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Research Article

Preoperative Diagnosis of Renal Tumors at the Stage of a Specialized Oncohematological Department

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Received: March 15, 2022; **Published:** April 27, 2022

Abstract

Nephroblastoma (or Wilms' tumor) is a relatively rare tumor of the kidney, which is characterized by clinical polymorphism, endowed with specific and nonspecific features that characterize it from the standpoint of clinical and paraclinical features. In the Russian Federation, with a total primary oncological incidence of approximately 15 per 100,000 child population per year, the detection rate of renal tumors is from 0.4 to 1.0 per 100,000 child population (average 0.6 per 100,000). Most often, the tumor manifests itself between the ages of 2 and 5 years (75% of cases).

Currently, problems remain in the identification of new molecular, histological and clinical risk factors, the search for biomarkers to stratify the intensity of treatment.

Specific symptoms are an increase in the volume of the abdomen and the presence of a palpable tumor. Nonspecific clinical signs are even more varied. In some patients, nonspecific clinical symptoms are associated with congenital malformations and syndromes.

In this paper, the most important symptom complexes of clinical manifestations of the oncological process are evaluated and data from paraclinical studies at the preoperative stage of a specialized department of a hospital of the III level of medical care are provided.

The study retrospectively selected patients with renal tumors in the amount of 46 people living in the territory of the Krasnoyarsk Territory.

The performed analysis is based on the analysis of medical records and evaluation of the obtained data in accordance with the study protocol.

Taking into account the data obtained by us, we consider it appropriate to identify the clinical symptom complex, which should become an alarm signal at the stage of pre-hospital examination, and in combination with specific symptoms, optimize specialized diagnostics.

As a visualization at the primary screening stage, an ultrasound diagnosis of a kidney tumor is performed. Computed tomography of the abdominal cavity with contrast has an advantage over ultrasound, it is a more informative and reliable study.

Distant metastases were found in 11 patients (24%). The most common organ belonging to metastatic foci is the lungs (6 cases or 13%).

Keywords: *Nephroblastoma; Wilms Tumor; Renal Tumor; Clinical Symptom Complex*

Introduction

Nephroblastoma (or Wilms' tumor) is a relatively rare tumor of the kidney, which is distinguished by clinical polymorphism, endowed with specific and nonspecific features that characterize it from the standpoint of clinical and paraclinical features. According to the literature, about 7% of all childhood malignant neoplasms are kidney tumors [1,2], while up to 85 - 90% of them are nephroblastomas - the so-called Wilms' tumor [3,4]. In the Russian Federation, with a total primary oncological incidence of approximately 15 per 100,000 child population per year, the detection rate of renal tumors is from 0.4 to 1.0 per 100,000 child population (average 0.6 per 100,000) [2]. Most often, the tumor manifests itself at the age of 2 to 5 years (75% of cases) [1,4], it can be congenital, but nephroblastoma is also observed in adults, with a frequency of 0.2 per million per year [5]. In childhood and adolescence, even more rare and little-studied kidney tumors are diagnosed, which are tactically identical to NB approaches to diagnosis and, in some cases, to treatment.

Currently, in the literature, data on the clinical and paraclinical features of kidney tumors are very diverse, not always structured, and the most common manifestations are not indicated, which allow discussing the symptom complex based on modern diagnostic approaches in verifying this pathology. The two largest collaborative groups that have studied the optimal treatment of Wilms' tumor are the National Wilms' Tumor Research Group of North America and the International Society of Pediatric Oncology, with participation from Europe and other countries [6]. The National Wilms Tumor Group recommends primary surgery before any adjuvant treatment, while the

International Society for Pediatric Oncology research is based on the use of preoperative chemotherapy [7]. Problems remain in the identification of new molecular, histological and clinical risk factors, the search for biomarkers [8] to stratify the intensity of treatment [9,10].

For the diagnosis of kidney tumors, clinical and paraclinical criteria are taken into account. Specific symptoms are an increase in the volume of the abdomen and the presence of a palpable tumor [8,11]. Nonspecific clinical signs are even more diverse: abdominal pain, constipation, increased blood pressure, nausea, vomiting, flatulence, appetite disorders, weight loss, increased blood pressure, intoxication, fever, dysuria, irritability, tearfulness, asthenia. In some patients, nonspecific clinical symptoms are associated with congenital malformations - aniridia, hemihypertrophy, urogenital malformations, anomalies of the musculoskeletal system (clubfoot, doubling of the ribs, congenital hip dislocation) [11] and syndromes such as Denis-Drash syndrome, WAGR -syndrome or Beckwith-Wiedemann syndrome [4,12]. Specific criteria are the detection of volumetric renal formations according to various imaging methods, microhematuria; nonspecific changes: micro and macrohematuria, leukocyturia, proteinuria, bacteriuria, anemia, leukocytosis, increased ESR, detection of data for congenital malformations of the kidney.

Purpose of the Study

To evaluate the most important symptom complexes of clinical manifestations of the oncological process and provide data from paraclinical studies based on the results of clarifying diagnostics for kidney tumors at the preoperative stage of a specialized department of a hospital of the III level of medical care.

Materials and Methods

The study retrospectively included all patients with renal tumors who underwent examination and treatment in the oncohematological department of the Krasnoyarsk Regional Clinical Center for Maternal and Child Health (KKKKTSOMD) from 2011 to 2019. in the amount of 46 people. All patients for the period of examination and treatment lived in the territory of the Krasnoyarsk Territory.

The performed analysis is based on the analysis of medical records and evaluation of the data obtained in accordance with the study protocol, which included: passport data, anamnesis, complaints, laboratory and instrumental examination methods, visualization data (computed tomography, ultrasound), information on the type and volume of surgical treatment, histological and immunohistochemical findings, physical examination data. Diagnostic and therapeutic methods were used in accordance with the Clinical Guidelines and the modern international protocol for the management of patients with renal tumors (mostly the SIOP Protocol 2001).

Results of the Study and their Discussion

The paper analyzes the main symptom complexes of clinical and paraclinical manifestations in patients with renal tumors who underwent diagnosis and treatment at the oncohematological department of the Krasnoyarsk Regional Clinical Center for Maternal and Child Health (KKKCMMD) in 2011 - 2019 before the stage of surgical intervention. The characteristics of clinical and laboratory parameters at the time of diagnosis of the tumor are given.

Renal tumors can be asymptomatic for a long time. For the first time, a dense, painless volumetric formation with a smooth (sometimes with an uneven surface) is detected in the abdomen of a child by a mother or pediatrician during dispensary observation, which is undoubtedly the most significant specific clinical manifestation of Wilms' tumor [6].

Nonspecific manifestations are diverse, but together they provide significant diagnostic information. Often a child complains of abdominal pain, the nature and localization of which are quite diverse. The cause of pain is either pressure on the surrounding organs, or the germination of the tumor in the diaphragm, liver or retroperitoneal tissue. The pains can be sharp or dull, cramping; sometimes they

simulate the clinical picture of acute appendicitis (subcapsular tumor ruptures are also likely) [11,13]. Along with this, dyspepsia, constipation, nausea, vomiting, loss of appetite are observed. Possible hyperthermia associated with urinary tract infection, general symptoms of intoxication, weight loss. Quite often (in 25%), on examination, arterial hypertension (secondary) is detected, which develops as a result of hyperreninemia and vasoconstriction or the spread of a tumor thrombus into the inferior vena cava up to the right atrium. [fourteen]. Sometimes the behavior of the child changes, which becomes irritable, whiny, gets tired quickly, loses interest in the environment. It is possible to develop a syndrome of physical inactivity, which covers not only the emotional sphere, but also the muscular system, accompanied by a decrease in muscle strength and motor activity [4].

According to our data, the following occurrence of specific and nonspecific symptoms was established in the study sample (Table 1). The most common symptom of the disease was an increase in the abdomen and the presence of a palpable tumor, which were recorded in the study group in 38 children (82%), 35 patients (76%) had abdominal pain, anemia was registered in 18 people (39%), constipation - in 12 children (26%), dysuria phenomena - in 8 people (17%), episodes of fever - in 7 cases (15%), repeated vomiting - in 2 patients (4%), there was an intestinal obstruction clinic that led to the need for emergency surgical intervention in one child (2%), as well as a case of severe pain in the bones of the lower leg associated with the presence of a metastatic lesion of clear cell sarcoma (2%). The manifestations generally coincide with the literature data, which describe a significant clinical variety of non-specific manifestations of nephroblastomas. At the same time, from the list of nonspecific initial manifestations, a significant frequency of abdominal pain, anemia, indications of constipation, dysuria and fever draws attention. Taking into account the data obtained by us, we consider it appropriate to identify the clinical symptom complex, which should become an alarm signal at the stage of pre-hospital examination, and in combination with specific symptoms, optimize specialized diagnostics.

	Abs	%
Specific features		
Increasing the volume of the abdomen	38	82
Palpable tumor	38	82
Non-specific signs		
Stomach ache	35	76
Anemia of the chronically ill	18	39
Constipation	12	26
Dysuria	8	17
Fever	7	15
Vomiting	2	4
Bone pain/fracture	1	2
Clinic of intestinal obstruction	1	2

Table 1: *The frequency of occurrence of specific and nonspecific symptoms in children with kidney tumors at the time of hospitalization in a specialized department.*

The primary diagnosis of a renal tumor involves a comprehensive approach aimed at excluding other kidney pathologies (kidney malformations, hydronephrosis, neurogenic tumors, other tumors of the retroperitoneal space, liver tumors, hamartomas) [3], as well as the identification of concomitant diseases.

	Abs.	%
Lag in physical development	5	11
Congenital malformations of the urinary tract	4	9
Pathology of the nervous system	3	6
Pathology of the gastrointestinal tract	3	6
Allergic diseases	1	2
Pathology of the upper respiratory tract	1	2
Rickets	1	2

Table 2: Concomitant pathological conditions in children with kidney tumors at the time of hospitalization in a specialized department.

The incidence of comorbidities in patients with renal tumors did not differ significantly compared to the population data at the time of admission to the oncohematology department. The sample is dominated by patients with a lag in physical development - 5 children (11%) and congenital malformations of the urinary tract in 4 patients (9%) (1 case of aplasia of the left kidney in combination with aplasia of the uterus, appendages, VUR 3-4 stage, hydronephrosis and horseshoe kidney)

Paraclinical data include laboratory and instrumental examinations.

In a clinical blood test, the most common is anemic syndrome, which is based on various causes, as well as monocytosis, eosinophilia, lymphocytosis, neutrophilia, an increase in ESR, indicating the severity of the tumor process and the likelihood of metastasis and/or tumor decay [14].

In the analysis of urine, microscopic examination often reveals microhematuria, proteinuria. Gross hematuria occurs in less than a quarter of patients and is a manifestation of tumor invasion into the pyelocaliceal system of the kidney [14].

As a visualization at the primary screening stage, ultrasound diagnostics was performed, as the most accessible method that allows you to reliably confirm the presence of a tumor mass and clarify the localization of the formation. Ultrasound of the abdominal cavity and retroperitoneal space is the first study and should be performed in all cases of the presence of mass formation in the abdomen in children. This rather simple and fast method is non-invasive and is necessary for the differential diagnosis of cysts and tumors, helps to assess the condition of the second kidney, detects metastases in the liver, retroperitoneal lymph nodes, and is indispensable during the period of observation of the patient after the completion of the treatment program [4]. Using this method, a kidney tumor can be diagnosed in 95% of cases before surgery.

The results of this study confirmed the presence of a tumor by ultrasound in all 46 patients, among which 42 (91%) people had damage to one kidney and 4 children (9%) had a bilateral process. The spread of tumor growth within one segment of the kidney was stated in 16 children (35%), 2 or more segments in 30 patients (65%).

In recent years, computed tomography of the abdominal cavity has been widely used in the diagnosis of Wilms' tumor. CT/MRI imaging, taking into account the peculiarities of the methods, has an advantage over ultrasound examination, and allows with greater information content and reliability to accurately determine the degree of involvement of the kidney tissue, as well as its capsule, germination of perirenal tissue, vessels, ureters, lymph nodes, infiltration of adjacent organs.

	Quantity	% From All Patients
Involvement within 1 kidney segment	12	26
Involvement more 1 kidney segment	34	74
Unilateral tumor	42	91
Bilateral tumor	4	9
Contrast accumulation data uneven	43	93
Contrast accumulation data intensive	3	6

Table 4: *Computed tomography imaging data.*

Computed tomography imaging data showed higher accuracy compared to ultrasound and the ability to state a greater involvement of kidney structures in the tumor process (involvement of more than one segment was diagnosed in 34 children (against 30 according to ultrasound data), correctly assess the stage of the tumor lesion and plan the necessary volume of the treatment program The CT/MRI information on laterality completely coincides with the assessment by ultrasound: 42 (91%) patients have a unilateral tumor and 4 (9%) have a bilateral tumor. The accumulation of specific contrast confirms the presence of tumor tissue, the uniformity of accumulation indicates a high density of neoplasm vessels, and the intensity indicates the activity of local blood flow in the identified structure, which indirectly indicates the activity of tumor tissue.

The median tumor volume in the considered sample was 375 ml. The distribution of patients, taking into account differences in the volume of tumor tissue (within specified intervals), showed the following: 9 patients (20% of the total number of patients) had the smallest volume up to 100 ml, 10 children (21%) had a volume of 100 to 300 ml, tumor mass from 300-500 ml was found in 11 people (24%), a volume of more than 500 ml was registered in 16 children, which accounted for 35% of all cases.

Tumor Volume	Me, (Q1-3)	Absolute Number of Cases	% From All Cases	M±Σ
до 100 мл	45 (19 - 60)	9	20	42 ± 29
100-300 мл	183 (152 - 226)	10	21	193 ± 49
300-500 мл	392 (360 - 448)	11	24	402 ± 62
более 500 мл	750 (592 - 865)	16	35	801 ± 267
все варианты	375 151 - 599	46	100	430 ± 351

Table 5: *The volume of the kidney tumor according to Computed tomography imaging data at the beginning of special therapy.*

Thus, very rarely a tumor is diagnosed in a volume of less than 100 ml; such variants are often detected as a clinical finding and, as a rule, do not have significant complaints at the diagnostic stage, including such specific ones as abdominal enlargement and the presence of a palpable tumor. The most common option for diagnosing a tumor in the presence of a volumetric formation was more than 500 ml. This approach is of clinical importance for further understanding the relationship between the size of tumors with clinical and paraclinical manifestations, as well as a number of secondary problems (risks of urinary tract infection, delayed physical development, manifestations of dyspepsia, anemia, asthenic syndrome, etc.). Often, a tumor with a volume of more than 500 ml is diagnosed as stage III of the disease, and if distant metastases are detected, stage IV.

Sign	Number of Observations	% Of All Patients
Metastases were absent	35	76
Metastases found:	11	24
Metastases to regional lymph nodes	11	24
Metastases to distant sites	8	17
Metastases to the brain	2	4
Metastases to the lungs	6	13
Metastases to the liver	2	4
Tumor thrombus in the inferior vena cava	2	4
Bone metastases	2	4
Metastases to the bone marrow	2	4

Table 6: *Distribution of examined patients with renal tumors, taking into account data on metastasis according to the results of CT/MRI/ bone scintigraphy/bone marrow cytology.*

Data on metastasis obtained using the imaging method (ultrasound, CT, MRI, abdominal and retroperitoneal organs, chest organs, brain, bone scintigraphy), as well as laboratory studies of bone marrow cytology, made it possible to identify metastatic foci in 11 patients according to the following loci of metastatic lesions: regional lymph nodes - 11 cases (24%), distant lymph nodes - 8 children (17%), lungs - 6 patients (13%), such localizations as the brain, liver, bone marrow, bones and tumor thrombus in the IVC, 2 children (4% for each localization). According to the data obtained, the presence of metastases was found in 24% of children at the stage of clarifying diagnosis, while some of the children had metastatic lesions at several loci at once. The most common distant metastases are in the lungs.

Conclusions

1. Non-specific symptoms (abdominal pain, anemia, constipation, dysuria and fever) make it possible to identify clinical symptom complexes, which, in combination with specific symptoms (the presence of a palpable tumor and an increase in the volume of the abdomen), require further examination in a specialized oncohematological department.

2. Of the concomitant conditions at the stage of preoperative diagnosis, the most frequent are physical developmental delay (11%) and the presence of congenital malformations of the urinary tract (9%).

3. Of the imaging modalities, ultrasound is mandatory for initial diagnosis and during the follow-up period of the patient during and after the completion of the treatment program. At the stage of a specialized examination, contrast-enhanced computed tomography expands diagnostic capabilities, allows you to clarify the volume of tissue involved in the tumor process of the kidney structures, assess the stage of the tumor lesion, as well as the presence of distant metastases, and plan the necessary volume of the treatment program. When assessing the size of the local focus, the highest the frequency of detection of a tumor formation with a volume of more than 500 ml (35% of all cases); it is important that small tumor sizes up to 100 ml were recorded in 20% of children (in every fifth patient). The average volume of the tumor mass at the time of surgery was Me 375 ml, (Q1 - 3 151 - 599 ml).

Distant metastases were found in 11 patients (24%). The most common organ belonging to metastatic foci is the lungs (6 cases or 13%).

Author's Contribution

Elena Aleksandrovna Karavaeva: Development of the article design, data collection, analysis of scientific material, analysis of the obtained data, publications on the topic of the article, preparation of the list of references, writing the text of the manuscript, preparation of the summary, scientific revision of the article, preparation of patient visualization.

Tatyana Evgenyevna Taranushenko: Development of the article design, analysis of the scientific material, analysis of the obtained data, publications on the topic of the article, preparation of the list of references, writing the text of the manuscript, preparation of the summary, scientific revision of the article.

Marina Vasilyevna Borisova: Publications on the topic of the article, data collection.

Tatyana Ivanovna Bulava: Data collection.

Tatyana Gennadyevna Kadricheva: Data collection.

Nadezhda Alexandrovna Gonchar: Data collection.

Evgeniya Aleksandrovna Guseynova: Data collection.

Source of Funding

Not specified.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Volume 11 Issue 5 May 2022