



## **CLINICAL AND MORPHOLOGICAL EVALUATION EFFECTIVENESS OF TREATMENT OF NEPHROBLASTOMA IN CHILDREN**

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### **Abstract:**

Nephroblastoma (Wilms tumor) is one of the most common malignant neoplasms in children. The tumor is named after the German surgeon Max Wilms, who described it in 1899. The tumor invades the kidney parenchyma and develops from degenerated (embryonic, epithelial and stromal) cells in varying proportions, destroying the affected kidney. The lymph nodes located in the region of the renal portal, para-aortic and hepatic portal are most often affected.<sup>1</sup> By hematogenous route, they mainly metastasize to the lungs, less often to the liver.

**Keywords:** nephroblastoma, tumors in childhood, nephroblastoma in children, frequency of nephroblastoma in childhood, malignant tumors, epidemiology of nephroblastoma

**INTRODUCTION:** In the structure of malignant tumors in children, nephroblastoma ranks 4th, behind hemoblastosis and soft tissue sarcomas. Its frequency varies from 0.4 to 1.0 per 10,000 newborns. Most often, nephroblastoma occurs in children aged 2 to 5 years, less often in newborns<sup>2</sup>.

The disease is observed in childhood with a frequency of 5-9 cases per 1 million children. Wilms tumor accounts for 7-8% of all malignant neoplasms in children. Most often, the tumor occurs between the ages of 2 and 5 years (75% of cases), it can be congenital, but nephroblastoma is also observed in adults (0.9% of tumors of this type). The frequency of detection of nephroblastoma does not depend on the gender of the child; There were no differences in the incidence of right and left kidney involvement. In 4-5% of sick children, the tumor is bilateral<sup>3</sup>.

The causes of nephroblastoma are not fully understood, but significant progress in research has been made in recent years. A key role in the development of this tumor is played by genetic factors, in particular defects in a number of genes - WT1, WT2 and WT3, which are associated with impaired formation of specific proteins involved in the regulation of the development of the primary nephron and act as kidney growth regulators and tumor suppressors. Abnormal activation of insulin-like growth factor 2 gene expression observed in many patients with nephroblastoma indicates dysregulation of

kidney development due to increased levels of mitogens in the fetus<sup>4</sup>.

A combination of nephroblastoma and developmental disorders such as aniridia (congenital). Daily iris failure), hypospadias, cryptorchidism, Beckwith-Wiedemann syndrome. For these anomalies, it is recommended to perform a kidney ultrasound every 3 months until the age of 7 years. Predisposing factors include certain diseases or exposure to ionizing radiation in the first half of pregnancy.

**MATERIALS AND METHODS:** At the initial stage of the disease, symptoms are usually absent or minimally expressed, so it is no coincidence that more than half of children with nephroblastoma are admitted to specialized departments with stages III-IV of the disease. Early manifestations of the disease: pale skin, general malaise, low body temperature, weight loss. The child's behavior changes - he becomes irritable, whiny, quickly gets tired and loses interest in his surroundings.

As the tumor grows, clinical manifestations increase. The rate of tumor growth varies. Slow growth over many months is possible, but more often the tumor grows quickly and gradually displaces or displaces surrounding organs and tissues.

In the area of the kidney, a tumor-like formation is usually palpable; the tumor is usually dense and smooth, less often lumpy. The tumor may be fixed to

<sup>1</sup> Григорьев К.И., & Бойченко Е.И. (2013). НЕФРОБЛАСТОМА У ДЕТЕЙ. Медицинская сестра, (2), 22-29.

<sup>2</sup> Мадаминова, З. А. (2014). Лечение нефробластомы у детей в Таджикистане. Онкопедиатрия, (3), 59.

<sup>3</sup> Детская гематология/онкология: Практическое руководство по детским болезням, Том IV / Под ред. А.Г. Румянцев и Е.В. Самохатова. – М.: Медпрактика-М, 2004. – 792 с.

<sup>4</sup> Григорьева К.И. Уход за детьми с онкогематологическими заболеваниями // Медсестра. – 2011 г.; 2:43-50.



the surrounding structures and not move during palpation<sup>5</sup>.

If the tumor is significant, edema of the lower extremities and ascites occur due to compression of large vessels. Possible nausea, vomiting, loss of appetite, abdominal pain, the nature and location of which are very different. The cause of pain is either pressure on surrounding organs, or tumor growth into the diaphragm, liver or retroperitoneal tissue; they can be sharp or dull and cramping; sometimes they simulate the clinical picture of acute appendicitis.

A common symptom of the disease is increased blood pressure (BP), which occurs in 75-90% of patients: systolic blood pressure is in the range of 110-140 mm Hg. Art. Art., diastolic – 90-100 mm Hg. Art.

Wilms tumor can occur in combination with two forms of nephrotic syndrome: glomerulosclerosis and Drasch syndrome.

Laboratory research methods help diagnose nephroblastoma. Urine tests can detect proteinuria, micro- or macrohematuria. Microhematuria is observed in 60% of children, macrohematuria – in 25%. A general blood test shows an increase in ESR and anemia.

In most cases, the tumor is unilateral, but bilateral lesions occur in 5-8% of children (stage V disease). The appearance of metastases worsens the patient's condition and leads to the appearance of new clinical symptoms associated with the localization of metastases. The time of appearance of metastases is determined by the size of the tumor, its histological structure and the age of the patient. The younger the child, the less often and later metastases occur<sup>6</sup>.

Surgery is the main treatment method for patients with Wilms tumor. The tumor and metastases must be removed. For unilateral tumors, the operation of choice is transperitoneal nephrectomy; For bilateral tumors, bilateral resection is performed in healthy tissues under the control of histological examination. The presence of distant metastases is not a contraindication to removal of the primary lesion. Nephrectomy is recommended to be performed no later than 6 weeks after the start of preoperative therapy.

Radiation therapy is used as an adjunct to surgical treatment both in the preoperative and postoperative periods<sup>7</sup>.

Nephroblastoma is considered a relatively radiosensitive tumor. Postoperative radiation therapy is carried out in the postoperative period for all patients with Wilms tumor stages II, III and IV, as well as stage I children over 2 years of age. Radiation therapy is sometimes avoided in children under 2 years of age. The dosage of radiation therapy largely depends on the age of the child. When irradiating the entire abdominal cavity, the hip joints must be carefully protected to avoid impaired bone growth, which in the long term can lead to slippage of the femoral head.

Chemotherapy as a mandatory component of combination treatment is used in patients with Wilms tumor at any stage of the disease. The main difficulties of chemotherapy are associated with the age of the child, especially in infants and newborns. The dosage of chemotherapy drugs for children under 12 months is reduced by 50% compared to the usual dose<sup>8</sup>.

The main goal of preoperative chemotherapy is to reduce the tumor and metastases, which is achieved in most patients: tumors are reduced in size by more than 50%<sup>9</sup>.

The number of complex operations is significantly reduced. They use vincristine, dactinomycin, etc. Preoperative chemotherapy allows for radical surgery, reduces the incidence of tumor rupture, and also allows one to determine the sensitivity of the tumor to the drugs used, which is taken into account in the treatment of the postoperative period and during chemotherapy to prevent metastases.

The intensity of postoperative chemotherapy and radiation therapy depends on the effectiveness of the initial chemotherapy; In patients with unfavorable tumor histology, more aggressive treatment regimens are used.

Postoperative treatment depends on the final stage of the disease. Treatment is carried out under the control of blood counts, since aggressive therapy primarily helps to suppress hematopoiesis - leukocytopenia and thrombocytopenia.

<sup>5</sup> Детская онкология: Национальные рекомендации / Под ред. М.Д. Алиева, В.Г. Полякова и др. – М.: Издательская группа РОНЦ, 2011. – 684 с.

<sup>6</sup> Дурнов Л.А., Шароев Т.А. Детская онкология: этапы развития, проблемы и успехи // Медсестра. – 2004 г.; 3:2-4.

<sup>7</sup> Peterman C.M., Fevurly R.D., Alomari A.I., et al.: Sonographic screening for Wilms tumor in children with CLOVES syndrome. *Pediatr Blood Cancer* 64 (12): 2017.

<sup>8</sup> Запруднов А.М., Григорьев К.И. Общий уход за детьми: Учеб. – М.: ГЭОТАР-Медиа, 2011, 4-е издание – 416 с

<sup>9</sup> Sandberg J.K., Chi Y.Y., Smith E.A., et al.: Imaging Characteristics of Nephrogenic Rests Versus Small Wilms Tumors: A Report From the Children's Oncology Group Study AREN03B2. *AJR Am J Roentgenol* 214 (5): 987-994, 2020.



Treatment of relapses. Patients with recurrent Wilms tumor are treated with aggressive chemotherapy and radiation therapy, and, if necessary, surgery. Relapse is the basis for the use of high-dose chemotherapy and the use of new drug combinations. A combination of ifosfamide, mesna and etoposide, as well as cisplatin and etoposide, is effective. The use of extremely aggressive chemotherapy usually leads to hematological complications, so such patients often undergo autologous bone marrow transplantation<sup>10</sup>.

**RESULT:** With Wilms tumor, the prognosis depends on the following factors: timely diagnosis; age of the patient at the time of diagnosis; stages of the disease; Histological differentiation of nephroblastoma. With favorable histology of Wilms tumor and appropriate treatment, more than 90% of children with nephroblastoma make a complete recovery. The risk of relapse after treatment is 15-20%. The two-year survival rate of patients with relapse of the disease does not exceed 40%.

**CONCLUSION:** Thus, since the main contingent of patients with nephroblastoma is admitted to the children's department of the hospital with stages III-IV of the disease, the use of block chemotherapy can not only significantly increase the effectiveness of complex treatment of this pathology in children, but also increase the chances of performing a nephrectomy.

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