WAGR syndrome

WAGR syndrome is a disorder that affects many body systems and is named for its main features: Wilms tumor, anirida, 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.

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.

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.

**Inheritance Pattern**

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.

**Other Names for This Condition**

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

Diagnosis & Management

Genetic Testing Information

• What is genetic testing?
https://primer/testing/genetictesting

• Genetic Testing Registry: Wilms tumor, aniridia, genitourinary anomalies, and mental retardation syndrome

• Genetic Testing Registry: Wilms tumor, aniridia, genitourinary anomalies, mental retardation, and obesity syndrome

Research Studies from ClinicalTrials.gov

• ClinicalTrials.gov
https://clinicaltrials.gov/ct2/results?cond=%22WAGR+Syndrome%22+OR+%22WAGR+syndrome%22

Other Diagnosis and Management Resources

• GeneReview: PAX6-Related Aniridia
https://www.ncbi.nlm.nih.gov/books/NBK1360

• GeneReview: Wilms Tumor Predisposition
https://www.ncbi.nlm.nih.gov/books/NBK1294

• MedlinePlus Encyclopedia: Undescended Testicle
https://medlineplus.gov/ency/article/000973.htm

Additional Information & Resources

Health Information from MedlinePlus

• Encyclopedia: Undescended Testicle
https://medlineplus.gov/ency/article/000973.htm

• Health Topic: Eye Diseases
https://medlineplus.gov/eyediseases.html

• Health Topic: Wilms Tumor
https://medlineplus.gov/wilmstumor.html
Genetic and Rare Diseases Information Center

- WAGR syndrome
  https://rarediseases.info.nih.gov/diseases/5528/wagr-syndrome

Additional NIH Resources

- National Human Genome Research Institute: Learning About WAGR Syndrome
  https://www.genome.gov/Genetic-Disorders/WAGR-Syndrome

Educational Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology: WAGR syndrome
  http://atlasgeneticsoncology.org/Kprones/WAGRID10032.html
- Boston Children's Hospital: Wilms Tumor in Children
  https://www.childrenshospital.org/conditions-and-treatments/conditions/w/wilms-tumor
- Centers for Disease Control and Prevention: Intellectual Disability
- Cincinnati Children's Hospital: Wilms Tumor
  https://www.cincinnatichildrens.org/health/w/wilms-tumor
- Great Ormond Street Hospital for Children (UK): Kidney Failure
  https://www.gosh.nhs.uk/conditions-and-treatments/conditions-we-treat/kidney-failure
- MalaCards: wilms tumor, aniridia, genitourinary anomalies, and mental retardation syndrome
  https://www.malacards.org/card/wilms_tumor_aniridia_genitourinary_anomalies_and_mental_retardation_syndrome
- March of Dimes: Chromosomal Conditions
  https://www.marchofdimes.org/baby/chromosomal-conditions.aspx
- Merck Manual Consumer Version: Wilms' Tumor
- Orphanet: WAGR syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=893

Patient Support and Advocacy Resources

- Aniridia Foundation International
  http://www.make-a-miracle.org
- Chromosome Disorder Outreach
  https://chromodisorder.org/
• International WAGR Syndrome Association  
  http://wagr.org/about-wagr/what-is-wagr-syndrome/

• Kidney Cancer Association  
  https://www.kidneycancer.org/

• National Organization for Rare Disorders (NORD)  

• Unique: Rare Chromosome Disorder Support Group (UK)  
  https://www.rarechromo.org/

• University of Kansas Medical Center Resource List: Sexuality and Sexual Differentiation Syndromes  
  http://www.kumc.edu/gec/support/ambig.html

Clinical Information from GeneReviews  
• PAX6-Related Aniridia  
  https://www.ncbi.nlm.nih.gov/books/NBK1360

• Wilms Tumor Predisposition  
  https://www.ncbi.nlm.nih.gov/books/NBK1294

Scientific Articles on PubMed  
• PubMed  
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28WAGR+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2520+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM  
• WILMS TUMOR, ANIRIDIA, GENITOURINARY ANOMALIES, AND MENTAL RETARDATION SYNDROME  
  http://omim.org/entry/194072

• WILMS TUMOR, ANIRIDIA, GENITOURINARY ANOMALIES, MENTAL RETARDATION, AND OBESITY SYNDROME  
  http://omim.org/entry/612469

Medical Genetics Database from MedGen  
• Wilms tumor, aniridia, genitourinary anomalies, and mental retardation syndrome  
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14673045

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  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3762943/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18241071

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23266638

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19096215

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