Wilms Tumor — Classification, Diagnosis, Stages and Treatment

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Nephroblastoma is a type of cancer that mostly occurs in children, with a slight female predominance. In some cases, it is followed by malformation syndromes. Usually, this kidney tumor is discovered incidentally during regular check-ups. It is considered a good example of curable malignancy and usually has a positive prognosis with interdisciplinary treatment.

Definition

Nephroblastoma or Wilms tumor is the most common renal tumor in young children and is also a common genitourinary malignancy in children.

It develops from the residues of the metanephric blastema. This type of tissue usually disappears before the 36th week of gestation. However, if parts of this embryonic tissue remain, it is referred to as nephroblastomatosis.

Nephroblastomatosis is considered a tumor precursor and can be found in 40% of children with Wilms tumor.
Epidemiology of Wilms’ Tumor

Incidence of Nephroblastoma

The incidence ratio of Wilms tumor is 1:10,000. Eighty-five percent of patients are usually younger than 6 years. Usually, diagnosis is made in the 2nd or 3rd year of life. Girls are slightly more often affected than boys, and there is a different incidence for children of different ethnicities. For example, the incidence in Asia is substantially lower than that in European or American children.

Etiology

Causes of Nephroblastoma

The genesis of nephroblastoma is much more complex than that of some other malignant tumors in children. About one-third of patients with nephroblastoma have mutations of the tumor suppressor gene \textit{WT1}: a deletion of genetic material on the short arm of chromosome 11. Other factors influencing tumor development are the loss of heterozygosity and genomic imprinting.

In 10% of cases, the tumor is associated with malformations such as the WAGR syndrome (Wilms tumor, aniridia, genitourinary malformations, mental retardation), Denys-Drash syndrome (pseudohermaphroditism, glomerulopathy, Wilms tumor), von Recklinghausen disease (type 1 neurofibromatosis), and Beckwith-Wiedemann syndrome (exomphalos-macroglossia-gigantism (EMG) syndrome).

Metastasis of Nephroblastoma

In 5% of cases, the nephroblastoma is bilateral. Metastasis mostly occurs in regional lymph nodes and \textit{lungs}.

**Note:** For children with WAGR syndrome, Denys-Drash syndrome, or Beckwith-Wiedemann syndrome, regular sonographic examinations every 3 months are indicated.

Classification

Histological classification of Nephroblastoma

The histological classification according to the SIOP (International Society of Pediatric Oncology) of 2002 identifies 3 groups based on different degrees of malignancy. Eighty percent of cases can be classified as intermediate malignancy, i.e., the standard histological finding.

Typically, blastema is present in the tumor, consisting of clusters of cells with hyperchromatic ovoid nuclei. Within the blastema, different structures can be observed, including rosettes, tubules, and pseudo-glomerular structures.
Clinical Presentation of Wilms’ Tumor

Symptoms of Nephroblastoma

The most common sign of nephroblastoma is a painless swelling of the abdomen. Only about one-quarter of the children complain of pain. In a few cases, hematuria can be observed. Non-characteristic symptoms include:

- Fever
- Constipation
- Diarrhea
- Weight loss
- Nausea or vomiting
- Lethargy and fatigue
- Abdominal pain or distension
- Gross hematuria

Approx. 10% of nephroblastoma is discovered only incidentally during a check-up because they are mostly asymptomatic.

Diagnosis of Wilms’ Tumor

Radiological Examination of Suspected Nephroblastoma
Using sonography, CT, or MRI, the dimensions of the tumor can be displayed and lymph node metastases can be detected. Moreover, a thrombus in the inferior vena cava can often be detected due to cone-shaped ingrowths of the tumor into the vessels. An urogram typically reveals that the tumor is spreading into the pyelocaliceal system. Imaging of the 2nd kidney before surgery is crucial since single or bilateral kidney tumors must be excluded. Imaging of the 2nd kidney before surgery is crucial since single or bilateral kidney tumors must be excluded.

**Note:** A biopsy is not indicated because of the risk of tumor cell seeding. Specific tumor markers do not exist for nephroblastoma. However, the determination of catecholamine degradation products in serum may be useful in some cases to distinguish possible neuroblastoma. Thus, urinalysis and urine catecholamine levels of vanillylmandelic acid and homovanillic acid should be measured.
Staging of Nephroblastoma

Staging of Nephroblastoma according to the National Wilms Tumor Study Group (NWT):

- **Stage I:** Tumor is limited to the kidney and is completely resectable
- **Stage II:** Tumor extends beyond the kidney but is completely resectable
- **Stage III:** Tumor resection only partially possible, or lymph nodes are affected
- **Stage IV:** Hematogenous metastases can be detected
- **Stage V:** The nephroblastoma is bilateral

Treatment

Treatment of nephroblastoma depends on the stage of the disease, histological subtype, and age of the child. Without treatment, the disease results in the death of the patient. Surgical removal of the tumor always involves the risk of rupturing the tumor and seeding into the abdomen, with a subsequently worse prognosis. Therefore, only for children under 6 months is surgery the primary mode of treatment.

For older children, the reduction of the tumor mass using neoadjuvant chemotherapy using agents such as vincristine and actinomycin D is the 1st step, with the goal of reaching stage I before surgery. For tumor patients with stage III or higher, radiation therapy becomes necessary. Radiation is delivered to the tumor bed after surgery and chemotherapy to eliminate residual disease. In the case of unilateral nephroblastoma, tumor nephrectomy is the next step.
Prognosis for Nephroblastoma

Prognosis is very good. The 5-year survival rate is 80%; for stage I patients, it is even higher at 90%.

**Prognostic factors:**
- Tumor size
- Grade of the tumor as anaplasia confers an unfavorable prognosis
- Older age is associated with poorer prognosis
- Lymph node involvement is associated with poorer prognosis

Follow-Up Surveillance and Aftercare of Wilms’ Tumor

During treatment, it is important to be aware of the possible presence of sinusoidal obstruction syndrome (formerly called veno-occlusive disease) affecting the small hepatic veins. It is a common side effect of the cytostatic drug actinomycin D, which represents the key substance in chemotherapy for nephroblastoma. For follow-up surveillance, abdominal sonography is a suitable method as it avoids further exposure to radiation.

Regular Aftercare of Nephroblastoma

To rule out any lung metastases, it is imperative to periodically perform X-ray of the lung. In the long term, special attention has to be paid to any growth disturbances in the skeleton and soft tissues, which could be a consequence of radiation.

References


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