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A Patient With Congenital Hypopituitarism And The Dynamics Of Clinical Manifestations Case From Practice

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ABSTRACT

In this article, the authors lead a case from practice. Given the clinical and hormonal characteristics, as well as specific changes according to MRI, the diagnosis of "congenital hypopituitarism" did not cause doubt. After the purpose of the chorionic gonadotropin of 1500 units 2 times a week for 2 months, there was a positive dynamics from the genital organs.

KEYWORDS

Congenital hypopituitarism, hormone deficiency, differential diagnosis.

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INTRODUCTION

Growth hormone deficiency (GHD) syndrome in children is a complex pathogenetic of various diseases with similar clinical symptoms. The incidence of STH deficiency in children ranges from 1: 10,000 to 1: 4,000 newborns. At the same time, the genetic basis of growth hormone deficiency in the presence of first-degree relatives with the same pathology is found only in 5-30% of cases [2]. Congenital hypopituitarism is characterized by multiple deficiencies of tropic hormones, primarily growth hormone, thyroid-stimulating hormone, prolactin, adrenocorticotropic hormone and gonadotropins. The incidence of congenital hypopituitarism ranges from 1: 3000 to 1:10 000 newborns [10], and in the neonatal period, this disease is diagnosed only in 23% of cases [2,4].

Most often, the aetiology of congenital hypopituitarism is mutations of various transcription factors involved in the ontogenesis of the pituitary gland (PROP1, PIT1, HESX1, etc.).

In addition, congenital hypopituitarism can occur as part of various syndromes caused by chromosomal deletions, and also be combined with malformations of the midline [3,11].

The clinical manifestations of this disease vary and directly depend on the combination and degree of tropic hormone deficiency. Most often, one of the first and obvious signs of congenital hypopituitarism is progressive growth retardation, which becomes apparent after 2-3 years of life and is caused by a deficiency of growth hormone. However, in the neonatal period, the manifestations of hypopituitarism are extremely nonspecific and are often disguised as various diseases of the liver and bile ducts, as well as infectious diseases or neurological disorders.Symptoms such as cholestasis and hypoglycemia usually come to the fore. If a newborn boy had an intrauterine deficiency of gonadotropins, this can lead to underdevelopment of the penis (micropenis) and/or cryptorchidism [1,6].

If a child has secondary adrenal insufficiency as part of congenital hypopituitarism, symptoms such as bradycardia decreased blood pressure, muscle hypotension and associated respiratory disorders may be observed. In addition, electrolyte disturbances in the form of persistent hyponatremia may occur. The frequency of neonatal manifestations of hypopituitarism with cholestasis syndrome and hypoglycemia has not been precisely determined. For the first time, Lizzard and Alberts in 1956 described a patient with hypopituitarism, one of the first manifestations of which was cholestasis and hypoglycemia. Since then, several series of cases have been described [1, 4].

The severity of cholestasis can vary widely from minimal to significant, requiring differential diagnosis with other liver diseases, including biliary atresia. These changes, as a rule, are transient and are completely stopped against the background of substitution therapy. Most international recommendations for the diagnosis of growth hormone deficiency (GHD), based on expert experience, have a low level of evidence. Determination of the level of GHD after stimulation tests below 7 μg/L confirms the diagnosis of severe GH deficiency with 100% sensitivity and 98% specificity in the presence of clinical signs of GH deficiency [4, 5].

For the detection of somatotropic insufficiency, a single measurement of the level of GHD is impractical, since its level is subject to an extremely variable circadian rhythm. In this case, investigate the concentration of insulin-like growth factor (IGF-1) [6].

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Magnetic resonance imaging (MRI) is used to assess changes in the chiasmatic-sellar region. At the same time, there are several changes in pathognomonic hypopituitarism. Among them, one can distinguish the MR picture of an "empty" or "partially empty" sella turcica, a "triad" including hypoplasia of the adenohypophysis, ectopia of the neurohypophysis, agenesis of the pituitary funnel. With mutations of the PROP1 gene, an enlargement and thickening of the adenohypophysis are revealed [7-9].

However, during the neonatal period, these MR images may not always correspond to the characteristic changes in hypopituitarism. Molecular genetic studies are not necessary to confirm the diagnosis, but in some situations, they can be used to assess the prognosis of the disease [8].

The main principle of the treatment of hypopituitarism is adequate hormone replacement therapy. On-time, the treatment started allows you to maximize the further physical and psychomotor development of the child [10, 12].

The blurring of clinical manifestations of hypopituitarism in the neonatal period, difficulties in interpreting hormonal parameters and the absence of characteristic MRI signs often lead to late diagnosis and untimely initiation of therapy. All of the above emphasizes the relevance of the study.

The objective of the study: to present the clinical manifestations and stages of diagnosis of congenital hypopituitarism using the example of clinical observation.

MATERIALS AND METHODS

On the basis of the Republican Specialized Scientific and Practical Medical Center of Endocrinology of the Ministry of Health of the Republic of Uzbekistan named after Academician Y.Kh. Turakulov in the children's department, a teenager with congenital hypopituitarism was examined, which was revealed by a specialist during the screening of 1,500 adolescents with delayed puberty at school No. 12 in the Sh. Rashidov district of the Jizzakh region. The patient did not present any complaints on his own. In our observation, the child was born full-term with normal indicators of weight and body length, in a satisfactory condition. The patient underwent a detailed biochemical blood test, a hormonal blood test with an assessment of the level of cortisol, ACTH, TSH, svT4, IGF-1, STH, LH, FSH, prolactin, free testosterone, as well as karyotyping, ECG, ultrasound of internal and sexual organisms, hand radiography, magnetic resonance imaging (MRI) of the brain.

RESULTS AND DISCUSSION

Complaints about: headaches, dry skin, constipation, decreased vision on the sides.

Anamnesis vitae. The male child, Meliboev Sardor, was born at the 39th week of gestation on November 22. 2007 with a bodyweight of 3210 g, a length of 50 cm. At birth, phenotype features were revealed: a small mouth, low auricles, a flat bridge of the nose (Fig. 1). The child's psycho-motor development took place on time.

Status praesens. Noteworthy is the short neck, low-set ears, flat bridge of the nose, short fingers and toes (Fig. 2) funnel chest. These are phenotypic signs of holoprosencephaly defects. The boy had a micropenis.

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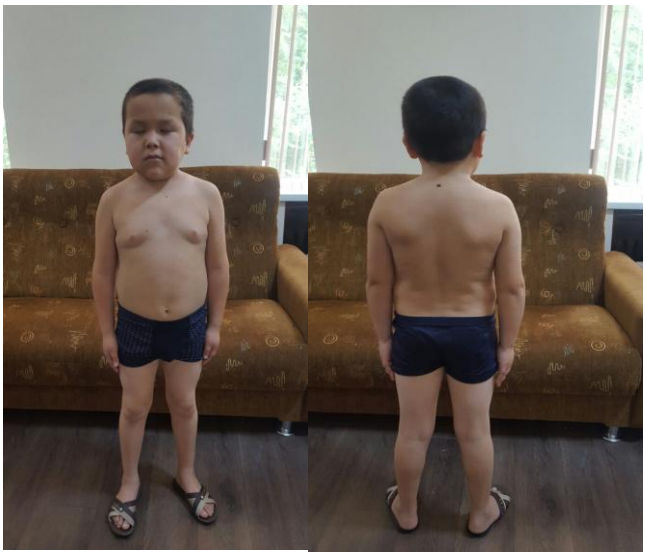

Fig. 1. Patient S. Meliboev, 14 years old

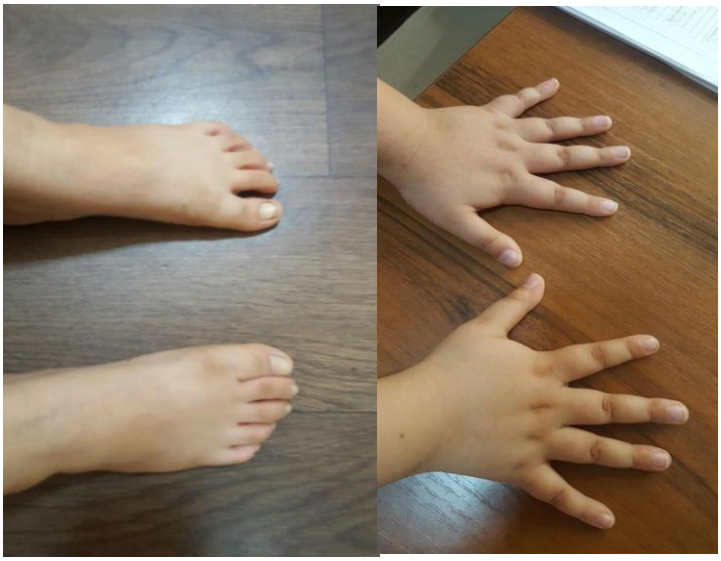

Fig. 2. Short toes and toes

The patient has all the symptoms of GH deficiency: short stature, lagging bone age. Deficiency of GH in our case was the cause of secondary hypothyroidism with corresponding symptoms - dry skin, constipation, chilliness, bradycardia, slowness of speech, movements.

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Laboratory data:

OAK: WBC leukocytes-6.5x10^9/l, Lymph # Lymphocytes 2.7×10^9/l, Mid # cells of medium sizes 0.7×10^9/ l, Gran # granulocytes 3.1×10^9/ l, Lymph% lymphocytes 42.1%, MID% of medium-sized cells 10.5% Gran% granulocytes 47.4%, rod 1%, segmented 60%, eosinophils 5%, basophiles -, monocytes 2%, lymphocytes 32, HGB hemoglobin-120g/l, RBC Erythrocytes - 4,75×10^{12}/l, HCT hematocrit 40.1%, MCV average volume of erythrocytes 84.6 f/l, MCH The average hemoglobin content in erythrocyte 26.9 P/g, MCHC average concentration of hemoglobin in erythrocyte 319 g/l, RDW-CV (Erythrocyte anisatosis) 13.2%, RDW-SD (Erythrocyte anisocytosis) Standard deviation 46.2 Φ/l, PLT platelets 316×10^9/ l, MPV average volumetric volume 8.1 F/l, PDW (platelet anisocytosis) 15.5, PCT thrombocrit 0.255%, ESR ESR 11 mm/h, coagulation time 1`15-4`10. General urine analysis: relative density 1018, reaction sour, protein traces of g/l, on non-cordan L - 2000, ER - 1000, epithelium flat 2-3%, mucus +, bacteria +++. Biochemical tests: urea 5.3 mmol/l; urea - 3.9 mmol/l, creatinine 37 MG/L; Alt 27 mmol/l; AST 34 mmol/l; Bilirubin shared 8.4 Mol/l; Potassium 3.2 mmol/l, sodium - 138 nmol/l, glycemia 4.6 mmol/l, calcium -2.4 mmol/l. Hormonal tests: ILL TTH 4.85 MME/L (0.4 - 6.2 Norm); STG - 0, 3 ng/ml (normally from 2 to 10), IFR -1 - 59 nmol/l (normally 344), VIT D 16.5 ng/ml, T4 - 0.60 NGG/DL (0 , 93 - 2.0) Testosterone 0.08 nmol/l (8,64-29.0.). ECG: moderate sinus tachycardia with Ch.S.S. 88-100 per minute. Moderately metabolic changes in myocardium left ventricle. Radiography of the right brush in direct projection - bone age corresponds to 8-10 years. Growth zones are open. Uzi genitals: testicular hypoplasia. MRI - pituitary - hypoplasia pituitary.

Inspection of the neuropathologist: Astheno-neurotic syndrome. Inspection of the urologist: urinary tract infection, complicated form. Chronic pyelonephritis in the phase of active inflammation.

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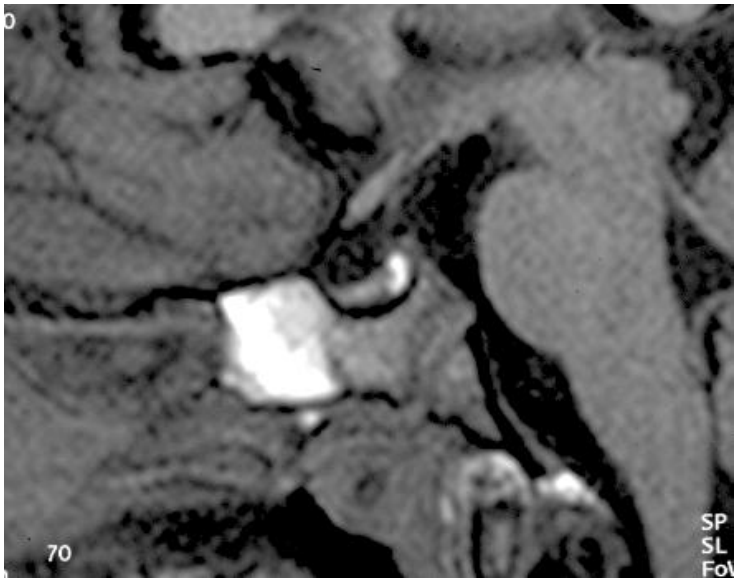

Fig. 3. MRI patient Melibeyev S., 14 years

Oculist: Dzn Border Clear. Fabric pale pink, veins convoluted, the arteries are narrowed, there are no pathological foci. Ou angiopathy vessels retina

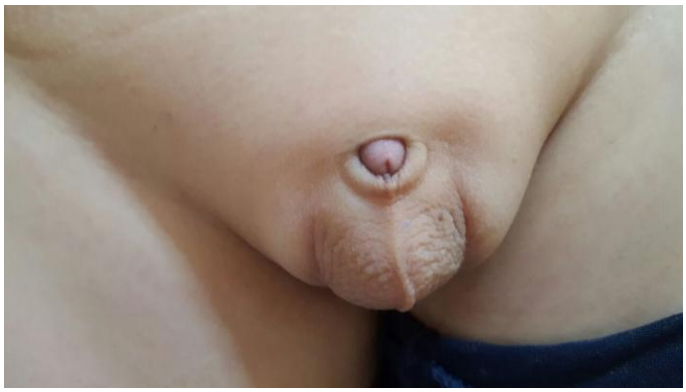

Fig. 4. State of the testicles to therapy xG

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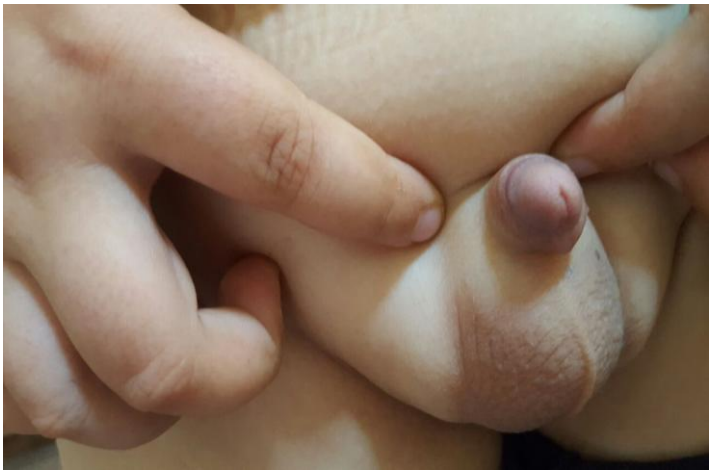

Fig. 5. The state of the testicles after therapy XG

The clinical diagnosis is set:

OSN. Congenital hypopituitarism.

Don OSN. Hypogonadotropic hypogonadism, STS - insufficiency. Secondary hypothyroidism.

Snoots. DZ. The deficiency of Vit D. false 2x supporting gencom the same. Obesity 1 Art. Hypochromic anaemia of easy degree. Urinary tract infection, complicated form. Chronic pyelonephritis in the phase of active inflammation. Angiopathy retinal vessels.

The child has treated: Levothyroxine 75 mg daily in the morning on an empty stomach constantly, chorionic gonadotropin 1000 meters 2 times a week in / m №10, chiculciferol WIT D to 5-6 CAPs 1 time in the morning constantly, vitamin complex VITA-Zinc in 5 ml x 2 3 times a day 1 month, Nitroxoline 2 Tab x 3 times a day - 3 days, Fusis 50 - 1 Tab X 1 time x 4 days.

After 1 month of therapy, there was a noticeable increase in the sizes of the testicles (Fig. 4, 5).

DISCUSSION

In our case, the child already in the neonatal period was manifested by signs of hypothyroidism, and in the 1st year of life, a pronounced lag at the rate of growth was revealed, the cause of which was STG deficiencies.
In this case, in addition to the loss of trophic functions of the pituitary, other specific features are noted: 1) hypoplasia of optic nerves, 2) Agnesia or hypoplasia of a transparent partition and/or corn body.

The loss of trail functions of the pituitary gland is very diverse: from an isolated STG deficiency to panhypopituitarism. It is worth noting that, according to Kelberman et al. (2009), HESX1 gene mutations lead to the development of insulated hypopituitarism, which may indicate a dose-dependent mechanism. Recent studies indicate the lack of correlation of the genotype-phenotype with a given disease, and most cases of septooptic dysplasia remain sporadic, without a mounted mutation [22, 23].

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Given the clinical and hormonal characteristics, as well as specific changes in MRI data, the diagnosis of "congenital hypopituitarism" in these cases is no doubt, despite the negative results of the genetic survey.

CONCLUSION

The diagnosis of congenital hypopituitarism in the neonatal period is a challenge. The presence of hypoglycemic syndrome in combination with cholestasis serves as a reason for holding a laboratory study of TSH levels, svT_4, ACTH, Cortisol and consultation of the endocrinologist. Timely hormonal diagnosis increases the effectiveness of treatment and avoids unjustified conducting invasive techniques, such as liver biopsy. In the time, adequate replacement hormone therapy began to improve such clinical symptoms as testicular hypoplasia.

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