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MODERN DIAGNOSIS OF NEPHROBLASTOMA IN CHILDREN

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ABSTRACT

Nephroblastoma is a highly malignant embryonic tumor originating from developing kidney tissues. The disease is the most common malignant neoplasm of the genitourinary tract in children. Most common before the age of 5 years with equal frequency in boys and girls, the relationship between maternal age and the likelihood of having a child with Wilms nephroblastoma is often associated with congenital anomalies.

The name Wilms tumor was named after the German surgeon from Heidelberg Max Wilms 1867 - 1918, who proposed in 1899 in his monograph a review of the literature on kidney tumors in children and substantiate the histogenesis of the tumor.

Wilms' tumor is a very high-grade solid tumor of the kidney. It is also called nephroblastoma (the "nephro" part of the word means kidney, and "blastoma" means tumor). At the turn of the last century, Max Wilms dealt with this disease and described it in detail for the first time. Wilms' tumor arises from a mutated primitive tissue that begins to develop during the prenatal development of the organism. It can be made from different types of fabric. Most often, this tumor grows from progenitor cells of the kidney tissue. But it may also contain other immature progenitors of other tissues (eg, muscle, cartilage, and epithelial tissue). Therefore, nephroblastoma is called a "mixed tumor". The malignancy of nephroblastoma is that it grows rapidly and begins to metastasize early. Approximately 10% of children who are diagnosed with Wilms tumor already have metastases at the time of diagnosis. As a rule, they affect neighboring lymph nodes with the kidneys, as well as the lungs and liver. In some children (about 5%), Wilms tumor immediately affects both kidneys. Typically, in these children, the tumor grows out of a tissue called nephroblastomatosis. It is immature embryonic kidney tissue. It is believed that Wilms tumor begins with it. More often than with other oncological diseases in childhood, children with certain anomalies or with hereditary cancer syndromes suffer from nephroblastoma [16].

Epidemiology of tumors in children. Epidemiology in pediatric oncology to a lesser extent (unlike adults) considers the relationship between the occurrence of tumors and geographic and other environmental factors. Perhaps this is due to not entirely reliable statistics, but, most likely, with their relative rarity - after all, there are only 42 children with a malignant tumor in a whole region with a million people. Even in such a large country as the United States, no more than 8,000 children fall ill annually, and in European countries about 21,000 annually. Another reason is that the environment, geographical, and climatic conditions act indirectly on young children through their mothers, therefore tumors in children is the epidemiology of their parents.

Wilms tumor is the most common kidney tumor in infants and children. The incidence of Wilms' tumor is 8.2 cases per 1 million children under 15, or one case per 10,000 infants. Approximately 650 cases of Wilms' tumor are diagnosed each year in the United States. The incidence is significantly lower in Asians. [16, 31].

In childhood and adolescence, Wilms tumor (nephroblastoma) accounts for about 5.5% of all cancers. It is the most common kidney cancer in children. At this age, it is considered one of the most common solid tumors. In Germany, the Children's Cancer Registry (Mainz) annually registers about 100 new cases of nephroblastoma in children and adolescents under the age of 14 years. That is, according to statistics, one child falls ill out of 100,000 children under 15 years of age. Since Wilms' tumor is an embryonic tumor, it most often affects children at an early age. 68% of cases are children from one to five years old, 16% are infants. Girls get sick a little more often than boys. But Wilms tumor also occurs in older children and adolescents. Adults get sick very rarely. A significant improvement in survival has been achieved for children and adolescents with cancer. From 1975 to 2010, childhood cancer deaths dropped by more than 50%. For children younger than 15 years of age with Wilms' tumor, the 5-year survival rate increased over the same time from 74% to 88%. Survivors of cancer in childhood and adolescence need to be closely monitored, as side effects of antitumor therapy may persist or develop months or years after treatment [16].

The male to female ratio in unilateral cases of Wilms' tumor is 0.92 to 1.00, but in bilateral cases it is 0.60 to 1.00. The mean age of diagnosis is 44 months in unilateral cases and 31 months in bilateral cases of Wilms tumor [15,29]. About 10% of children with Wilms tumor have an associated congenital malformation syndrome [21].

Nephroblastoma, or Wilms' tumor, is a congenital embryonic malignant tumor of the kidney with a frequency of 1:100,000 in children under 14 years of age per year. The tumor is detected mainly at the age of 1-6 years, girls and boys are ill with the same frequency. In 5% of cases, bilateral nephroblastomas are observed. Up to 1/3 of patients with nephroblastoma have malformations: aniridia, hemihypertrophy, malformations of the genitourinary system, malformations of the musculoskeletal system associated with Beckwith-Wiedemann syndromes, WAGR syndrome, Denys-Drash syndrome, type I neurofibromatosis. Nephroblastoma is characterized by hematogenous and lymphogenous metastasis, while lymphogenous metastasis is early. The lymph nodes in the gates of the kidneys, para-aortic lymph nodes and lymph nodes of the gates of the liver are affected. With nephroblastoma, a tumor thrombus may occur in the inferior vena cava. Hematogenous metastasis is more often detected in the lungs, less often in the liver. In the primary diagnosis, 20-25% of patients with nephroblastoma have metastasis: lungs - 10%, liver - less than 5%, peripheral retroperitoneal lymph nodes - 10% [12].

Occupational hazards, bad habits, various physical and chemical influences primarily and mainly affect parents, and through them, children. Leading pediatric oncologists from different countries under the epidemiology of tumors in children in all their works mean the relationship of malignant neoplasms with obstetric pathology, with viral infections during pregnancy in the mother, with vaccination of mothers during pregnancy, congenital and family factors, sex and age, defects development. Leading scientists in the field of epidemiology in a large review, which they call "epidemiological", gives an epidemiological assessment of the relationship between

malignant tumors and birth defects. They conventionally divide tumors in children into 3 groups. The 1st group includes leukemia, nephroblastoma, cancer of the liver and adrenal glands, neuroblastoma. These tumors are often combined with various congenital malformations. Acute leukemia is characterized by a combination with Down's disease, and for other tumors of this group (except for neuroblastoma) with hemihypertrophy. With neuroblastoma, aniridia (congenital absence of the iris) often occurs. The second group consists of brain tumors. They are most often combined with malformations of the central nervous system (some tendency to develop gliomas is noted in patients with nodular sclerosis and neurofibromatosis). Group 3 includes genital tumors, which also often occur simultaneously with malformations [13].

Etiology of tumors in children. Dlya ob"yasneniya proiskhozhdeniya opukholey u detey ispol'zuyutsya teorii, kotoryye prinyaty v obshchey onkologii. No imeyutsya gipotezy, kharakternyye dlya detskoy onkologii. Odnoy iz nikh yavlyayetsya teoriya Kongeyma, predlozhennaya yeshche v 70-kh godakh XIX stoletiya. Soglasno etoy teorii, opukholi proiskhodyat iz persistiruyushchikh embrional'nykh zachatkov, voznikshikh iz-za narusheniya embriogeneza. Vo vremya vnutriutrobnogo razvitiya ploda proiskhodit smeshcheniye embrional'-nykh zachatkov tkaney. Ne ispol'zovannyye pri stroitel'stve organizma, eti ektopirovannyye kletki mogut dlitel'noye vremya ne proyavlyat' sebya. Pri prisoyedinenii vnutrennikh i vneshnikh razdrazhiteley eti zachatki mogut dat' opukholevyy rost. Soglasno teorii Fisher-Vazel'sa, sformulirovannoy v 20-kh godakh proshlogo stoletiya, pridayetsya naibol'sheye znacheniye voznikno-venii opukholevogo rosta usloviyam, pri kotorykh tkan' v techeniye dlitel'nogo sroka poluchayet moshchnyye fiziologicheskiye ili patologicheskiye impul'sy k rostu. Oni mogut voznikat' vsledstviye povtornoy gibeli ili regeneratsii tkaney (chastoye vozdeystviye rentgenovskikh luchey) libo pod vliyaniyem bystrogo rosta tkaney v opredelennyye vozrastnyye periody. Bol'shoy interes predstavlyayet teoriya immunologicheskogo kontrolya. Soglasno etoy teorii, u prakticheski zdorovogo cheloveka zalozhena vozmozhnost' zlokachest-vennogo prevrashcheniya kletok, kotoraya sderzhivayetsya zashchitnymi silami organizma. Eta teoriya nakhodit svoye podtverzhdeniye v tom, chto u detey s polomkami immunnoy sistemy chashche voznikayut zlokachestvennyye opukholi. Kontseptsiya o roli immunnykh mekhanizmov v razvitii zlokachestvennykh novoobrazovaniy byla vydvinuta v 1909 godu Erlikhom, a zatem rasshirena mnogimi issledovatelyami. Issledovaniya poslednikh let podtverdili sushches-tvennoye znacheniye faktora immunodepressii v razvitii opukholey. Eta teoriya, kotoraya takzhe imenuyetsya kontseptsiyey immunologicheskogo nadzora, imeyet ne tol'ko storonnikov, no i mnogikh protivnikov, kotoryye utverzhdayut, chto ona ne ob"yasnyayet proiskhozhdeniya bol'shinstva opukholey u detey.

Ещё

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Результаты перевода

To explain the origin of tumors in children, theories that are accepted in general oncology are used. But there are hypotheses specific to pediatric oncology. One of them is the Konheim theory, proposed back in the 70s of the XIX century. According to this theory, tumors originate from persistent embryonic buds that have arisen due to a violation of embryogenesis. During the intrauterine development of the fetus, the embryonic tissue rudiments are displaced.

Unused in the construction of the body, these ectopic cells may not manifest themselves for a long time. When attached to internal and external stimuli, these rudiments can give tumor growth. According to the Fischer-Wazels theory, formulated in the 20s of the last century, the greatest importance is attached to the occurrence of tumor growth under conditions under which the tissue receives powerful physiological or pathological impulses to grow for a long time. They may occur as a result of repeated tissue death or regeneration (frequent exposure to x-rays) or under the influence of rapid tissue growth during certain age periods. Of great interest is the theory of immunological control. According to this theory, a practically healthy person has the possibility of malignant transformation of cells, which is restrained by the body's defenses. This theory is supported by the fact that children with impaired immune systems are more likely to develop malignant tumors. The concept of the role of immune mechanisms in the development of malignant neoplasms was put forward in 1909 by Ehrlich, and then expanded by many researchers. Recent studies have confirmed the essential importance of the immunosuppression factor in the development of tumors. This theory, which is also called the concept of immunological surveillance, has not only supporters, but also many opponents who claim that it does not explain the origin of most tumors in children.

The most interesting theory for pediatric oncology is the theory of the origin of tumors associated with transplacental blastomogenesis. According to this theory, most neoplasms in children arise through the passage of carcinogens through the placenta. Almost all drugs used in obstetric practice pass through the placenta. There are works based on large statistical material indicating the transplacental effects of tobacco and alcohol on offspring. Some drugs used in agriculture (pesticides) act transplacentally. Hereditary-genetic theory. About 101 genetically determined syndromes are known that predispose to the development of neoblastic processes in childhood. It has been proven that genetic factors play the main role in the etiology of a number of congenital tumors in children. This is primarily characteristic of retinoblastoma and nephroblastoma. The development of the most common embryonic tumors is associated with structural changes in the chromosomal apparatus, as a result of which the action of suppressor tissues of specific mechanisms is switched on and, possibly, certain oncogenes are activated. Factors of the external and internal environment, which can be the causes of tumors in children, are called carcinogenic. There are physical, chemical, viral carcinogenesis. Of the physical factors, various types of ionizing radiation deserve special attention. Children are more sensitive than adults to radiation. Irradiation of the thyroid zone can cause the development of a malignant tumor in it, especially in girls. The development of secondary tumors after radiation therapy is one of the most serious complications of this type of treatment. No one knows exactly why children get Wilms tumor. But scientists have found that the tumor is associated with changes in certain genes and chromosomes.

Today, the so-called Wilms tumor gene 1 [WT1 gene] on chromosome 11 has been studied the most. The WT1 gene is located on the short arm of chromosome 11 (11p13). WT1 is a transcription factor that is essential for the normal development of the genitourinary system and is important for the differentiation of the renal blastema [32]. WT1 mutations are observed in 10–20% of cases of sporadic Wilms tumor [22,30,32].

Wilms tumor with WT1 mutation is characterized by the following:

1. Evidence for activation of the WNT pathway by activation of mutations in the CTNNB1 gene is common [10,18,30]. Loss of heterozygosity (LOH) at 11p15 is commonly observed as paternal unibreed disomy for chromosome 11 is a common mechanism for the loss of the remaining normal WT1 allele [30,24].
2. Nephrogenic remnants are benign foci of embryonic kidney cells that persist abnormally in the postpartum period. Intralobar nephrogenic malformations occur in about 20% of cases of Wilms tumor. They are observed with high frequency in cases with genetic syndromes with WT1 mutations, such as WAGR and Denis-Drash syndromes [9]. Intralobar nephrogenic malformations are also observed in cases of sporadic WT1 and MLLT1 mutations [23,34]. WT1 germline mutations are rare (2–4%) in nonsyndromic Wilms tumor [5,25]. WT1 and 11p15 LOH mutations were associated with relapse in very low risk Wilms tumor patients in one study of 56 patients who did not receive chemotherapy [27]. These results need to be confirmed but may provide biomarkers for patient stratification in the future. Germline WT1 mutations are more common in children with Wilms tumor and have one of the following:

- WAGR syndrome, Denis-Drash syndrome [28], or Fraser syndrome [33]
- Anomalies of the genitourinary system, including hypospadias and cryptorchidism.
- Bilateral Wilms tumor.
- Unilateral Wilms' tumor with nephrogenic remnants in the opposite kidney.
- Stromal and rhabdomyomatous differentiation.

WT1 germline point mutations cause genetic syndromes that are characterized by nephropathy, 46XY sexual development disorder, and various risks of Wilms' tumor [3,6]. Syndromic conditions with germline WT1 mutations include WAGR syndrome, Denis-Drash syndrome [28], and Fraser syndrome [33]. Fraser syndrome is characterized by progressive nephropathy caused by focal segmental glomerulosclerosis, gonadoblastoma, and XY pseudohermaphroditism. WT1 mutations in Fraser syndrome usually occur in intron 9 at the KTS site and create an alternative splicing variant, thereby preventing the formation of the usually more common WT1 + KTS isoform [19]. It is important for the normal development of the kidneys in children. And if any changes occur in it, then a tumor or other anomalies may occur. Scientists have also found other genes on chromosome 11 and on other chromosomes that are involved in the process of Wilms tumor formation. If the structure of the chromosome is damaged, or a certain chromosome begins to change its number, then the risk of getting nephroblastoma increases. Wilms tumor often occurs in children who already have a congenital cancer syndrome, such as WAGR syndrome (combines several symptoms of abnormal development). Children with WAGR syndrome are at high risk (approximately 50%) of developing Wilms tumor [21]. WAGR syndrome results from deletions on chromosome 11p13 that include a set of contiguous genes that include the WT1 and PAX6 genes. Inactivation of mutations or deletions in the PAX6 gene results in aniridia, while deletion of WT1 increases the risk of Wilms' tumor. Loss of the LMO2 gene is associated with a more frequent development of Wilms tumor in patients with congenital aniridia and deletions of the WAGR region [8]. Sporadic aniridia in which WT1 is not removed is not associated with an increased risk of Wilms tumor. Accordingly, children with familial aniridia, usually occurring over many generations, without renal abnormalities, have a normal WT1 gene and are not at increased risk of Wilms' tumor [4,26]. Wilms tumor in children with WAGR syndrome is characterized by an excess of

bilateral disease, intralobar nephrogenic remnants, early age at diagnosis, and stromal-dominated histology in FH tumors [2]. Mental retardation in WAGR syndrome may be secondary to deletion of other genes, including SLC1A2 or BDNF [20], Beckwith-Wiedemann syndrome (increase in body weight and internal organs). An increased incidence of Wilms tumor is observed in patients with a number of genetic disorders, including WAGR syndrome (Wilms tumor, aniridia, genitourinary anomalies and mental retardation), Beckwith-Wiedemann syndrome, hemihypertrophy, Denis-Drash syndrome, and Perlman syndrome [14]. Other genetic causes that have been observed in cases of familial Wilms tumor include germline mutations in REST and CTR9 [7,17], Denis Dresh syndrome (genital underdevelopment). Denis-Drash syndrome is characterized by a nephrotic syndrome caused by diffuse mesangial sclerosis, XY pseudohermaphroditism, and an increased risk of Wilms' tumor (>90%). WT1 mutations in Denis-Drash syndrome are most often missense mutations in exons 8 and 9, which encode the DNA-binding region of WT1 [28] and type 1 neurofibromatosis (Recklinghausen's disease). Children with these diseases have developmental disabilities and an increased risk of developing cancer. If someone in the family had a Wilms tumor, then the child from this family also has an increased likelihood of getting nephroblastoma. Even if he does not have any developmental disabilities due to heredity. "Family" cases of Wilms tumor are quite rare (about 1%), and in these children the tumor usually affects both kidneys.

Studies evaluating genotype/phenotype correlations of WT1 mutations have shown that the risk of Wilms' tumor is highest for truncating mutations (14 of 17 cases, 82%) and lower for missense mutations (27 of 67 cases, 42%). The risk is lowest for KTS splicing site mutations (1 case in 27.4%). Bilateral Wilms tumor was more common in cases with WT1 truncating mutations (9 out of 14 cases) than in cases with WT1 missense mutations (3 out of 27 cases) [3,6]. These genomic studies confirm previous estimates of increased risk of Wilms tumor in children with Denis-Drash syndrome and low risk of Wilms tumor in children with Fraser syndrome.

In most affected children, Wilms' tumor occurs for the first time (an isolated case in the family), that is, they have neither a genetic syndrome nor any other hereditary disease in the family. Scientists have not found a relationship between the environment and its influence on the occurrence of nephroblastoma [11].

Symptoms. At first, because of Wilms' tumor, the children do not hurt anything and they do not complain about anything. In sick children, the stomach is dense and it seems to “bulge” forward. Parents attribute this to a good appetite. Often, during a routine medical examination, a pediatrician accidentally finds nephroblastoma by probing a large tumor in the child's abdomen (about 10% of cases), and there are no other symptoms. Very rarely, the first symptom of nephroblastoma in children is abdominal pain, or there are blood impurities in the urine. The child may also lose weight, have a high fever, indigestion (such as constipation), high blood pressure, and cough due to lung metastases. If the child already has certain genetic syndromes and developmental anomalies, then they help to suspect that he has a Wilms tumor. The most common sign of Wilms' tumor is a palpable or no tumor in the abdomen. Nephroblastoma can be asymptomatic for a long time. Sometimes, pain in the abdomen is noted. Hematuria can be detected by microscopic examination. Hypertension occurs in approximately 25% of patients.

Histological structure and histological classification. Tumors of the kidney are characterized by histological heterogeneity. About 80% of nephroblastoma is the "classic" variant of the tumor.

Histological staging according to Smidt / Harms provides for the allocation of 3 degrees of malignancy of kidney tumors in children associated with the prognosis of the disease.
Histological classification of kidney tumors according to Smidt/Harms:
According to the degree of malignancy: low, medium, high
1. By risk group: low risk, standard risk, high
According to histological variants of tumors: low (mesoblastic nephroma, fetal rhabdomyomatous nephroblastoma, cystic, partially differentiated nephroblastoma); medium: "classic" variant without anaplasia, nephroblastoma with focal anaplasia; high: nephroblastoma with diffuse anaplasia, clear cell sarcoma, rhabdoid tumor of the kidney.
In the classification of kidney tumors, Wilms' tumor refers to nephroblastic tumors, other neoplasms of the kidney are not Wilms' tumors. Classification of kidney tumors in children (2007)
• Nephroblastic tumors - Wilms tumor
• Mesenchymal tumors - clear cell sarcoma of the kidney, ATRO of the kidney, mesoblastic nephroma
• Metanephron tumors - metanephron adenoma, metanephron adenofibroma, metanephron stromal tumor, ossifying renal tumor in infants
• Epithelial tumors - renal medullary carcinoma, papillary cell renal carcinoma
• Other tumors - PNET, synovial sarcoma, anaplastic sarcoma of the kidney.
Clinical staging: Currently, the SIOP and NWTS groups use a single nephroblastoma staging system, which is decisive for treatment: Stage I - the tumor is localized within the kidney, complete removal is possible; Stage II - the tumor spreads beyond the kidney, complete removal is possible, including germination of the kidney capsule, with spread to the perirenal tissue and / or into the kidney hilum, damage to regional lymph nodes, damage to extrarenal vessels, damage to the ureter; Stage III - the tumor spreads beyond the kidney, possibly incomplete removal, including, in the case of incisional or aspiration biopsy, pre- or intraoperative rupture, peritoneal metastases, damage to intra-abdominal lymph nodes, with the exception of regional ones, tumor effusion into the abdominal cavity, non-radical removal; Stage IV - the presence of distant metastases; Stage V - bilateral nephroblastoma.
Variants of bilateral nephroblastomas include: A - lesion of one of the poles of both kidneys, B - lesion of one kidney with involvement of the hilum in the tumor process (total or subtotal) and one of the poles of the second kidney, C - lesion of both kidneys with involvement of the hilum (total or subtotal).
The classification of nephroblastoma according to the TNM system currently retains mainly historical significance. This classification is based on the allocation of 4 stages. It includes clinical and postoperative staging.
Clinical (cTNM) classification of nephroblastoma: Primary tumor (category T) (Tx - primary tumor was not assessed, T0 - primary tumor was not detected, T1 - tumor of one kidney with an area of up to 80 cm2, T2 - tumor of one kidney with an area of more than 80 cm2 (measurement area is made by multiplying the largest vertical and horizontal dimensions, while the dimensions include the kidney tissue along with the tumor), T3 - a rupture of a unilateral tumor that occurred before the start of treatment, T4 - a bilateral tumor); Lymph node involvement (category N) (Nx - regional lymph nodes not assessed, N0 - regional lymph

nodes not affected, N1 - metastases to regional lymph nodes); Distant metastases (category M) (Mx - diagnosis of possible distant metastases was not carried out, M0 - distant metastases were not detected, M1 - distant metastases were detected).

The calculation of the area is made according to the excretory urogram, ultrasound, CT or MRI.

The aim of our study is to improve modern diagnostic methods in the study of pathomorphological changes that develop in the kidneys of children with nephroblastoma.

The main objectives of the study are to identify macroscopic and microscopic changes in the renal tissues in nephroblastoma in children, to study the changes in renal tissues that develop in nephroblastoma in children using the immunohistochemical method, to substantiate the criterion for the relationship between pathomorphological and immunohistochemical changes during development nephroblastoma in children.

When evaluating the pathomorphological features of nephroblastoma, data on autopsied corpses are given, as well as a general description of the research methods used. In this study, a retrospective analysis of extracts from case histories, data obtained during autopsy, copies of materials obtained in laboratory studies, the results of clinical, laboratory studies, which were obtained during autopsy in the department of pathomorphology of the Republican Specialized Scientific and Practical Medical Center of Oncology, is carried out. and radiology from 2008 to 2021.

In our research, based on the results of the study, we study the relationship of pathomorphological changes that develop in the kidneys with nephroblastoma in children and between death. A full and comparative analysis of the relationship between pathomorphological and immunohistochemical changes in renal tissues is carried out.

Diagnosis of Wilms tumor. If, after an external examination of the child and in the history of the disease, the pediatrician has a suspicion of Wilms' tumor, then the doctor issues a referral to the children's oncological hospital on suspicion of Wilms' tumor, various tests and studies must be carried out: firstly, to confirm the diagnosis, and secondly, to find out the specific form of nephroblastoma and find out how much the disease has already spread throughout the body. Having received answers to these questions, you can begin to plan the optimal treatment tactics and give a prognosis. An important role (after an external examination) for the diagnosis is played by such diagnostic methods from images as ultrasound (ultrasound), magnetic resonance imaging (MRI) and computed tomography (CT). With their help, Wilms' tumor can be distinguished from other diseases (for example, from neuroblastoma, from lymphoma or from neuroblastomatosis) with a certainty of up to 95%. Also, the images can accurately assess the size of the tumor and the degree of its prevalence throughout the body. But the condition for the most accurate diagnosis is the high quality of equipment and the extensive experience of the doctor who performs diagnostics using images. This is especially important here. Because in Germany, microscopic (histological) confirmation of the diagnosis, that is, when a tumor sample is taken and then examined under a microscope, is usually carried out after the initial course of chemotherapy. Clarification of the diagnosis and search for metastases. Sometimes it happens that it is impossible to accurately distinguish Wilms' tumor from other diseases, such as neuroblastoma, from the images. Then an additional examination is ordered. For example, MIBG scintigraphy is done to distinguish nephroblastoma from neuroblastoma. Or they look for certain tumor markers in the body, which can be found if the child has a neuroblastoma.

With nephroblastoma, they are not in the body. Other studies should confirm or rule out metastases in the body. Therefore, in order to find metastases in the lungs, an x-ray or computed tomography of the chest is always prescribed.

Depending on the treatment plan and to check how certain organs work, additional studies are carried out before the start of treatment. So, especially before a course of chemotherapy in children, they check how the heart works (echocardiogram - EchoCG), check hearing (audiometry) and kidneys (using nuclear medicine methods). If any changes occur during treatment, then they must be compared with the initial results of the examination. Depending on this, the tactics of treatment can be adjusted. Examination of tissue samples: Only when the preoperative course of chemotherapy is completed (it lasts from 4 to 6 weeks) and the images clearly confirm the diagnosis, a biopsy of the tumor is taken. Tumor tissue is examined under a microscope (histological analysis) and molecular genetic analysis is done. A tumor biopsy is performed during surgery, when the tumor itself is removed. Only in exceptional cases, an operation or a biopsy with a fine needle is performed before the start of treatment in order to obtain a sample of tumor tissue [1].

Morphological diagnosis. As with all other malignant tumors, the diagnosis of nephroblastoma is based on morphological findings. However, in relation to nephroblastoma, an exception is allowed from the rule of conducting a biopsy before starting chemoradiotherapy. During a biopsy, a violation of the integrity of the pseudocapsule occurs, and the tumor detritus enclosed in the pseudocapsule, which has a mushy nature, is dispersed throughout the abdominal cavity or along the needle, which increases the spread of the tumor, changes the clinical stage of the disease (automatically transfers to stage 3) and worsen the prognosis of the disease. Therefore, in patients >6 months and <16 years of age, the diagnosis of nephroblastoma is made on a conservative examination. This is facilitated by the presence of clear diagnostic signs of nephroblastoma, which reduce diagnostic errors to a negligible minimum. Histological diagnosis is established after preoperative chemotherapy. Confirmation of the diagnosis in a reference laboratory is mandatory. At the same time, some foreign protocols suggest the initial removal of a kidney with a tumor or its biopsy, even with dubious tumor resectability. In accordance with the NWTS strategy, this approach makes it possible to avoid errors in conservative diagnosis and conduct a thorough revision of the abdominal organs, excluding or detecting metastasized lymph nodes and a tumor of the opposite kidney (according to NWTS, in 30% of cases of bilateral nephroblastoma, the tumor of the second kidney does not visualized by conservative diagnostic methods). Diagnosis of the primary tumor is based on the identification of typical signs of nephroblastoma and the exclusion of other diseases. The circle of differential diagnoses includes malformations of the kidney, hydronephrosis, neurogenic tumors and other tumors of the retroperitoneal space, liver tumors, hamartoma. Diagnosis of nephroblastoma and determination of the stage includes laboratory and instrumental studies. Laboratory studies include: a clinical blood test, a general urinalysis, a biochemical blood test, and a study of catecholamines in urine and blood serum (to rule out neuroblastoma) [13].

Thus, the review of the literature showed that in the domestic and foreign literature the issue under study has not been sufficiently studied. Nephroblastoma is one of the serious diseases in children among oncopathologies, which requires dynamic monitoring of hemodynamic parameters and the timely administration of both pharmacological and mechanical means of

prevention. Prevention of the development of Wilms' tumor is one of the important steps to increase the survival of children with nephroblastoma.

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