Wilms Tumor

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The bilateral kidneys are positioned in the retroperitoneal cavity. They are part of the urinary system, which consists of the bilateral kidneys and ureters, urinary bladder, and urethra (see **Figure 1**). The kidneys are vital organs that filter blood and excrete metabolic products and waste in the form of urine. They preserve bodily fluid and regulate blood pressure and acid-base balance, among other functions. Wilms tumor, also called *nephroblastoma*, is a malignant tumor arising from the renal parenchyma.[1] This tumor was named after German physician and surgeon Dr Max Wilms (1867-1918) who described this tumor in 1899.[1,2] Wilms tumor is the most common malignant pediatric renal mass and the fourth most common pediatric cancer.[1,2]

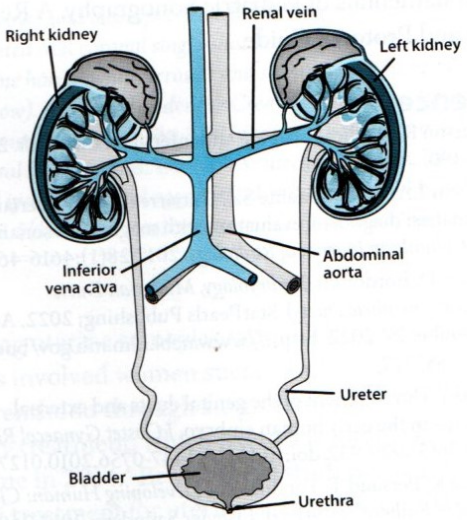

Figure 1. *Anatomy of the urinary system.* © *ASRT 2016.*

Epidemiology and Associated Disorders

Wilms tumor accounts for 7% of all childhood cancer and more than 85% of pediatric renal mass cases.[3] Approximately 80% to 90% of Wilms tumors are discovered before 6 years of age.[1,2] However, this mass can occur at any time from infancy to early adolescence.[1,4,5] The mean age of occurrence is 2 to 5 years, and the median age is 3.5 years.[1,2,4] When coinciding with a syndrome, the age of occurrence tends to be earlier, between 2 and 24 months of age.[1]

Female patients have a marginally higher predisposition for developing Wilms tumor compared with male patients, and presentation in girls occurs at a later age.[4] Patients of African descent are at greatest risk for developing Wilms tumor.[4] The rates of occurrence among patients with European and North American descent are relatively the same. Prevalence of Wilms tumor among patients of East Asian descent is collectively the lowest.[2] Furthermore, patients of Asian descent demonstrate greater survival rates, a lower rate of disadvantageous tumor histology, and lower-stage tumor classification.[2]

Wilms tumor is primarily a unilateral condition, with less than 5% of cases occurring bilaterally.[1] For a unilateral Wilms tumor, the age at diagnosis is between 3.5 and 4 years. Bilateral Wilms tumor is diagnosed

earlier on average, between 2.5 and 2.75 years of age.[5] In the United States, Wilms tumor occurs in approximately 1 in 10 000 pediatric patients, with 650 new cases diagnosed yearly.[4] With technological advances in the United States, patients with Wilms tumor have a 5-year survival rate of 92%. In resource-poor countries, the survival rate is lower, at 78%.[2]

Causes and Risk Factors

Many cases of Wilms tumor occur sporadically, with approximately 1% to 2% of cases being familial.[1] For patients with a relative who was diagnosed with Wilms tumor, the relative typically is not the parent.[2] The cause of Wilms tumor is not well understood, but it is presumed to be related to genetic modification associated with embryonic genitourinary tract development. Wilms tumor could evolve from nephrogenic rests or preservation of metanephric tissue, which ordinarily regresses in youth but can occur in 1% of infantile kidneys.[2] Near age 3, renal cells mature; however, with Wilms tumor, renal cells fail to fully mature, and immature cells begin developing into a mass.[4] Anomalous metanephric cells are identified in all bilateral Wilms tumor cases. Abnormal metanephric cells are identified in 35% of cases of unilateral Wilms tumor.[4] Infants aged 1 year or less who exhibit perilobar nephrogenic rests are at increased risk for developing a contralateral Wilms tumor.[2]

Wilms tumor is affiliated with genetic markers, including *WT2* overgrowth and *WT1* nonovergrowth syndromes.[2] Overgrowth syndromes associated with Wilms tumor include Perlman syndrome; Beckwith-Wiedemann syndrome; Sotos syndrome, also called *cerebral gigantism*; and Simpson-Golabi-Behmel syndrome. WAGR syndrome is an associated nonovergrowth syndrome that affects many bodily systems; WAGR is an abbreviation for the primary characteristics of the syndrome: Wilms tumor, aniridia, genitourinary anomalies, and intellectual retardation (disability). Aniridia is a partial or complete lack of the ocular iris. Female patients with WAGR syndrome also might have underdeveloped, or streak, ovaries, which can lead to development of gonadoblastoma. Patients with WAGR syndrome have a 50% likelihood of developing Wilms tumor. This relates to an anomaly on the chromosomal *WT1* gene pertaining to gonadal and renal development.[2] *WT1*, *WTX*, and *CTNNB1* gene alterations have been noted in one-third of patients with Wilms tumors.[2] *MYNC* and *TP53* genes also have been correlated with Wilms tumor, with alterations in the *TP53* gene and heterozygosity deficit at chromosomes 1q, 1p, 16q, and 11p15 carrying a worse prognosis (see **Figure 2**).[2]

Other associated nonovergrowth syndromes include Bloom syndrome, Frasier syndrome, Trisomy 18 (Edward syndrome), Li-Fraumeni syndrome, and Denys-Drash syndrome.[1,2] Denys-Drash syndrome, also called *Drash syndrome*, involves progressive renal failure. Approximately 90% of patients with end-stage renal failure related to Drash syndrome develop Wilms tumor.[2] Isolated conditions related to Wilms tumor include sporadic aniridia, hemihypertrophy, and an array of genitourologic disorders, including cryptorchidism, hypospadias, varicocele, renal fusion (horseshoe kidney), renal ectopia, and renal duplication. Approximately 10% of female patients have associated congenital uterine abnormalities.[1,2] Reproductive and urinary system anomalies coincide because of their close developmental relationship during embryogenesis.

Clinical Manifestation

Many young children with Wilms tumor are asymptomatic and present with a palpable region of upper abdominal swelling. Often in the infantile period, this swelling is noted by the parent or caregiver when changing or bathing the child. Other symptoms more commonly noted in older children include[4]:

- anemia
- constipation

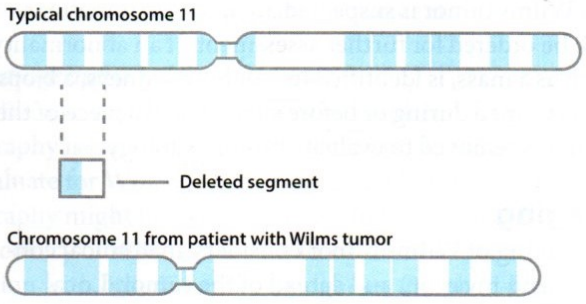

Figure 2. *Illustration comparing the typical structure of chromosome 11 with an abnormal version caused by the deletion of a segment (loss of heterozygosity), which is associated with Wilms tumor. Public domain image from Wikimedia Commons.*

- decreased appetite
- elevated blood pressure (due to high renin production)
- fever
- gross hematuria (present in 20% of cases)
- nausea
- upper abdominal pain
- urinary tract infection
- vomiting

If nephrectomy is performed to resect the kidney affected by Wilms tumor, hypertension normalizes.[2] Acquired von Willebrand disease affects approximately 8% of patients with Wilms tumors.[1] In late stages, metastases can occur. The most common site for Wilms tumor to metastasize is the lung, which accounts for 85% of metastatic cases arising from Wilms tumor. At diagnosis, approximately 10% to 20% of patients have coinciding lung metastases.[1] Dyspnea or tachypnea might occur when Wilms tumor metastasizes to the lung.[2]

Diagnosis

Diagnosis of Wilms tumor begins with a physical examination of the patient and obtaining the patient's personal and family medical history, including medications and past and current medical conditions. The clinician might order a urinalysis and blood tests.[4] The urinalysis can differentiate a Wilms tumor from another tumor, such as neuroblastoma, by assessing for a substance in the urine called *catecholamines*.[6] Blood tests might include a complete blood count, coagulation study, blood chemistry profile to gauge renal function and evaluate blood calcium and electrolyte levels, and cytogenetic studies to check for alteration of specific genes.[7] If a Wilms tumor is suspected, imaging examinations will be ordered for further assessment. If an abnormality, such as a mass, is identified in 1 or both kidneys, a biopsy is performed during or before surgery, and a piece of the tumor is removed to evaluate tumor histology.

Staging

Staging of Wilms tumor considers anatomical confinement, invasion, and spread of the tumor. Local invasion and metastasis worsen the prognosis of the disease.[8] With stage I, Wilms tumor is restricted to the kidney without extending past the renal capsule, and complete renal resection is a viable treatment option.[4,8] No vascular invasion is involved with this stage.[4] Stage I is the most prevalent stage, composing 40% to 45% of all diagnosed Wilms tumors.[2,4] Stage II involves local spread to the renal collecting system, renal capsule, and areas surrounding the affected kidney such as the renal vein.[4,8] The second stage constitutes 20% of all diagnosed Wilms tumors.[2,4] When Wilms tumor is deemed stage III, disease has spread past the affected kidney. This stage might involve regional lymph nodes along the abdominal aorta or inferior vena cava or in the peritoneal cavity.[4] In stage III, metastases are confined to the abdomen. Surgical margins where renal resection is performed typically contain tumor cells, allowing cancer to continue to spread.[4,8] Twenty percent to 25% of Wilms tumors are stage III at diagnosis.[2] Hematogenous metastasis is classified as stage IV. In these cases, the malignant Wilms tumor has spread via the vascular system from its site of origin to distant sites, including the lungs, distant lymph nodes, brain, bones, or liver.[4,8] At diagnosis approximately 10% to 15% of Wilms tumors are stage IV.[2,4] Stage V entails bilateral renal involvement. When both kidneys are involved, each kidney should be separately staged.[8] Between 5% and 10% of Wilms tumors are stage V at diagnosis.[4]

Imaging Features

Imaging examinations provide detailed information related to renal anatomy and pathology. When a mass is present, medical imaging can determine its site of origin and whether the mass has spread. The Wilms tumor staging system corresponds with imaging features of Wilms tumor. The primary imaging used to assess the upper urinary system for Wilms tumor includes sonography, computed tomography (CT), and magnetic resonance (MR) imaging. Plain-film radiography is not an adequate method for evaluating Wilms tumor but can provide information that leads to further investigation of the abdomen.

CT and MR evaluations produce cross-sectional images over a large area of the body, which is useful for assessing the potential spread of cancer. Sonography allows for real-time assessment of anatomy and perfusion of structures. Sonography is quick, cost efficient, portable, and does not use ionizing radiation to produce images. The main drawback is its small field of view

compared with CT and MR imaging.[4] Because of the limited field of view, assessing tumor metastases with sonography alone is challenging; therefore, sonographic evaluation often is performed in conjunction with another cross-sectional imaging modality.

Sonography

Sonography is the first-line imaging modality used for evaluation of Wilms tumor (see **Figure 3**). It uses acoustic energy to produce a diagnostic image. Typical retroperitoneal renal sonography assesses the bilateral kidneys and urinary bladder. If a complete abdominal evaluation is ordered, assessment also includes the:

- biliary tree
- gallbladder
- great vessels
- liver
- pancreas
- spleen

Sonography can localize the origin of a mass and differentiate between alternative etiologies that can cause renal distension such as hydronephrosis.[1] On a sonogram, Wilms tumor in the kidney appears as a large mass that varies from homogeneous to heterogeneous.

Wilms tumors can grow larger than 12 cm in diameter and cause secondary hypertension because of hilar vessel compression.[9] Wilms tumors might contain areas of fat, calcification, and necrosis. Sonography can assess perfusion in the renal vein and inferior vena cava. This finding is useful in identifying hilar vessel compression and a thrombus associated with Wilms tumor that might cause adverse patient symptoms. In North America and Europe, combining sonography with another cross-sectional imaging modality, such as CT or MR imaging, to stage Wilms tumors is standard, with CT being the most used cross-sectional modality to determine the extent of Wilms tumor.[1]

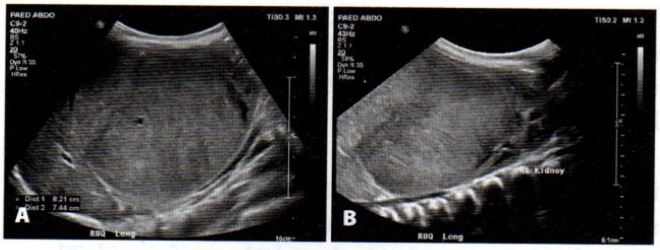

Figure 3. *Sagittal ultrasound imaging of the right upper abdominal quadrant demonstrating presence of Wilms tumor arising from the superior pole of the right kidney, measuring up to 8.2 cm. Case courtesy of James Harvey, Radiopaedia.org (rID: 80200). Reprinted with permission under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported license. creativecommons.org/licenses/by-nc-sa/3.0/legalcode*

Computed Tomography

CT uses ionizing radiation to produce a diagnostic cross-sectional image and to assess the spread of Wilms tumor. For tumor representation, CT should be performed in the portal venous phase. Mostly because of their developing tissues, pediatric patients are part of a radiosensitive population. Multiphase CT of the abdomen has no additional imaging value, and providers should refrain from ordering this examination in adherence with the ALARA (as low as reasonably achievable) principle. The purpose of ALARA is to reduce the extent of radiation exposure by ordering only pertinent examinations that will benefit the patient's diagnosis and treatment plan.

On CT images, Wilms tumors appear as bulky, spherical, inhomogeneous intrarenal masses with soft-tissue density (see **Figure 4**). A pseudocapsule or well-defined rim of compressed renal parenchyma surrounding the tumor is common. Areas of fat-density are not uncommon, and calcified regions are identified in 13% to 15% of cases.[1,10] Wilms tumor also has been described as having a patchy enhancement pattern or exophytic growth. This tumor might compress surrounding anatomical structures. Approximately 10% of patients demonstrate compression of the collecting system, renal tumor infiltration, and venous tumor extension. Twenty-five percent of cases show vascular encasement.[10]

Radiography

Because of the lack of renal detail, plain-film radiography is not the imaging modality of choice to evaluate for Wilms tumor. However, plain-film radiography might be a starting point in the incidental discovery of Wilms tumor, leading to further investigation with other imaging modalities. On plain-film radiographs, Wilms tumors appear as enlarged, inhomogeneous, soft-tissue opacity tumors that displace surrounding anatomic structures such as the malleable adjacent bowel.[1]

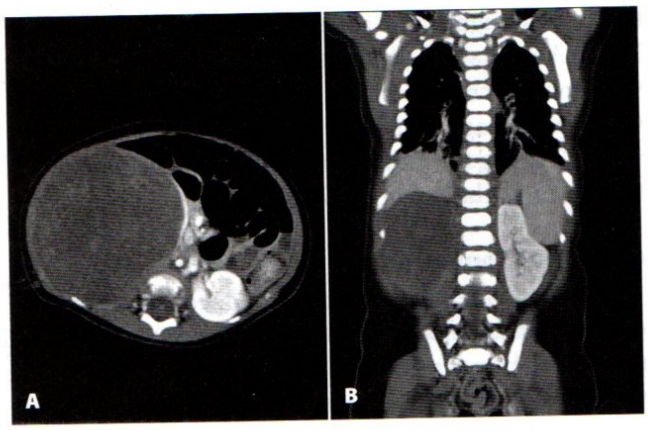

Figure 4. *Axial (A) and coronal (B) computed tomography representation of confirmed Wilms tumor arising from the right kidney. Case courtesy of James Harvey, Radiopaedia.org (rID: 80200). Reprinted with permission under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported license. creativecommons.org/licenses/by-nc-sa/3.0/legalcode*

Magnetic Resonance Imaging

MR imaging uses a magnetic field to create detailed cross-sectional images and can assess for spread of Wilms tumor like a CT scan but without the use of ionizing radiation. This makes MR imaging a beneficial resource for staging Wilms tumors in this patient population. The drawback to MR imaging is the time required to obtain an imaging sequence. Young patients might require sedation to complete an MR evaluation of the urinary system and regions possibly affected by metastases.

On all MR imaging sequences, Wilms tumors appear inhomogeneous. Blood product might be identified with Wilms tumor on MR imaging. A T1 sequence produces a hypointense mass appearance; T1 imaging with gadolinium contrast produces heterogeneous enhancement of the tumor. A T2 sequence produces a hyperintense mass appearance. MR imaging also can accurately identify involvement of the inferior vena cava.[1]

Treatment Options

To determine the appropriate course of treatment, Wilms tumor should be differentiated from other renal etiologies that have similar clinical signs or symptoms, including[1,4]:

- angiomyolipoma
- childhood renal cell carcinoma
- clear cell sarcoma
- cystic partially differentiated nephroblastoma
- neuroblastoma
- pediatric cystic nephroma
- renal abscess
- renal rhabdoid tumor

In this pediatric group, tumor histology coincides with surgical intervention and a preceding routine biopsy is not recommended in unilateral cases.[2] Factors that affect treatment include laterality, Wilms tumor staging, and familial predisposition.

Treatment options include open or minimally invasive surgery, chemotherapy, and, in select cases, radiation therapy. The benefit of open surgery compared with a minimally invasive technique is the ability to provide a large number of lymph nodes for sampling.[2] Tumor histology will determine use of adjuvant radiation therapy. When radiation therapy is warranted, it should be performed within 2 weeks of surgical intervention for best outcomes.[2] Chemotherapy drugs used to treat Wilms tumor might be used individually or together depending on disease stage. These drugs include doxorubicin, cyclophosphamide, carboplatin, and etoposide, and, in stage I and II cases, dactinomycin and vincristine.[4]

Surgical removal of the affected kidney, called *nephrectomy*, is the treatment plan of choice for patients with early stages of unilateral Wilms tumor. Regional lymph node sampling is performed to determine whether the tumor has spread.[4] After renal resection, patients might undergo systemic chemotherapy, particularly if there is loss of heterozygosity of chromosomes 1p, 1q, 11p15, and 16q or the patient presents with a mutation in the *TP53*.[2] Radiation therapy might be indicated after nephrectomy based on tumor histology and if regional lymph node sampling results are positive for spread.[4]

For more advanced stages of Wilms tumor that involve metastatic spread of cancer and in bilateral cases, systemic high-dose chemotherapy and radiation therapy to the focal regions of spread might be performed. The goal of this treatment is to shrink the tumor and preserve the unaffected renal tissue, so the patient is not reliant on dialysis.[2] Often, Wilms tumor spreads to lung tissue. Treatment response to pulmonary metastases dictates the therapy options used. For stage IV Wilms

tumor, systemic chemotherapy involves a combination of drugs that might include vincristine, dactinomycin, and doxorubicin. After the tumor has decreased to a more favorable size, surgery is performed to remove the mass.

Patient prognosis depends heavily on tumor stage at diagnosis and tumor histology. In the United States, the 5-year survival rate for patients with Wilms tumor is 92% owing to new technologies and treatment therapies.[4] The 5-year survival rate for Wilms tumor is lower in countries lacking medical resources. If recurrent Wilms tumor is identified, it often is found in the tumor fossa or in areas where metastatic spread occurred such as the liver or lungs.[1]

Conclusion

Wilms tumor, a malignant renal mass most often found in children and adolescents, is associated with several genetic markers, residual metanephric tissue, and nephrogenic rests. It is the most common pediatric renal malignancy, accounting for more than 85% of pediatric renal masses and 7% of all childhood cancers. The median age of occurrence is 3.5 years, but Wilms tumor can occur at any age from infancy through early adolescence. Wilms tumor has a distinct imaging appearance and can be diagnosed and staged using sonography, CT, and MR imaging. Patient prognosis and treatment depend on laterality, staging, and familial predisposition for Wilms tumor. Current treatment options include surgery, chemotherapy, and radiation therapy. As new technologies and treatments for Wilms tumor emerge, prognosis improves.

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References

1. Gaillard F, Bell D. Wilms tumor. Radiopaedia. Updated October 18, 2023. Accessed October 19, 2023. https://radiopaedia.org/articles/wilms-tumour
2. Leslie SW, Sajjad H, Murphy PB. *Wilms Tumor.* StatPearls Publishing; 2022. Accessed December 4, 2022. https://www.ncbi.nlm.nih.gov/books/NBK442004/
3. Servaes SE, Hoffer FA, Smith EA, Khanna G. Imaging of Wilms tumor: an update. *Pediatr Radiol.* 2019;49(11):1441-1452. doi:10.1007/s00247-019-04423-3
4. Wilms' tumor. National Organization for Rare Disorders. Published September 10, 2019. Accessed December 4, 2022. https://rarediseases.org/rare-diseases/wilms-tumor/
5. The Children's Hospital of Philadelphia. Wilms tumor (kidney tumor). Children's Hospital of Philadelphia. Published January 28, 2012. Accessed December 4, 2022. https://www.chop.edu/conditions-diseases/wilms-tumor-kidney-tumor
6. Tests for Wilms tumors. American Cancer Society. Published 2022. Accessed December 4, 2022. https://www.cancer.org/cancer/wilms-tumor/detection-diagnosis-staging/how-diagnosed.html#:~:text=Kidney%20biopsy%2Fsurgery,and%20checked%20under%20a%20microscope
7. Paulino A. Wilms tumor workup. Approach, considerations, imaging studies, surgical examination and biopsy. Published December 9, 2021. Accessed December 4, 2022. https://emedicine.medscape.com/article/989398-workup
8. Gaillard F, Worsley C. Wilms tumor (staging). Radiopaedia. Updated August 30, 2022. Accessed October 19, 2023. https://radiopaedia.org/articles/wilms-tumour-staging-1?lang=us
9. Laquerre J. Pathologic processes of the urinary tract. In: Laquerre J. *Lange Review: The Fundamentals of Pediatric Sonography: A Registry Review and Protocol Guide.* Vol 1. McGraw-Hill Education; 2023:153-170.
10. Olukayodé AA, Richard IO, Rachael AA, Babajide OB, Ireti OF, Gbolahan OA. Pattern of computed tomography scan findings in children with Wilms' tumor in a tertiary hospital in Lagos, Nigeria. *Indian J Med Paediatr Oncol.* 2014;35(1):31-35. doi:10.4103/0971-5851.133713.