syndrome is characterized by hyperprolactinemia, which acquires a transient character during dynamic observation: from normal to moderately elevated [10]. E. A. Mizetskaya et al. suggest that when conducting a test with parlodel, there is a rapid (after 2 hours) decrease in the prolactin level, and after 4 hours its content reaches the norm, which is a criterion for the primary nature of PTS; in secondary PTS, the prolactin level does not normalize. Celani et al. studied the prolactin level in a test with TRH in patients with primary PTS and patients with prolactinomas. The results of the study showed that in both cases the prolactin response to TRH was reduced, so the value of such a test for differential diagnosis is questionable. It is worth noting that more than half of patients with hyperprolactinemia have reduced concentrations of luteinizing and follicle-stimulating hormones in the blood.This position is based on the absence of correlation between the degree of compression of the pituitary gland itself and clinical symptoms and is confirmed by polymorphism and instability of clinical neuroendocrine disorders. The functional state of the pituitary gland in PTS syndrome changes in half of the patients, and in some cases PTS can be combined with pituitary adenomas [5]. Endocrine disorders in PTS syndrome can manifest themselves as a change in the tropic functions of the pituitary gland without clinical symptoms. PTS syndrome is characterized by hyperprolactinemia, which, during dynamic observation, acquires a transient character: from normal to moderately elevated [10]. E. A. Mizetskaya et al. suggest that when conducting a test with parlodel, there is a rapid (after 2 hours) decrease in the prolactin level, and after 4 hours its content reaches the norm, which is a criterion for the primary nature of PTS; in secondary PTS, the prolactin level does not normalize. Celani et al. studied the prolactin level in the TRH test in patients with primary PTS and patients with prolactinomas. The results of the study showed that in both cases the prolactin response to TRH was reduced, so the value of such a test for differential diagnosis is questionable. It is worth noting that more than half of the patients with hyperprolactinemia have reduced concentrations of luteinizing and follicle-stimulating hormones in the blood. This position is based on the absence of correlation between the degree of compression of the pituitary gland itself and clinical symptoms and is confirmed by polymorphism and instability of clinical neuroendocrine disorders. The functional state of the pituitary gland in PTS syndrome changes in half of the patients, and in some cases PTS can be combined with pituitary adenomas [5]. Endocrine disorders in PTS syndrome can manifest themselves

as a change in the tropic functions of the pituitary gland without clinical symptoms. PTS syndrome is characterized by hyperprolactinemia, which, during dynamic observation, acquires a transient character: from normal to moderately elevated [10]. E. A. Mizetskaya et al. suggest that when conducting a test with parlodel, there is a rapid (after 2 hours) decrease in the prolactin level, and after 4 hours its content reaches the norm, which is a criterion for the primary nature of PTS; in secondary PTS, the prolactin level does not normalize. Celani et al. conducted a study of prolactin levels using a TRH test in patients with primary PTS and patients with prolactinomas. The results of the study showed that in both cases the prolactin response to TRH was reduced, so the value of such a test for differential diagnosis is questionable. It is worth noting that more than half of patients with hyperprolactinemia have reduced concentrations of luteinizing and follicle-stimulating hormones in the blood. Hyperprolactinemia in PTSD syndrome in some cases is not a factor preventing pregnancy, which can proceed favorably even with concomitant osteoporosis [25]. When studying the adrenocorticotropic function of the pituitary gland, only an insignificant proportion of patients showed an increased level of ACTH. Half of the patients have a decreased concentration of ACTH in the blood serum and secondary adrenal insufficiency, which is often mild and in some cases is accompanied by a deficiency of somatotropic hormone (STH) [31]. Of interest is the description of two patients with PTSD syndrome and ACTH hypersecretion with normal cortisol levels, which may be associated with the production of ACTH peptide with low biological activity and subsequent infarction of corticotrophs and the development of PTSD. The functional activity of the adrenal cortex in some patients with PTSD is reduced, which is confirmed by the stimulation test with ACTH. On the contrary, there is a long-term observation of a patient with all the signs of hypercorticism, in whom MRI excluded both corticosteroma and pituitary adenoma, and no ectopic source of ACTH production was found. Repeated control studies came to one diagnosis: PTSD syndrome [36]. A study of the pituitary-thyroid axis function showed that secondary hypothyroidism was observed in 1/10 patients and was accompanied by a decrease in the level of triiodothyronine, thyroxine and an increase in the level of thyroid-stimulating hormone in the blood. The same number of patients were found to have a subclinical form of hypothyroidism, diagnosed by a stimulation test with TRH. Characteristic disorders of sexual function in women are oligomenorrhea and amenorrhea. Impaired gonadotropic function in men is often manifested by decreased libido, oligospermia, and infertility. In a detailed study of the pituitary-ovarian (testicular) axis, secondary hypogonadism was observed in a number of cases. The results of the luteinizing hormone-releasing hormone test in men confirmed the pituitary nature of hypogonadism, and in women - the hypothalamic nature [14]. Secretion of STH in patients with primary PTS in more

than half of the cases tends to decrease, as shown in a study on stimulation of insulin hypoglycemia, and the frequent association of PTS syndrome with diseases accompanied by STH deficiency confirms these data. An example is the combination of PTS with congenital septo-pituitary dysplasia syndrome (agenesis of the septum pellucidum or corpus callosum, hypoplasia of the optic nerve, deficiency of STH, ACTH, thyroid-stimulating hormone and excess prolactin) [24]. In general, patients with PTS syndrome more often have a change in the function of the anterior pituitary gland, less often - the posterior lobe. A case of diabetes insipidus of central origin in combination with hypogonadism is known, and according to computed tomography data, a defect of the diaphragm of the sella turcica and PTS syndrome were revealed [42]. To date, many cases of a combination of diabetes insipidus and PTS syndrome have been described,which suggests [34] a high probability of developing central diabetes insipidus against the background of PTS syndrome. It should be taken into account that panhypopituitarism and hypopituitarism are often observed with PTS syndrome [38]. We give an example of one case from practice: a 64-year-old woman was examined for persistent hyponatremia [35]. After a complete clinical and laboratory examination, a diagnosis of panhypopituitarism was made, and according to MRI of the brain - PTS syndrome. It is important to note that the weakening of the tropic functions of the pituitary gland is sometimes less pronounced in primary PTS than in secondary PTS, and does not always require replacement therapy. This fact can be explained by the fact that the presence of a pituitary tumor makes the disorders more profound.

2. Neurological disorders. According to observations of neurologists of the A. M. Vein Clinic, patients with PTSD syndrome have a high degree of emotional-personal, motivational and vegetative disorders [1]. The appearance of clinical symptoms and worsening of the disease are directly related to the exacerbation of a chronic stress situation. In all patients, a stressful environment affects the level of brain mediators, changing the production of inhibitory and releasing factors of the hypothalamus, which subsequently affects the function of the pituitary gland. The state of stress worsens the course of arterial hypertension, which is often present in patients with PTSD, leading to an increase in the frequency of vegetative crises, affecting the cerebrospinal fluid dynamics. The discordance of the hypothalamic-pituitary connections in PTSD syndrome inevitably disrupts all functions of the hypothalamus, reducing adaptive properties and increasing susceptibility to stress. In turn, this leads to an increased response to stress, which is manifested by a worsening of the disease, aggravation of emotional-motivational and vegetative disorders. Schematically, pathological changes in patients with PTSD syndrome can be presented as follows. Pathology from the central nervous system: - cephalgic syndrome caused by tension headache or increased

intracranial pressure, - cerebroasthenic syndrome without vascular lesions: memory loss, rapid fatigue, tearfulness, decreased tone, leveled by rest and taking nootropic, vasodilator drugs; - vestibular syndrome: dizziness, unsteadiness and uncertainty of gait. Pathology from the autonomic nervous system: - complaints of a cardiovascular, gastrointestinal, respiratory nature. In connection with the provision on increased pressure of the cerebrospinal fluid in PTSD syndrome, the dependence of intracranial hypertension and pituitary function was studied. It has been shown that prolonged increased pressure on the anterior pituitary gland resulted in decreased pituitary function [41]. Impaired cerebrospinal fluid circulation was observed in the majority of patients with pituitary hypofunction, in fewer cases with normal pituitary function, and in concomitant hyperprolactinemia it occupied an intermediate position. Demineralization and erosion of the sella turcica, which also indicate increased intracranial pressure, were combined with both normal and impaired pituitary function. There is strong evidence that patients with panhypopituitarism had a history of cerebrovascular episodes or meningoencephalitis before the development of pituitary insufficiency. It is possible that these patients experienced acute attacks of increased intracranial pressure, which were not compensated for by an increase in the sella turcica. Thus, subsequent pituitary dysfunction in some patients is secondary to impaired cerebrospinal fluid circulation.

3. Visual impairment. Visual impairment varies in nature and severity [52]. Typically, it may be a decrease in visual acuity in one or both eyes, changes in the visual fields [4], photophobia. Long-term observation reveals fluctuations in the visual fields, visual acuity, and the state of the optic nerve heads, which can be explained by changes in cerebrospinal fluid circulation in the basal cisterns and the degree of sagging of the optic nerves into the sella turcica. Ophthalmological examination in patients with PTSD is extremely important, since changes in the visual fields and optic nerve heads can be observed in open-angle glaucoma or glaucoma with low or normal intraocular pressure, which is not uncommon and can be combined with PTSD [44]. In this regard, it is necessary to diagnose glaucoma as the cause of visual field defects, since the treatment tactics for these diseases are different. Visual impairment in secondary PTS syndrome has slightly different roots: after surgery on the pituitary gland, the optic chiasm sags into the sella turcica; after X-ray therapy, there is a high risk of negative effects of radiation on the vascular system, the development of vasculitis and visual impairment due to narrowing of the blood vessels. As PTS syndrome was studied, it was found that in half of the cases it can be associated with other endocrine diseases [12, 35, 36]. This is confirmed by the combination of PTS with multiple endocrine tumor syndrome type 1 [43], diabetes mellitus, corticotropinoma [32], etc. An association of PTS syndrome and Itsenko-Cushing‘s disease is not uncommon [44].

There are also reports in the literature on an association with Addison's disease in a patient who took glucocorticoids for 14 years, and an MRI of the brain revealed a picture of PTS [9]. When studying the hormonal status, an impaired release of luteinizing and follicle-stimulating hormones was noted, which could be a manifestation of both hypogonadism and PTSD syndrome. Finally, PTSD syndrome can quite often be combined with various congenital anomalies (for example, with Hand-Schüller-Christian syndrome [46]). In 1995, a case of PTSD was described in which STH deficiency was noted in combination with DIDMOAD syndrome [40]. The prevalence of PTSD syndrome in children, according to the literature, is underestimated, although it ranges from 1 to 58% [41]. It has been established that perinatal events, changing the blood supply to the pituitary gland or infundibulum, contribute to the formation of PTSD. It is noteworthy that some authors consider it important to take into account the presence of unfavorable perinatal factors in the development of PTSD, while others argue that they have no etiological significance. In both adults and children, PTSD may be associated with hypofunction and hyperfunction of the pituitary gland [43]. The most common endocrine disorders are: isolated growth hormone deficiency [48, 41] (possibly associated with a biologically inactive form of growth hormone),hypogonadotropic hypogonadism, premature puberty [32], delayed puberty. In addition, it should be noted that PTS syndrome can be combined with polyglandular deficiency syndrome in children. Conflicting opinions regarding the incidence of STH deficiency and polyglandular deficiency in children can only be explained by the polymorphism of this disease. Thus, the high incidence of endocrine disorders in PTS syndrome emphasizes the exceptional importance of assessing the function of the pituitary gland in individuals with this disease. Diagnostics The diagnosis of PTS syndrome is based on the results of various examination methods. Craniography data in the lateral projection are usually as follows: no changes in the bone structure and size of the sella turcica, closed cylindrical shape of the sella turcica. In 1/3 of patients, signs of increased intracranial pressure are found: hyperpneumatization of the sinus of the sphenoid bone, increased vascular pattern, digital impressions of the bones of the cranial vault, an increase in the size of the sella turcica with changes in the bone structure. Characteristic craniographic signs are usually more pronounced in secondary PTS. Radiography cannot be used as the sole criterion for diagnosing PTS, since the frequency of detection of intrasellar tumors and PTS syndrome during this study is almost the same. However, there are still frequent cases when an enlarged sella turcica is assessed as a pituitary adenoma and unjustified surgical intervention is undertaken, so further examination should be carried out. Previously, a reliable method for diagnosing PTS syndrome was pneumoencephalography, in which the cavity of the sella turcica is filled with gas to

one degree or another. In 76% of cases, air contrasts well with the basal cisterns and penetrates into the cavity of the sella turcica. In 24% of cases, pneumoencephalography data do not allow us to judge the presence of PTS. At present, this technique has no practical application due to its high trauma and low diagnostic value. Computed tomography combined with the introduction of contrast agents intravenously or directly into the cerebrospinal fluid has a higher resolution [30, 38]. In typical cases, the changes are localized below the diaphragm of the sella turcica; the bottom of the sella turcica is symmetrically located in the frontal projection and has a closed shape. The sella turcica is enlarged mainly in the vertical size, there are no signs of thinning and erosion of the cortical layer, a two-contour bottom is visible on the sagittal section, the lower line of which is thick and clear, and the upper is blurred. Computed tomography in patients with secondary PTS often reveals a decrease in tissue density in its cavity, but this sign is also characteristic of endosellar pituitary adenomas and non-neoplastic cysts, so further diagnostics should be directed towards searching for hormone hyperproduction. It is proposed to consider that the volume of the pituitary gland is up to 150 mm3,revealed by computed tomography data is a criterion for PTS [40]. In cases where computed tomography data reveals a zone of reduced echogenicity, it is necessary to perform computed cisternography with amipak. According to the methodology of this study, the contrast agent penetrates the existing arachnoid coele and provides good contrast of PTS, but in 2% of cases this procedure is uninformative. Let us give the following example: a patient with hyperprolactinemia was diagnosed with PTS according to CT data of the brain, and an MRI study revealed a microprolactinoma localized in the lower part of the sella turcica. Moreover, computed tomography is associated with allergic reactions to endolumbar administration of amipak. Computed tomography with contrast and pneumoencephalography are invasive methods and are combined with a significant radiation load. A modern diagnostic method for detecting PTSD is a non-invasive method of intrascopic diagnostics - MRI, based on the phenomenon of nuclear magnetic resonance. The method allows conducting research without the use of ionizing radiation, the introduction of iodine substances, the study can be carried out repeatedly and in 3 mutually perpendicular planes [45]. The state of the pituitary gland and the cerebrospinal fluid-conducting system is most clearly and informatively assessed in the sagittal section. When comparing the MRI picture of the brain in healthy individuals and patients with PTSD, it was found that the relative signal intensity of the deformed pituitary gland is significantly lower, especially on the T-echo image [30]. The MRI picture of PTS looks like this [2]: in the area of the unchanged sella turcica there is a zone of low signal intensity, which has a clear glow when performing "MR myelography", which is interpreted as the presence of fluid contents in the

intrasellar area - cerebrospinal fluid, the pituitary gland is deformed and takes the shape of a sickle or a crescent 2-4 mm thick and is flattened along the bottom of the sella turcica. Many studies devoted to MRI of the brain in PTS syndrome allow us to conclude that the diagnostic value of MRI in this pathology reaches 100%. Domestic and foreign researchers of the problem of diagnosing PTS syndrome recommend MRI of the brain in patients taking dopamine agonists, thyroid hormones for a long time, as well as in patients diagnosed with hypopituitarism, since these factors lead to the formation of PTS. Treatment. Treatment of neuroendocrine disorders in PTS syndrome depends on the clinical picture and hormonal levels. Dehydration and vascular therapy are indicated to improve hemodynamics in the chiasmal-sellar region. The severity of motivational and psychovegetative disorders determines the introduction of vegetotropic and psychotropic drugs into the spectrum of therapeutic measures. The threat of vision loss is an indication for surgical intervention [8].Currently, transsphenoidal extradural insertion of a removable silicone-filled balloon [18] is widely used abroad [40]. An alternative approach is tamponade of the sella turcica with fat [39], muscle, cartilage or bone [3] with the possibility of performing a simultaneous adenomectomy [7]. With the help of the listed methods, the severity of headaches and visual disturbances decreases within a few days, which would be difficult to achieve in some cases by therapeutic measures. A method for treating progressive vision loss in this disease has also been proposed - transsphenoidal chiasmopexy [28|, and lumboperitoneal shunting is successfully used in patients with intracranial arterial hypertension and PTSD. There is an opinion that the combination of spontaneous spinal rhinorrhea and progressive visual impairment in combination with severe intracranial hypertension is an indication for surgical treatment, for example, tamponade of the sella turcica with muscle, cartilage [49]. The prognosis of PTS syndrome is determined by the degree of endocrine, neurological and ophthalmological disorders. With adequate symptomatic therapy, a favorable course of the disease can be ensured.

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