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A CLINICAL CASE OF HYPOPITUITARISM IN AN EIGHT-YEAR PATIENT

A clinical case of hypopituitarism, a rare disease, is diagnosed in an eight-year patient. The early diagnosis of the condition was complicated by specific clinical manifestations. The delayed diagnosis and late replacement therapy resulted in retarded growth of the child.

Keywords: hypopituitarism, retarded growth, hypophisis (pituitary gland), replacement therapy.

Introduction. Hypopituitarism [ICD-10 code: E23.0] is a thyroid disorder resulting from the deficiency of one or several hormones produced by the hypophisis (pituitary gland). It is a rare disease which can be congenital or acquired; thus it can occur in infants, children, teenagers and adults [1,4]. The congenital causes include perinatal traumas (birth asphyxia, birth traumas), disturbed development of the pituitary gland, ectopic position of the neurohypophesis, Pallister-Hall syndrome (hypothalamic hamartoma and polydactyly), genetic disturbances (isolated deficiency of GH, PIT1 and PROP1 mutations, septo-optic dysplasia, gonadotrophin deficiency) and disturbed development of the central nervous system (anencephaly, holoprosencephaly, aplasia or hypoplasia of pituitary gland) [5]. Acquired causes of hypopituitarism include infiltrative disturbances (tuberculosis, sarcoidosis, X-histiocytosis, lymphocytic hypophisis and tumors [7].Most commonly the disease results from PIT1 and PROP1 gene mutations which are caused by transcription factors.

Severe deficiency of somatotropic hormone and prolactin are characterized by PIT1 gene mutation. Deficiency of thyrotrophic hormone may vary by its expression. Retarded growth from the birth, secondary hypothyreoidism and low prolactin level will be diagnosed clinically. Development of adrenal insufficiency and secondary hypogonadism is not characteristic [1,8].

Perinatal signs of hypopituitarism are absent in children with mutation in PROP1. Mean weight and height at birth are within the normal features. Hypoclycemia and long-lasting jaundice of the newborn are not common [1,3,8]. The diagnosis is made when the parents complain of short stature. Deficiency of thyrotrophic hormone can be present at birth and it most commonly occurs together with the deficiency of growth hormone. Hypothyroidism is not expressed. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) deficiencies are revealed at puberty. Insufficient production of adrenocorticotropic hormone (ACTH) is less common, its deficiency is usually revealed at puberty and adulthood [6].

Neuroimaging of hypothalamic-pituitary area commonly reveals hypoplastic or normal anterior and posterior lobes of the pituitary gland [2].

It is known that the early diagnosis of the disease corresponds to expression of the symptoms and thus possible diagnosis of congenital hypopituitarism. In 2019 Child et al declared the median age of hypopituitarism diagnosis to be 11 years [6]. At the same time Boros et al suggested that those patients diagnosed with hypopituitarism after 10 years of age should be referred as late ones when making a final diagnosis [3].

Objectives: The article is aimed at describing the clinical case of hypopituitarism in an eight-year patient.

The research was agreed by the local committee of biomedical ethics in Yakutsk scientific center “Complex medical problems” in accordance with the Helsinki declaration #54, signed in 20.12.2021 #1, declaring ethical responsibility. The legal representatives of the patient signed agreement in a case history, which allows referring to the data anonymously. All the personal data of the patients were deidentified.

In 27.11.2023 the patient M. was admitted to the department of endocrinology and gastroenterology of M.E. Nikolaev Republican hospital #1 of the Republic of Sakha (Yakutia) at the age of 8 years. He complained of short stature, rapid fatigue and constant constipations. The patient is Russian.

Past medical history shows that retarded growth was noticed at the age of 5 years. The patient was referred to the in-patient department for further check-up. The retarded growth was noticed at the age of 4-5 years as his father said.

Past history shows that he was born from the third pregnancy which ran normally. He was born on the 40th week, weight at birth was 3300 gr, and height was 53cm. Nervous and psychological development was not disturbed and corresponded to his age. He rarely was ill with infectious diseases of the respiratory tract, he had chicken-pox. No known allergies were noticed.

Family history: mother’s height – 160 cm, father’s height – 170 cm, brother’s height (12 years) – 150 cm (-1.12 SDS).

Objective examination: Height – 122 cm (-2.32 SDS), weight – 20 kg, BMI – 14.8 kg/m2 SDS BMI (-1.36 SDS).

The condition is satisfactory. General state is normal with clear consciousness. Appetite is not disturbed. No meningeal signs, focal neurological symptoms are absent. The Romberg test is negative. The patient sleep is satisfactory. The body

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habitus type is hyposthenic with moderate diet. The bony and muscular system has no abnormalities. The pharynx is not hyperemic. Mucous membranes of the mouth and pharynx are clear and pale. Nasal breathing is not complicated and free. The osteoarticular system shows no anomalies. The lymphatic nodes are not enlarged. The thoracic cage is regular. On percussion the lungs tone is clear on all sides. Breathing is vesicular, with no rales and wheezes. Cardiac tones are clear and rhythmic. Abdomen is soft and painless. The liver and the spleen are not enlarged. The right foot is swollen. No peripheral swollen areas are noticed. Urination is free and painless. Urine is light and transparent. The outer genitals are formed correctly and have the male type. Puberty corresponds to Tanner stage 1.

The full blood count (28.11.2023): leukocytes – 11.42 (RI 4.27-11.40); lymphocytes – 4.29 (RI 0.97-4.28); eosinophils – 6% (RI 0.00-4.70).

Urine test (28.11.2023): the results correspond to the norm.

Biochemical blood test results (28.11.2023): biochemical blood test results correspond to the norm.

Hormone profile (28.11.2023): Thyroid stimulating hormone (TSH) – 11.00 IU/L (RI: 0.40-7.00), free T4 – 15.17 pmol/L (RI: 8.00-17.00) antibodies to thyroid peroxidase (Ab to TPO) – 0.19 U/mL (RI: 0.00-30.00). Conclusion: high level of thyroid stimulating hormone.

Insulin tolerance test (06.12.2023): 0II – 0.28 ng/mL, 15II – 1.42 ng/mL, 45II – 1.16 ng/mL, 60II – 1.04 ng/mL, 90II – 0.58 ng/mL, 120II – 1.06 ng/mL. Conclusion: insufficient production of somatotropic hormone.

MRI and magnetic resonance angiography of the brain (03.12.2023): No focal and space-occupying lesions in the brain structures were revealed. No hemodinamically significant changes in the vessels of the brain were found out.

X-ray of the wrist with wrist joints (radiocarpal articulations) (28.11.2023): bone age corresponds to 5.5-6 years.

Digital lateral skull X-ray (28.11.2023): Intracranial hypertension. Adenoid hypertrophy grade 2-3.

Discussion. A short stature patient passed a regular check-up at the department of endocrinology. The child was a full-term newborn with normal height and weight in a satisfactory condition. Due to unspecific manifestations of the disease at the early childhood the diagnosis was complicated.

Congenital hypopituitarism is diagnosed after hormone examination. The patient has confirmed deficiency of somatotropic hormone according to glucose intolerance test. Insulin-like growth factor 1 is also examined, as a single identification of somatotropic hormone is incorrect to diagnose a disease because of its high variety.

Taking into account height indices, low concentration of insulin-like growth factor 1 the following diagnosis was made: hypopituitarism with isolated deficiency of somatotropin.

The isolated deficiency of somatotropin is the commonest in most cases. It is a rare case with incidence from 1 per 4,000 to 1 per 10,000. Etiology of most cases remains unknown.

The treatment efficiency depends on early identification of hormone deficiency. This patient is administered a replacement therapy with recombinant somatotropin.

Conclusion. Congenital hypopituitarism is a rare disease with unspecific manifestations which complicates early diagnosis and due time therapy.

The patients with hypopituitarism need a life-long surveillance and replacement therapy.

Early reveal and diagnosis of hypopituitarism in children, administration of adequate replacement therapy with hormone require clinical suspicion and awareness of the local pediatricians. It is important to remember that this disease can be caused not only by isolated somatotropin but also deficiency of other tropic hormones of the pituitary gland resulting in certain clinical picture.

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