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Primary Diagnostics Renal Tumors in Children and Adolescents (On the Example of the Krasnoyarsk Territory)

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Abstract

Aim: The purpose of this study is to present data on the incidence and epidemiology of renal tumors in the pediatric population of the Krasnoyarsk Territory and to clarify individual features of the tumor at the stage of primary diagnosis.

Materials and Methods: This publication presents the results of an exploratory study aimed at clarifying the relevance and importance of scientific and practical tasks for the study of nephroblastoma in children and adolescents in the Krasnoyarsk Territory.

The design of the study was based on a retrospective analysis of a cohort sample (46 patients with renal tumors), which included all children and adolescents admitted for examination and treatment at the oncohematological department of the Krasnoyarsk Regional Clinical Center for Maternal and Child Health from 2011 to 2019. All patients lived in the Krasnoyarsk Territory at the time of diagnosis verification and throughout the duration of specific therapy.

Results and Discussion: The study, carried out for the first time on the territory of the Krasnoyarsk Territory, made it possible to present data on the incidence and incidence of renal tumors in the pediatric population of the Krasnoyarsk Territory and to establish individual features of tumors, taking into account the stage of the disease and the risk group.

For the first time, data are presented on the primary incidence of renal tumors in children of a separate territory of Eastern Siberia over a 9-year observation period, which averaged 0.87 per 100,000 children with alternating periods of rise and decrease in the detection of the pathology under consideration. In the structure of oncohematological diseases in children of this region, kidney tumors occupy the 4th place.

The age structure of patients was established, the main symptom complex of the manifestation of the pathology under consideration was noted, and the distribution of children with kidney tumors was indicated, taking into account the prognostic risk groups and the stage of the disease.

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Introduction

In world practice, a lot of experience has been accumulated in the treatment of renal tumors in children in general and nephroblastomas in particular [1,2].

Treatment success rates for renal conditions indicate significant therapeutic success and improved prognosis, largely due to close collaboration between multidisciplinary teams from different countries. For many countries, SIOP research has become a key to public health development, as in North America great advances have been made in the Wilms National Growth Study Group (NWTSG). Other foreign teams, such as the UK Children's Tourism Research Organization (UKCCSG) and the UK Wilms Increasing Incidence Research Organization, have also made major contributions to research on the scientific and practical aspects of childhood nephroblastoma [3]. The current consensus on the results of the best results of observations is a multimodal approach, applied surgery, chemotherapy and radiation.

In rare cases of malignant diseases in children, the tumor takes the 4th place, yielding to hemoblasts, neoplasms of the central nervous system and lymphomas and accounts for 5.5% to 7%

of all malignant tumors of early age [3]. According to literature data in the Russian Federation, with a general oncological incidence of approximately 15 per 100,000 child population per year, the survival rate of Wilms tumor is from 0.4 to 1.0 per 100,000 child population (average 0.6 per 100,000) [4]. In Europe, the incidence rate of kidney tumors in children is 0.88 per 100,000 children per year. 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. The average in countries such as Finland, Sweden, the US, Australia, Italy, the Netherlands and the UK reduced 0.7 per 100,000 children per year. At the same time, the highest incidence rate is in Finland (0.95 per 100,000) and the lowest in the UK (0.51 per 100,000) [5-7].

In most pathogens, neoplasms were detected in the age group of 0 to 4 years [8,9].

NB is a congenital embryonic malignant tumor of the kidney, the histological picture of which is extremely diverse. Classical NB microscopically represents a combination of three cell types: Blastema, stromal and epithelial. Each cell type may be present to varying degrees or absent. The severity of each histological feature has a different prognostic value [10,11]. Typically, Wilms' tumor occurs sporadically, in 2% of cases it has a family character. It is extremely rare for bilateral kidney damage with nephroblastoma in children. Bilateral Nephroblastoma (BN) is recorded in 4% to 10% of all nephroblastomas in children [12].

Wilms tumor is often combined with congenital developmental anomalies, and may also be part of a genetic syndrome that predisposes to the development of nephroblastoma. In 12% to 15% of cases, children with Wilms' tumor have genitourinary tract malformations, of which more than 50 variants have been described (hypoplasia, dystopia, shape anomaly, absence or duplication of the kidney, vascular malformations, hypogonadism, etc.). Genetically determined diseases are detected in approximately 5% of children with Wilms tumor. Patients with some WT1-associated syndromes (including WAGR and Denis-Drash), Perlman syndrome, mosaic intermittent aneuploidy, and Fanconi anemia with a biallelic BRCA2 mutation have a high risk of developing Wilms' tumor (>20%). A moderate risk of developing nephroblastoma (5% to 20%) was noted in groups of children with Fraser and Beckwith-Wiedemann syndromes, which developed as a result of 11p15 disomy, and Simpson-Golaby-Bemel syndrome. Patients with isolated hemihypertrophy, Bloom and Li-Fraumeni syndromes, congenital hyperparathyroidism in combination with jaw tumors, MULIBREY dwarfism, and various chromosomal aberrations are included in the low-risk group for developing nephroblastoma (<5%) [13].

Cellular precursors of nephroblastoma have not been reliably established. Currently, the generally accepted theory of the genetic nature of cancer, which is based on the existence of suppressor genes that can suppress tumor growth (mutation in the Wilms Tumor gene 1 (WT1), located on chromosome 11. A breakdown in the 11p15 locus causes the tumor to lose specific heterozygosity and leads to tumor progression; mutation of the TP53 gene, a tumor growth suppressor that prevents clonal progression). Defects in these genes determine the progression of tumor growth and are divided into 2 groups: “cell cycle guardian” genes and “general control” genes [14,15].

NB is the most common primary renal malignancy in children, accounting for up to 85% of all renal neoplasms [1]. Histological staging according to Smidt/Harms, in accordance with the Stockholm classification of 1994, taking into account the changes introduced by the International Society of Pediatric Oncologists SIOP in 2007, is carried out after removal of the neoplasm and provides for the allocation of three histological risk groups that affect the prognosis of the disease (low, intermediate and high risk groups) depending on the structure of the tumor [11].

In general, it is known that the malignancy of NB is determined by the rapid growth of the tumor and the high rate of development of metastases.

Despite significant advances in the study of nephroblastoma in children, the importance of the problem under consideration for health care remains relevant, which is dictated by a number of circumstances:

- There is a certain need for a comparative assessment of the quality of the organization of oncological care in various territories and medical institutions that provide specialized and highly qualified care to patients.
- The importance of a dynamic assessment of morbidity rates, the structure of pathology, age and sex characteristics, clarification of the risk of relapses and adverse outcomes, as well as life expectancy in nephroblastomas is obvious.
- There is no doubt about the importance of a comparative analysis of new (and traditional) treatment and diagnostic approaches for renal tumors in children, as well as the feasibility of comparing the results of individual clinics with data from other centers providing care for these patients.

The purpose of this study is to provide information on the detection rate of renal tumors based on the data of patients in the Krasnoyarsk Territory applying to the Children's Oncological Center (KTCOMC) and to clarify individual features of the tumor at the stage of primary diagnosis.

Materials and Methods

This publication presents the results of an exploratory (pilot), dynamic, single-center study aimed at clarifying the incidence and features of early diagnosis of kidney tumors for the period 2011-2019, in order to obtain comparative data, analyze and improve care in the pediatric population of the Krasnoyarsk Territory. The work uses the continuous method of the studied population, i.e. the sample included all children from 0 to 17 years old with the pathology in question.

The design of the study was based on a retrospective analysis of a cohort sample (46 patients with renal tumors), which included all children and adolescents admitted for examination and treatment at the oncohematological department of the Krasnoyarsk Regional Clinical Center for Maternal and Child Health (KRCCMCH) from 2011 to 2019. All patients were residents of the Krasnoyarsk Territory, including 3 children who arrived from the Republics of Khakassia and Tyva at the time of diagnosis verification and the period of specific therapy.

The article presents the calculated incidence rates of renal tumors according to the number of children and adolescents in the Krasnoyarsk Territory (the number ranged from 548, 151 in 2011 to 633, and 520 in 2019).

The paper presents the results of the hospital registry, which made it possible to perform an analysis to clarify the features of the diagnosis and course of nephroblastoma (passport data, anamnesis, complaints, physical examination data, laboratory and instrumental examination methods, visualization data, information about the type and volume of surgical treatment, histological and immunohistochemical conclusions).

This publication considers a separate fragment (primary data on patients with kidney tumors) of a planned study.

Results

The paper analyzes the structure of primary patients with oncohematological profile for 2011 to 2019 in the Krasnoyarsk Territory (Table 1).

According to the frequency of occurrence, renal tumors follow after hemoblastoses, tumors of the central nervous system and lymphomas and slightly exceed the number of tumors of soft tissues and bone tumors. The share of renal tumors in the structure of oncohematological pathology, first diagnosed in childhood, accounts for 6.4% and for the period 2011 to 2019 in absolute terms is from 3 to 7 children per year, i.e. in different years, the eventfulness of the considered pathology differed by 2 or more times.

According to the results of the study, it was found that the primary incidence rate of kidney tumors among children and adolescents in the Krasnoyarsk Territory in different years of the analyzed period ranged from 0.5 to 1.26 cases per 100 thousand, which made it possible to form a target cohort of 46 cases over a nine-year period (Table 2).

The calculation of a non-standardized incidence rate was characterized by an alternation of significant rises to 1.26/100 000 and 1.12/100 000 in 2012 and 2018, respectively, with a significant decrease to the minimum values - 0.55/100 000 and 0.50/100 000 in 2011 and 2016. The presented results, in general, correspond to the statistical data for the Russian Federation and European indicators.

According to the well-known published reports in the literature, the average age of children at the time of tumor detection corresponds to a period of 0 to 4 years [6]. According to our data, the average age of sick children was 4 ± 0.5 years, while the maximum of sick children (71.7% or 33 children) were aged from 1.5 to 5.5 years (18 months to 5 years 6 months). The youngest patient was a 2-month-old child; the oldest was a 16-year-old girl.

No gender differences were found among the patients; the studied cohort included 24 girls and 22 boys.

There were no indications of a burdened family nephroblastoma.

The paper considers the clinical features of renal tumors at the stage of primary treatment. In the studied cohort of patients, the following complaints prevailed: Abdominal pain in 34 patients (74% of all cases), an increase in the size of the abdomen in 30 patients (65%), constipation in 8 patients (17%), fever in 7 patients (15%), lagging in physical development in 4 patients (8.7%), arterial hypertension, recorded only in one child (2%). The most common pre-hospital misdiagnosis was: Urinary tract infection and vesicoureteral reflux in 3 cases, respectively (6.5% each), suspected bowel dysfunction in 2 cases (4%), parasitosis in 2 cases (4%), the absence of any formulated preliminary diagnosis in 3 children (6.5%).

At the pre-hospital stage, the presence of a tumor was suspected in 24 patients (52%).

In four cases (8.7 ± 4%), additional imaging studies revealed abnormalities in the development of the urinary system (double renal artery, renal aplasia, horseshoe kidney, vesicoureteral reflux).

Bilateral nephroblastomas were found in 4 people (8.7%).

In the conditions of a specialized oncohematological department, on the basis of regulatory documents (Order of the Ministry of Health of Russia dated December 29th, 2012 N 1687n "On approval of the standard for specialized medical care for children with nephroblastoma" and clinical recommendations "Nephroblastoma in children" approved on January 1st, 2019), each patient was prescribed a comprehensive treatment and diagnostic a program that includes surgical, drug and radiation treatment.

According to the results of histological examination, the vast majority of renal tumors were nephroblastomas (40 out of 46 cases); other morphological variants were clear cell sarcoma (4 cases) and metanephrogenic tumor (2 cases). The presented data correspond to the literature descriptions of the structure of kidney tumors, according to which NB is one of the most common solid neoplasms in preschool children (among primary malignant kidney tumors in children, NB accounts for up to 85% of all cases) [1].

To resolve the issue of subsequent treatment tactics, risk groups and the stage of the disease were taken into account.

Based on the histological variants of renal tumors, we divided

Table 1: The structure of primary patients with oncohematological profile for 2011-2019 (absolute values are shown for ages 0-18).

Nosological groups	2011	2012	2013	2014	2015	2016	2017	2018	2019	Всего	%
Leukemia	29	39	27	30	33	29	31	34	33	285	40
Lymphoma	6	12	6	9	12	10	11	13	12	91	12.7
Tumors of the central nervous system	12	14	7	7	4	10	10	8	14	86	12
Tumors of the kidneys	3	7	5	5	5	3	6	7	5	46	6.4
Bone tumor	4	5	7	3	6	5	5	3	7	45	6.3
RMS	2	4	5	3	6	9	2	5	6	42	5.9
Neuroblastoma	3	1	1	3	6	3	4	8	7	36	5
GKO	1	4	5	3	2	4	2	3	3	27	3.8
Retinoblastoma	2	3	4	1	1	2	1	4	2	20	2.8
Histiocytosis	3	2	2	1	3	3	2	2	2	20	2.8
Liver tumor	2	3	0	0	2	2	5	0	2	16	2.2

Table 2: Primary incidence of renal tumors in 2011 to 2019.

Years	Child population	Number of new cases of NB (aged 0-18 years)	0-5 years	6-14 years	15-18 years	Incidence (per 100,000 cases)
2011	548151	3	2	1	0	0.55
2012	556517	7	5	1	1	1.26
2013	565584	5	4	1	0	0.88
2014	578493	5	4	1	0	0.86
2015	588344	5	1	3	1	0.85
2016	602844	3	2	1	0	0.5
2017	615254	6	4	2	0	0.98
2018	624692	7	4	3	0	1.12
2019	633520	5	4	1	0	0.79
TOTAL	5313399	46	30	14	2	Me=0.87

patients into prognostic risk groups (probability of recurrence and/or other adverse outcome) and found that only 2 patients were in the low risk group, 25 people in the intermediate risk group, and 19 children in the high risk group. The prevalence of children with intermediate and high risk corresponds to the literature data.

Taking into account the peculiarities of tumor growth in the group under consideration, the following stages of the disease (volume of lesions and metastasis) were established: 6 children (13%) had stage I, 16 children (34.8%) had stage II, 9 children (19.6%) had stage III, IV - 11 patients (23.9%), stage V - 4 people (8.7%). It is important that more than 50% of children (III, IV, V stages) had a more unfavorable course of the tumor process, needed more aggressive methods of treatment, and were characterized by a worse prognosis.

The average time from the moment of seeking treatment to the start of therapy in the group of children with renal tumors was 3.8 (Q1-Q3=2-4) months. In comparison with the average indicators in the Russian Federation, a feature of the presented data is the diagnosis mainly at stages II and IV of the disease, which may be due to a number of reasons (late diagnosis of renal tumors due to the large territorial extent of the Krasnoyarsk Territory, untimely application of parents for medical care, lack of oncological alertness of the pediatric service, as well as failure to perform imaging research methods at the initial stages of an outpatient examination outside a specialized oncology department).

Discussion

The article presents the incidence rates of renal tumors according to the appeals to the KRCCMCH of the children and adolescents in the Krasnoyarsk Territory for the period 2011 to 2019 with alternating periods of rise and decrease in the detection of the pathology in question. The data obtained in children and adolescents 0 to 18 years of age in the territory of the Krasnoyarsk Territory do not contradict the average published data for Russia and Europe [4,5].

The nine-year follow-up period made it possible to form a hospital registry database, analyze the features of clinical manifestations, age and gender composition of patients, establish the absence of a family predisposition to the development of renal tumors, estimate the average time for clarifying diagnosis, and present the distribution of patients by risk groups and stages of the disease. The obtained data are comparable with the results of other researchers on this problem [5,7]. At the same time, the performed study convinces of the need for pediatricians to pay closer attention to children with the pathology under consideration at the stage of primary treatment (cancer alertness in relation to children with abdominal pain and enlarged abdomen) in order to reduce the time for establishing a diagnosis, as well as to expand the use of ultrasound screening of the kidneys (as at medical examination of children, and at suspicion on tumors of kidneys).

The low diagnostic significance of a family history, as well as the severity and significant variety of clinical symptom complexes associated with renal tumors (attention is drawn to the rarity of detected arterial hypertension); determine the need to optimize research methods using genetic analysis (especially if bilateral kidney damage is suspected).

Conclusions

1. The study, carried out for the first time on the territory of the Krasnoyarsk Territory, made it possible to present data on the incidence of renal tumors in pediatric and adolescent populations and to establish individual features of tumors, taking into account the stage of the disease and the risk group.

2. Incidence (detection rate) of renal tumors according to the data of primary visits to the specialized oncohematological center of the Krasnoyarsk Regional State Budgetary Institution of Health Care "Krasnoyarsk Regional Clinical Center for Maternal and Childhood Care" in children and adolescents aged 0 to 18 years over a 9-year follow-up period averages 0, 87 per 100 thousand of the child population and is characterized by alternating periods of rise and decrease in the frequency of cases of the pathology under consideration. In the structure of oncohematological diseases in children and adolescents in the Krasnoyarsk Territory, kidney tumors occupy the 4th place, which corresponds to the statistics of the Russian Federation and individual European countries.

3. In the largest number of children (68%), kidney tumors were diagnosed at the age of 1 to 5 years (the average age at the time of diagnosis was 4 years) in the absence of gender differences and indications of an aggravated anamnesis.

4. The leading clinical manifestations are abdominal pain (74% of all cases), an increase in the size of the abdomen (65%). The average time from the moment of seeking treatment to the start of therapy was 3.8 (Q1-Q3=2-4) months.

5. The distribution of children with kidney tumors indicates a significant predominance of intermediate and high risk groups for an unfavorable outcome during the course of the disease, as well as the detection of nephroblastomas mainly at stages II and IV of the

disease.

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