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Review article Disease

A REVIEW ON WILMS TUMOR

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ABSTRACT

Wilms' tumor is a type of childhood cancer that starts in the kidneys. It is the most common type of kidney cancer in children. About 9 of 10 kidney cancers in children are Wilms tumors. Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer. Most Wilms tumors or unilateral, which means they affect only one kidney. Most often there is only one tumor, but a small number of children with tumors have more than one tumor in the same kidney. About 5% to 10% of children with Wilms tumors have bilateral disease (tumors in both Kidneys). Wilms tumor often become quite large before they are noticed. The average newly found Wilms tumor is many times larger than the kidney in which it started. Most Wilms tumors are found before they have spread (metastasized) to other organs. Other type of kidney cancers in children are Mesoblastic nephroma, Clear cell sarcoma of kidney (CCSK), malignant rhabdoid tumor of the kidney, renal cell carcinoma.

Keywords: Wilms tumor, pathology, genetics, management

INTRODUCTION

Wilms tumor, or nephroblastoma, is the most common renal cancer in the pediatric age group. It is also the most common pediatric abdominal cancer and the fourth most common pediatric cancer overall. Wilms tumor is typically found in children younger than five years old. The tumor is named after the German physician, Dr. Max Wilms, who first described it in 1899 [1].It is also one of the successes of paediatric oncology with long term survival above 90% for localised disease and 75% for metastatic disease. Successful management of Wilms' tumor necessitates meticulous attention to correct staging of the tumor and a collaborative effort between paediatric oncologists, specialist surgeons, radiologists, pathologists, and radiation oncologists. Although current treatment protocols are based on risk assignment to minimise toxicity for low risk patients and improve outcomes for those with high risk disease, challenges remain in identifying novel molecular, histological and clinical risk factors for stratification of treatment intensity. Knowledge about Wilms' tumor biology and treatment is evolving rapidly and remains a paradigm for multimodal malignancy treatment. Future efforts will focus on the use of biomarkers to improve risk stratification and the introduction of newer molecularly targeted therapies that will minimise toxicity and improve the outcomes for patients with unfavourable histology and recurrent disease.

Types of Wilms Tumor

There are two kinds of Wilms tumors, divided by how the cells look under a microscope. Favorable histology. More than 9 out of 10 Wilms tumors fall into this group. It means there isn't a lot of difference among the cancer cells. Children with this type have a good chance of being cured. Unfavorable or anaplastic histology. This type has a variety of deformed cancer cells. It can be much harder to cure.[2]

Epidemiology

Wilms tumor is the most common incidence is slightly higher for girls than boys among white patients. In contrast, a greater incidence among boys than girls has been observed in the east-Asian population almost entirely along ethnic

groups rather than geographic areas, suggesting that genetic factors play the most important role in its etiology.[3]

Signs &Symptoms

Signs and symptoms of Wilms' tumor vary widely, and some children don't show any obvious signs. But most children with Wilms' tumor experience one or more of these signs and symptoms: An abdominal mass you can feel, Abdominal swelling, Abdominal pain. Other signs and symptoms may include Fever, Blood in the urine, Nausea or vomiting or both, Constipation, Loss of appetite, Shortness of breath, High blood pressure.[4]

Risk factors

A risk factor is anything that increases a persons chance of developing a tumor. Although risk factors often influence the development of a Wilms tumor, most do not directly cause it. Some children with several risk factors never develop a tumor, while others with no known risk factors do. Most often, the risk of a Wilms tumor is not inherited, but there can be genetic reasons for the tumors development. Genetic changes. Children may have a mutated (changed), damaged, or missing gene. This change can also cause other birth defects. About 15% of children with a Wilms tumor were born with other health problems. WAGR syndrome: WAGR syndrome is a condition that causes a number of birth defects. Children with this syndrome have a 33% chance of developing a Wilms tumor. WAGR stands for Wilms tumor, Aniridia (no iris in the eye), Genitourinary abnormalities, which are changes to the reproductive and urinary organs, or gonadoblastoma, which is a rare tumor of the reproductive organs, Intellectual disability, once called mental retardation. [5] Beckwith-Wiedemann syndrome: This condition causes enlarged internal organs and limbs. Children with this syndrome have a higher risk of developing a Wilms tumor, kidney cysts, and tumors of the liver (hepatoblastoma), pancreas, and adrenal glands. Denys-Drash syndrome: This is a condition in which a boy's sex organs do not develop correctly. Boys with this syndrome have a higher risk of developing a Wilms tumor. Family history. A small number of children with a Wilms tumor have a relative in their family with the disease.[6]

Diagnosis

Medical appointment will probably include

A physical exam and medical history. The doctor will ask about the symptoms and whether cancer or urinary tract problems run in your family. A blood test to check how well your child's kidneys and liver are working, their red and white blood cells, and their blood clotting, A urine test to look for blood, Imaging tests like an ultrasound, MRI, or CT scan of your childs belly[7] .If the doctor finds a tumor in your childs kidney, they may: Take a small sample to look at under a microscope (biopsy),Order more imaging tests to find out whether the disease has spread, Do a bone scan to look for diseased bone,Abdominal ultrasound. This imaging test uses high-frequency sound waves and a computer to create pictures of internal organs, blood vessels and tissues. Bone scan, This imaging test, which is used to detect bone cancer, uses a special radioactive material that is injected into a vein. The substance collects in areas of diseased bone and is sensed by special cameras that pick up radioactivity. Abdominal computerized tomography scan (CT or CAT scan), This imaging test uses X-rays and computer technology to produce detailed cross-sectional images (slices) of the body, including the bones, muscles, fat and organs. It can show a mass in the kidneys and whether the cancer has spread to other organs such as the lungs.Chest X-ray, This imaging test produces images of the heart, lungs and bones.Magnetic resonance imaging (MRI), An MRI scan uses radio waves and strong magnets with computer technology. MRI shows more detailed images than CT and ultrasound and can help doctors see if the cancer has invaded one of the major blood vessels located near the kidney.Blood and urine tests, These laboratory tests help evaluate kidney and liver function.Biopsy, A sample of tissue is removed and examined under a microscope; this helps confirm the diagnosis and aids in the treatment plan.

Wilms Tumor Staging

The doctor will use test results to figure out how far a tumor has spread. This is called staging. The stages of a Wilms tumor are, Stage I: Its in only one kidney. Surgery can remove it all. Stage II: Cancer has moved into the area around the kidney, but surgery can remove it all. Stage III: Cancer hasn't spread outside the child's abdomen. Surgery can't remove it all. Stage IV: Cancer has spread to parts of the body that are farther away, like the lungs, bones, or brain, or to lymph nodes outside the belly. Stage V: There are tumors in both kidneys. [6]

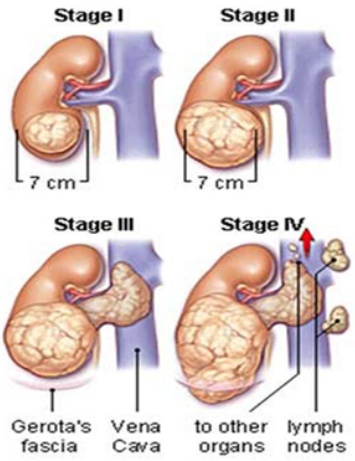

Fig 1: 1stages of wilms tumor [8]

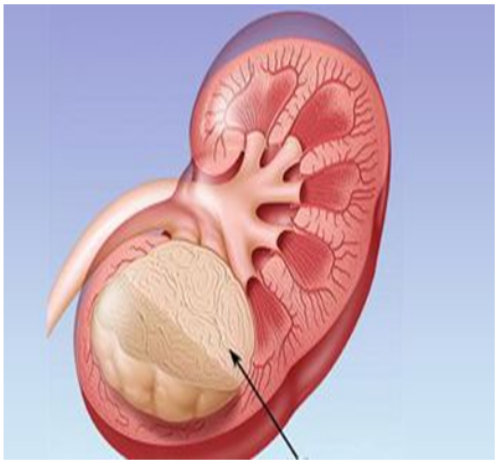

Fig 2: Human Kidney[9]

Pathophysiology

Nephrogenic rests are precursor lesions [10], Nephrogenic rests are found in 40% of unilateral and >90% of bilateral Wilms tumors [11]. Not clear how nephrogenic rests progress to tumor. Two main types of nephrogenic rests: Perilobar nephrogenic rests, Intralobar nephrogenic rests, Perilobar nephrogenic rests in children under 1 year of age are associated with a markedly increased risk of developing a contralateral Wilms tumor.

Chemotherapy

1.Neoadjuvant chemotherapy indications include :Bilateral Wilms tumor, Inoperable tumor, Intravascular extension into IVC above hepatic veins, Tumor in solitary kidney.2.Adjuvant Chemotherapy : Regimen EE4A -18 week course, Actinomycin D and Vincristine, Stage I/II FH WT, Stage I focal or diffuse anaplasia WT. Regimen DD4A -24 week course, Actinomycin D, Vincristine, Doxorubicin, Stage III/IV FH WT, Stage II - IV Focal analapsia. Regimen I-24 week course, Vincristine, Doxorubicin, Cyclo-phosphamide, Etoposide. [12]

Surgical principles

A. Standard procedure: Radical nephrectomy + lymph node sampling through a transperitoneal approach. Surgery helps in Assessing Tumor extent involvement, Lymph node sampling, Any liver metastasis biopsy, Any peritoneal seeding biopsy.Formal retroperitoneal lymph node dissection is not indicated but lymph node sampling in the hilar, periaortic, pericaval, iliac and celiac lymph node regions are mandatory. The incidence of post-operative complications in the NWTSG was 11%. The most serious complication intra-operatively is tumor embolus into pulmonary artery and sudden death. Common post-operative complications are Hemorrhage, Intestinal obstruction and Intestinal obstruction which in first post-op week is mostly due to intussusception and after that is due to adhesive obstruction**.** *B. Role of contralateral exploration:* Contralateral exploration is mandatory according to NWTSG with formal opening of Gerota's fascia and inspection of anterior and posterior surface of kidney and biopsy of any suspicious lesion. The chance of missing a bilateral WT after imaging studies is 0.35%. Hence, the routine practice of contralateral exploration is controversial. *C. Intravascular tumor extension:* Neoadjuvant chemotherapy will be helpful in avoiding a tumor embolus during mobilization. An infradiaphragmatic infrahepatic non-adherent caval vein thrombus generally can be removed by cavotomy or using a Fogarty or Foley balloon catheter. Patients with intravascular extension above the level of the hepatic veins should receive preoperative chemotherapy. Recent reports showed that preoperative therapy in patients with suprahepatic caval or atrial extension led to a marked decrease in size of tumor thrombus and even complete regression of thrombus without embolization. As an alternative in adverse cases, embolectomy under cardiopulmonary bypass is required. *D. Parenchymal sparing surgery:* Partial nephrectomy, Enucleation. The above procedures can be done if following criteria are satisfied: Tumor involving one pole and less than one-third of kidney, Normal functioning remaining kidney, No tumor extension into renal collecting system and renal vein, Clear demarcation between tumor and kidney and adjacent structures.[13] Parenchymal sparing surgery is indicated in Bilateral WT, Renal insufficiency as in Denys-Drash syndrome, Solitary kidney WT**,** Syndromes associated with increased incidence of nephrogenic rests.

Adults Wilms tumor

Wilms tumor in adults is rare and the estimated incidence is only 0.2 cases per million. There are approximately 300 cases of adult WT reported in the literature.54–59 Kilton et al59 suggested diagnostic criteria for adult WT that include primary renal tumor in the age group of above 15 years, with histologic features of embryonic glomerulotubular structures with immature spindle or round cell stroma and no areas of tumor diagnostic of renal cell carcinoma. The genomic alterations involved in adult WT maybe different than WT in children, with the majority of chromosomes displaying uniparental disomies and microdeletions in genes involved in organogenesis. Adult WT has more aggressive clinical course and a higher tumor stage at the time of presentation, as well as worse outcome than pediatric WT probably because of the difficulty in diagnosis, inadequate staging, and undertreatment. Adult WT is a difficult tumor to study, because some of the previously considered adult WT may in fact be other more aggressive entities such as primary renal Ewing sarcoma and primary renal synovial sarcoma.[14]

Extra Renal Wilms Tumor (ERWT)

ERWT is a rare form of WT that occurs outside the kidney. It accounts for 3% of WTs with approximately 100 well-documented cases. It has been reported in a variety of locations including the retroperitoneum, inguinal and paratesticular region, female genital tract, bladder, thorax, and lambosacral region. On the basis of the National Wilms tumor study, the diagnosis of an ERWT should fulfill 3 criteria. First, a primary tumor in the kidney should be excluded. Second, the triphasic histology pattern (blastemal, epithelial, and stromal) should be present. Third, there should be no evidence of teratoma or renal cell carcinoma on thorough examination of the entire tumor. No staging system for ERWT has been worked out, although the staging similar to that used for intrarenal WT may be applicable. The prognosis of ERWT also seems to be similar to that of intrarenal WT. The origin of ERWT is unclear; possibilities include origin from heterotopic metanephric blastema, persistent mesonephric duct remnants, and intermediate mesoderm. [14]

CONCLUSION

The outcome of children with Wilms tumor has improved significantly over the last few decades. New treatment protocols are designed to maintain a high cure rate for these children while reducing toxicity. Future targets for treatment are expected to emerge based on the molecular genetics of Wilms tumor. Such a biology-driven approach to risk stratification and introduction of novel therapies should continue to improve the success of first line treatments and minimize the overall burden of therapy. Surgery will continue to play a crucial role in the management of all patients, while radiotherapy is applied to a carefully selected

diminishing proportion. Hence, it is essential that the surgeon performing nephrectomy for childhood renal tumors is an integral part of the oncological discussions and understands fully the impact of different outcomes of surgery on the overall management plan.

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