WAGR Syndrome

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genetic conditions

1. Introduction

WAGR syndrome is a disorder that affects many body systems and is named for its main features: Wilms tumor, aniridia, genitourinary anomalies, and intellectual disability (formerly referred to as mental retardation).

People with WAGR syndrome have a 45 to 60 percent chance of developing Wilms tumor, a rare form of kidney cancer. This type of cancer is most often diagnosed in children but is sometimes seen in adults.

Most people with WAGR syndrome have aniridia, an absence of the colored part of the eye (the iris). This can cause reduction in the sharpness of vision (visual acuity) and increased sensitivity to light (photophobia). Aniridia is typically the first noticeable sign of WAGR syndrome. Other eye problems may also develop, such as clouding of the lens of the eyes (cataracts), increased pressure in the eyes (glaucoma), and involuntary eye movements (nystagmus).

Abnormalities of the genitalia and urinary tract (genitourinary anomalies) are seen more frequently in males with WAGR syndrome than in affected females. The most common genitourinary anomaly in affected males is undescended testes (cryptorchidism). Females may not have functional ovaries and instead have undeveloped clumps of tissue called streak gonads. Females may also have a heart-shaped (bicornate) uterus, which makes it difficult to carry a pregnancy to term.

Another common feature of WAGR syndrome is intellectual disability. Affected individuals often have difficulty processing, learning, and properly responding to information. Some individuals with WAGR syndrome also have psychiatric or behavioral problems including depression, anxiety, attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), or a developmental disorder called autism spectrum disorder that affects communication and social interaction.

Other signs and symptoms of WAGR syndrome can include childhood-onset obesity, inflammation of the pancreas (pancreatitis), and kidney failure. When WAGR syndrome includes childhood-onset obesity, it is often referred to as WAGRO syndrome.

2. Frequency

The prevalence of WAGR syndrome ranges from 1 in 500,000 to one million individuals. It is estimated that one-third of people with aniridia actually have WAGR syndrome. Approximately 7 in 1,000 cases of Wilms tumor can be attributed to WAGR syndrome.

3. Causes

WAGR syndrome is caused by a deletion of genetic material on the short (p) arm of chromosome 11. The size of the deletion varies among affected individuals.

The signs and symptoms of WAGR syndrome are related to the loss of multiple genes on the short arm of chromosome 11. WAGR syndrome is often described as a contiguous gene deletion syndrome because it results from the loss of several neighboring genes. The *PAX6* and *WT1* genes are always deleted in people with the typical signs and symptoms of this disorder. Because changes in the *PAX6* gene can affect eye development, researchers think that the loss of the *PAX6* gene is responsible for the characteristic eye features of WAGR syndrome. The *PAX6* gene may also affect brain development. Wilms tumor and genitourinary abnormalities are often the result of mutations in the *WT1* gene, so deletion of the *WT1* gene is very likely the cause of these features in WAGR syndrome.

In people with WAGRO syndrome, the chromosome 11 deletion includes an additional gene, *BDNF*. This gene is active (expressed) in the brain and plays a role in the survival of nerve cells (neurons). The protein produced from the *BDNF* gene is thought to be involved in the management of eating, drinking, and body weight. Loss of the *BDNF* gene is likely responsible for childhood-onset obesity in people with WAGRO syndrome. People with WAGRO syndrome may be at greater risk of neurological problems such as intellectual disability and autism than those with WAGR syndrome. It is unclear whether this increased risk is due to the loss of the *BDNF* gene or other nearby genes.

Research is ongoing to identify additional genes deleted in people with WAGR syndrome and to determine how their loss leads to the other features of the disorder.

3.1 The genes and chromosome associated with WAGR syndrome

- BDNF
- PAX6
- WT1
- chromosome 11

4. Inheritance

Most cases of WAGR syndrome are not inherited. They result from a chromosomal deletion that occurs as a random event during the formation of reproductive cells (eggs or sperm) or in early fetal development. Affected people typically have no history of the disorder in their family.

Some affected individuals inherit a chromosome 11 with a deleted segment from an unaffected parent. In these cases, the parent carries a chromosomal rearrangement called a balanced translocation, in which no genetic material is gained or lost. Balanced translocations usually do not cause any health problems; however, they can become unbalanced as they are passed to the next generation. Children who inherit an unbalanced translocation can have a chromosomal rearrangement with extra or missing genetic material. Individuals with WAGR syndrome who inherit an unbalanced translocation are missing genetic material from the short arm of chromosome 11, which results in an increased risk of Wilms tumor, aniridia, genitourinary anomalies, and intellectual disability.

5. Other Names for This Condition

- 11p deletion syndrome
- 11p partial monosomy syndrome
- WAGR complex
- WAGR contiguous gene syndrome
- Wilms tumor, aniridia, genitourinary anomalies, and mental retardation syndrome
- Wilms tumor-aniridia-genital anomalies-retardation syndrome
- Wilms tumor-aniridia-genitourinary anomalies-MR syndrome

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