

Wilms Tumor

Subjects: Genetics & Heredity

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Wilms tumor is a form of kidney cancer that primarily develops in children. Nearly all cases of Wilms tumor are diagnosed before the age of 10, with two-thirds being found before age 5.

Keywords: genetic conditions

1. Introduction

Wilms tumor is often first noticed because of abdominal swelling or a mass in the kidney that can be felt upon physical examination. Some affected children have abdominal pain, fever, a low number of red blood cells (anemia), blood in the urine (hematuria), or high blood pressure (hypertension). Additional signs of Wilms tumor can include loss of appetite, weight loss, nausea, vomiting, and tiredness (lethargy).

Wilms tumor can develop in one or both kidneys. About 5 to 10 percent of affected individuals develop multiple tumors in one or both kidneys. Wilms tumor may spread from the kidneys to other parts of the body (metastasize). In rare cases, Wilms tumor does not involve the kidneys and occurs instead in the genital tract, bladder, abdomen, chest, or lower back. It is unclear how Wilms tumor develops in these tissues.

With proper treatment, children with Wilms tumor have a 90 percent survival rate. However, the risk that the cancer will come back (recur) is between 15 and 50 percent, depending on traits of the original tumor. Tumors usually recur in the first 2 years following treatment and develop in the kidneys or other tissues, such as the lungs. Individuals who have had Wilms tumor may experience related health problems or late effects of their treatment in adulthood, such as decreased kidney function, heart disease, and development of additional cancers.

2. Frequency

Wilms tumor is the most common kidney cancer in children. In Europe and North America, Wilms tumor affects 1 in 10,000 children. In the United States, 500 children develop Wilms tumor each year. The incidence of Wilms tumor seems to vary among populations, with African Americans having a higher-than-average risk of developing this cancer and Asians having a lower-than-average risk.

Wilms tumor rarely develops in adults; only about 300 such cases have been described.

3. Causes

Changes in any of several genes are involved in the formation of Wilms tumor. Wilms tumor is often associated with mutations in the *WT1* gene, *CTNNB1* gene, or *AMER1* gene. These genes provide instructions for making proteins that regulate gene activity and promote the growth and division (proliferation) of cells. *WT1*, *CTNNB1*, and *AMER1* gene mutations all lead to the unchecked proliferation of cells, allowing tumor development.

Changes on the short (p) arm of chromosome 11 are also associated with developing Wilms tumor. Two genes in this area, *IGF2* and *H19*, are either turned on or off depending on whether the copy of the gene was inherited from the mother or the father. This parent-specific difference in gene activation is a phenomenon called genomic imprinting. In some cases of Wilms tumor, abnormalities in the process of genomic imprinting on chromosome 11 lead to a loss of *H19* gene activity and increased activity of the *IGF2* gene in kidney cells. The resulting loss of *H19* gene activity, which normally restrains cell growth, and increase in *IGF2* gene activity, which promotes cell growth, together lead to uncontrolled cell growth and tumor development in people with Wilms tumor.

In most cases of Wilms tumors involving one kidney and nearly all cases involving both kidneys, the tumors are thought to arise from immature kidney tissue that never developed properly. These immature tissues are known as nephrogenic rests. It is likely that genetic changes are involved in the presence of nephrogenic rests and that additional genetic changes trigger nephrogenic rests to develop into a tumor.

Genetic conditions that share a genetic cause with Wilms tumor can also have this cancer as a feature. These conditions include WAGR syndrome, Denys-Drash syndrome, and Frasier syndrome, which are caused by mutations in the *WT1* gene. Wilms tumor has also been seen in individuals with Beckwith-Wiedemann syndrome, which can be caused by changes in the genomic imprinting of the *IGF2* and *H19* genes. Wilms tumor can be a feature of other genetic conditions caused by mutations in other genes.

Many children with Wilms tumor do not have identified mutations in any of the known genes. In these cases, the cause of the condition is unknown. It is likely that other, unknown genes are also associated with the development of Wilms tumor.

3.1 The genes associated with Wilms tumor

- *AMER1*
- *CTNNB1*
- *H19*
- *IGF2*
- *TP53*
- *WT1*

4. Inheritance

Most cases of Wilms tumor are not caused by inherited genetic factors and do not cluster in families. Approximately 90 percent of these cancers are due to somatic mutations, which means that the mutations are acquired during a person's lifetime and are present only in the tumor cells.

Mutations that are present in cells throughout the body (called germline mutations) are responsible for the remaining 10 percent of Wilms tumor cases and cause either Wilms tumor without any other signs or symptoms or syndromes in which Wilms tumor is one of multiple features. These cases follow autosomal dominant inheritance, which means one copy of the altered gene in each cell can cause a Wilms tumor-related syndrome or increase a person's chance of developing the cancer alone. Most of these cases result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development.

The *AMER1* gene is located on the X chromosome (one of the two sex chromosomes), so when Wilms tumor is caused by mutations in this gene, the condition follows an X-linked dominant pattern. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to increase a person's chance of developing cancer. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell increases their cancer risk.

In many cases, the genetic basis for Wilms tumor and the mechanism of inheritance are unclear.

5. Other Names for This Condition

- embryonal adenosarcoma
- embryonal nephroma
- kidney Wilms tumor
- kidney, adenomyosarcoma, embryonal
- kidney, carcinosarcoma, embryonal
- kidney, embryoma
- kidney, embryonal mixed tumor
- nephroblastoma
- nephroma
- renal adenosarcoma
- renal cancer, Wilms
- renal Wilms tumor
- tumor, Wilms

- Wilms' tumor

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