CLINICAL CASE

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CASES OF ADRENOCORTICAL CANCER IN CHILDREN IN THE REPUBLIC OF SAKHA (YAKUTIA)

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The article describes cases of primary tumor of the adrenal cortex and adrenocortical cancer in two children. In one case, the tumor turned out to be hormone-active, with increased cortisol secretion with the development of Icengo-Cushing syndrome. In the first case, stage II of the tumor process was established, in the second – stage IV. The children received combined treatment, surgery and chemotherapy. In the first patient, the treatment was successful, the child is in remission for 4 years, in the second case, the outcome is fatal, due to the progression of the malignant process.

Keywords: adrenocortical cancer, children.

Introduction. Adrenocortical cancer (ACR) is a rare high–grade tumor originating from the cortical layer of the adrenal gland. The incidence of ACR is 0.2 cases per 1 million children per year, and its share of all malignant neoplasms in children and adolescents is about 0.2%. [1]. There are 2 peaks in the incidence of ACR: this is the 1st and 4th decade of life, in children it is the age of up to 5 years. Girls get sick more often than boys [5].

Most ACS are sporadic, but in children it is often associated with hereditary syndromes (Lee–Fraumeni, Gardner, multiple endocrine neoplasia type 1). In childhood, secretory active ACR is diagnosed in 70-80% of cases, and the most common symptom occurring in 50-80% of cases is virilization [4]. According to Dark A.S. et al. (2021) in children with ACR, in 71.1% of cases, pathological secretion of one hormone or more occurred. Clinical Cushing's syndrome was observed in 26.3% of patients [1, 2]. The prognosis (outcome) of the disease depends on the stage of the tumor. Thus, in patients with stage I and II of cancer, the five–year survival rate is 80 and 50%, respectively, and in patients with stage III and IV - 20 and 10% [3].

The purpose of the study: to present cases of ACR, a rare pathology in children.

Material and methods of research. The article presents a description of two children with ACR who passed through the oncology department of the Pediatric Center of the Republican Hospital No. 1 – National Center of Medicine (PDC RB No. 1-NCM).

Results and discussion. The first patient. The girl, 11 months old, was admitted to the department with complaints of overweight, emotional lability, a rash on her face, stopped walking and resting on her legs.

The child's mother is 43 years old, the father is 41 years old. A girl from 6 pregnancies, 2 births. The first and second half of pregnancy proceeded with the threat of termination. Delivery on time at 37 weeks, operative. Body weight at birth is 3030 g, body length is 50 cm. The Apgar score is 8/9 points, she screamed immediately, the scream is loud. Attached to the breast immediately, sucked actively. The umbilical cord residue disappeared on the 5th day in the hospital. They were discharged home on the 7th day. Breastfeeding for up to 6 months, then artificial. Psychomotor, mental development by age.

3 months before hospitalization, increased appetite appeared, including at night, and began to gain weight. Over time, the girl began to limp on her right leg, then stopped walking, resulting in turning to the reception and diagnostic department of the PSC AI RS (Y) "RH No. 1-NCM". During ultrasound of the abdominal cavity, the formation of the adrenal gland, liver was detected.

The condition of the child at admission is severe, due to the tumor process. Well-being is moderately disturbed. The child's height is 75 cm, weight is 10 kg, BMI is 17.78. Matronism, moon-shaped face, bulemia, can't follow through the night without feeding. The skin is of normal color, clean, hypertrichosis. Acne on the cheek, chin (fig. 1). Peripheral lymph nodes are not enlarged. Does not walk, rests on the legs with difficulty. Breathing is puerile, there are no wheezes. The heart tones are rhythmic, clear. Heart rate – 120 beats per minute. Arterial pressure (BP) 201/124 mmHg. The abdomen is enlarged in size, there is a dense formation in the right hypochondrium, protruding 7 cm from under the costal arch. Stool is formed. Urination is not disturbed.

In the hemogram at admission – moderate polycythemia (leukocytes 15.6 thousand / ml, erythrocytes 5.16 million / ml, hemoglobin 160 g / l, hematocrit 44.8%, ESR – 2 mm / h). The daily rhythm of cortisol and ACTH was 655.6 nmol/l and 46.67 pg/ml at 08:00 and 606.6 nmol/l and 53.06 pg/ml at 22:00, respectively (cortisol norm 28-966, ACTH up to 46). The level of cortisol in the daily urine is 724.8 mcg / day at a rate of up to 190 mcg / day. The levels of metanephrine and normetanephrine in the daily urine were within the normal range. Electrolyte disturbances in the form of hypokalemia – 2.3 mmol / l.

During computed tomography (CT), MRI of the abdominal organs with contrast enhancement (CU) in the projection of the right adrenal gland, a formation

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with clear, somewhat uneven contours, heterogeneous structure due to small linear and ring-shaped calcinates, dimensions on axial sections of 6.0 * 6.6 cm and vertical size of 7.2 cm was revealed. After CU, hypodensic decay sites were detected in the formation. The formation squeezed the right lobe of the liver, displaced and squeezed down the right kidney, displaced the inferior vena cava inside (Fig. 2). The left adrenal gland was unchanged. In addition, cysts and concretions of both kidneys, doubling of the left kidney with incomplete doubling of the ureters were found. Osteoscintigraphy with technetium showed no signs of focal bone damage.

To verify the diagnosis, a fine needle biopsy of the formation was performed. The material was sent to the Federal State Budgetary Institution "NMRC PHOI named after Dmitry Rogachev". Histological conclusion: the pathological change and immunophenotype correspond to an adrenocortical tumor, reliable determination of its malignant potential is not possible due to the small volume of material. Taking into account high arterial hypertension, therapy with Amlodipine at a dose of 2.5 mg / day and Bisoprolol 1 mg / day was prescribed. In the future, the girl was sent for specialized treatment at the FSBI "National Medical Research Center of Endocrinology" (NMRCE) of the Ministry of Health of the Russian Federation in Moscow.

Correction of antihypertensive therapy was carried out in the children's department of the NMRCE and the diagnosis was verified: cortisol-producing adrenal tumor. Then the girl was transferred to the surgery department, where an operation was performed – an open removal of the right adrenal gland with a tumor. The result of histological examination of the formation is Adenocortical cancer of the right adrenal gland (5 points on the Weineke scale), Ki67 15-20%. According to the instrumental methods of investigation, metastatic lesions of regional lymph nodes and distant metastases were not detected.

After the operation, replacement therapy with Cortef and Cortineff was started. The child's condition improved, she began to get up, walk with support, anxiety disappeared, external manifestations of Cushing's syndrome decreased, blood pressure normalized (100-110 / 65-75 mmHg). Given the high degree of malignancy, as well as iatrogenic damage to the tumor capsule, as a result of an earlier puncture biopsy, the girl was prescribed chemotherapy, Mitotan (Lysodren). Against the background of mitotane therapy (the dose of the drug was corrected according to its concentration in blood serum) at the age of 1 year 7 months, an estrogen–like side effect developed - an increase in mammary glands, the size of the uterus by ultrasound up to 8-9 years, a slight increase in estrogens. There was no acceleration of bone age. Hypothyroidism was detected, probably associated with taking a chemotherapy drug, and therefore L-thyroxine was connected to therapy. In the future, against the background of taking mitotan, there was a progressive increase in the mammary glands, the appearance of mucous secretions from the genital tract. At the control examination in NMRCE at the age of 2 years, there were no signs of relapse and metastases, chemotherapy was canceled. Permanent replacement therapy with gluco- and mineralocorticoids and L-thyroxine is recommended.

Currently, the girl is 5 years old, physical development corresponds to age, speech development delay. A year ago, Cortef and Cortineff were canceled, 9 months ago – L-thyroxine.

The second patient. A boy, 3 years old, was admitted to the department with complaints of an increase in the size of the abdomen. According to the ultrasound examination of the abdominal organs, a huge abdominal formation was visualized, the exact localization of which could not be determined.

In the oncology department, examinations were conducted to clarify the anatomical localization and nature of the formation, and an assessment of the prevalence of the process was also performed. Computed tomography revealed in the left half of the abdominal cavity a huge solid formation emanating from the left adrenal gland of a heterogeneous structure due to areas of softening and calcification, the size of 12,3*9,2*15.4 see, after contrast enhancement, the formation moderately unevenly accumulates a contrast substance. The formation squeezes, shifts down, does not separate from the left kidney, shifts up the spleen, stomach, intestinal loops are pushed to the right (fig. 3). The left adrenal gland is not traced against the background of the tumor. In S5 of the left lung, a lesion up to 0.9 cm in size was detected, with an intensive accumulation of contrast agent, regarded as metastasis. There is also a small lesion up to 0.2-0.3 mm in the S9 of the right lung Intra-thoracic lymph nodes up to 0.7-0.8 cm in size.

Taking into account the age of the child, the localization of the tumor, a differential diagnosis was made between tumors of the adrenal cortex and neuroblastoma. The study of hormonal status (thyroid-stimulating hormone, adrenocorticotropic hormone (ACTH), renin, cortisol) revealed no pathology. Neuron-specific enolase within normal values. Scintigraphy of the skeleton with technetium of the lesion of the bones of the skeleton did not reveal.

To verify the diagnosis, a fine needle biopsy of the formation was performed. Histological examination showed that the tumor is alveolar-nested structure, with extensive foci of necrosis. Neoplastic tissue is constructed from medium-sized and large cells with abundant eosinophilic or optically empty cytoplasm. Nuclei with pronounced pleomorphism, there

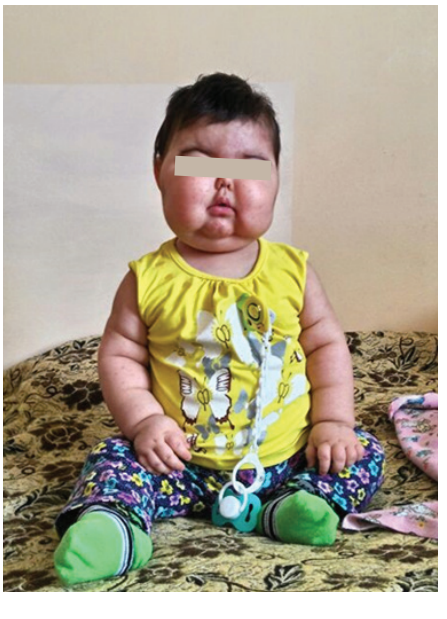

Fig. 1. A girl of 11 months with Itsengo-Cushing syndrome, with a hormone-active ACR

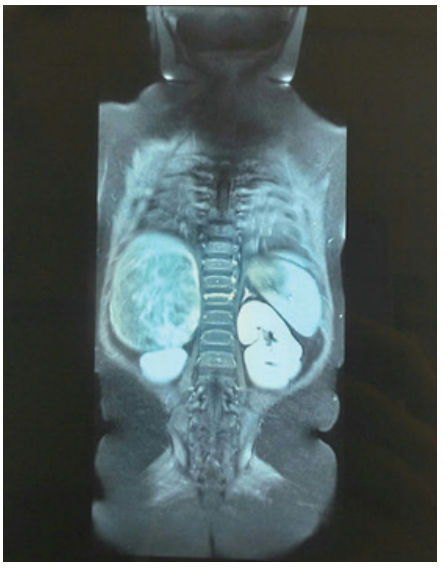

Fig. 2. MRI of the abdominal organs of the girl 11 months. Formation of the right adrenal gland

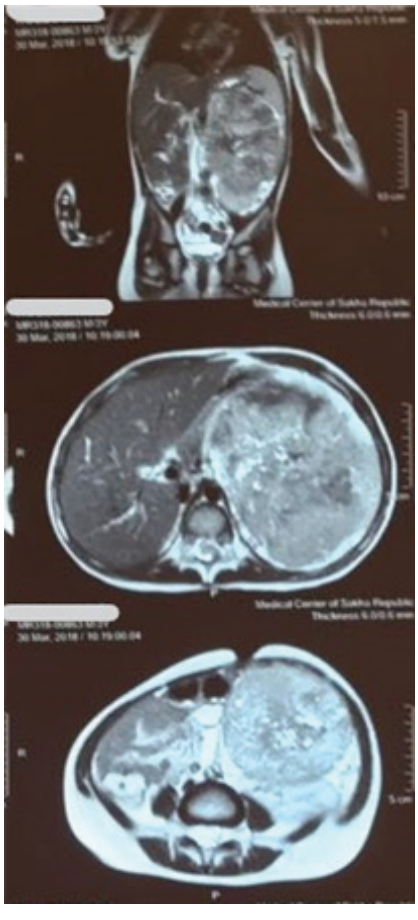

Fig. 3. Abdominal CT with contrastenhance 3 years old boy, demonstrating a large heterogeneous mass in the left adrenal gland. The overall size of this mass was1742 cm3

are large hyperchromic nuclei with the presence of pseudo-inclusions. Mitotic activity of 7 mitosis figures in 5 fields of view at magnification of the microscope x 400. An immunohistochemical study was performed with antibodies to Chromogranin A, HMB45, Inhibincc1, Ki67 up to 40-45%. The reaction with the rest of the antibodies is negative. Histological conclusion: correspond to adrenocortical carcinoma, ICD-0 code 8370/3.

The tactics of the child's treatment were discussed with leading pediatric oncologistsNational Medical Center of Pediatric Hematology and Oncology (NMC PHO) named after D. Rogachev. 2 courses of chemotherapy according to the EDP/M scheme (etoposide, doxorubicin, cisplatin, mitotan) were carried out in the oncological department of the PC NMC.

For the surgical stage of treatment, the child was sent to the Federal Center (NMC PHO) named after D. Rogachev, where the operation was performed: laparotomy, arteriolysis and venolysis of the left renal pedicle, adrenalectomy on the left, ipsilateral retroperitoneal lymph

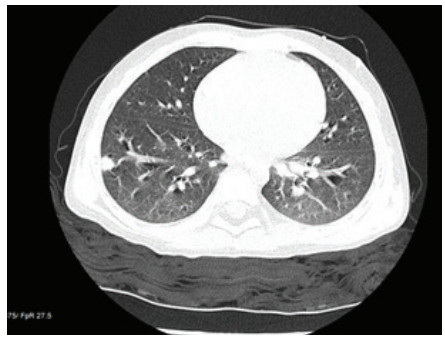

Fig. 4. Axial sections of contrastenhanced breast CT, demonstrating metastases of S9 right lung

dissection. Histological conclusion: Adrenocortical carcinoma (8 criteria on the Weiss scale; 28.4 points on the VanSlooten scale, 5 criteria on the AFIP scale for tumors of the adrenal cortex in children). Taking into account the histological type of the tumor and the prevalence of the tumor process, chemotherapy according to the EDP/M scheme was continued at the place of residence. During the control examination after 4 courses of chemotherapy, according to lung RCT, there was an increase in the formation of the right lung in S9 to 8mm (fig. 4), a decrease in the focus in S5 of the left lung. For histological verification and removal of the formation, resection of the formation in S9 of the right lung was performed. Histological examination showed that the tumor tissue with nodular growth of a solid structure, constructed from fields of cells with abundant eosinophilic cytoplasm and large nuclei with pronounced polymorphism (the histological structure of the tumor is identical to that in previous biopsies). Therapeutically induced changes are not pronounced. Perifocal hemorrhages, focal lymphocytic infiltration. Thus, histologically, metastasis to the lung was confirmed.

In total, 8 courses of chemotherapy were carried out according to the EDP/M scheme. Taking into account the stabilization of the process and the intensity of polychemotherapy, the child was left under dynamic observation while taking mitotan. After 6 months, the progression of the disease was established: during the control examination, an increase in the previously detected solid formation in the basal zone of the right lung, with clear contours, dimensions, was noted 3,4*3,3*3,0 cm, with moderate accumulation of contrast agent.Education is distributed in segments S2, S4. Management and treatment tactics were discussed jointly with leading pediatric oncologists of the D.Rogachev National Research Medical Center. Based on the data of the international literature and practical recommendations for the treatment of cancer of the adrenal cortex RUSSCO, an attempt was made to treat with second-line therapy according to the gemcitabine/capecitabine scheme. However, after 2 blocks according to this scheme, there was a continued growth of metastases in the lungs. Due to the lack of standards for the treatment of children with relapses / progression of ACR, tumor progression in the treatment of 2 lines, curative methods are considered exhausted. The child was referred for palliative care at the place of residence.

Conclusion. Thus, the clinical picture of adrenal cortex cancer depends on the hormonal activity of the tumor, the hyperproduction of certain steroid hormones, which contributes to an earlier diagnosis. Hormone-inactive tumors go on for a long time without clinical manifestations, they are often detected during examination for another disease. In the first case, in an 11-month-old girl, the tumor proceeded with hyperproduction of cortisol with the development of Icengo-Cushing syndrome, in the second patient the tumor was hormonally inactive. The prognosis of the disease depends on the stage of the tumor. In the first case, stage II of the tumor process was established, in the second – stage IV with distant metastases. The children received combined treatment, surgery and chemotherapy. In the first patient, the treatment was successful, the child is in remission for 4 years, in the second case, the outcome is fatal, due to the progression of the malignant process.

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