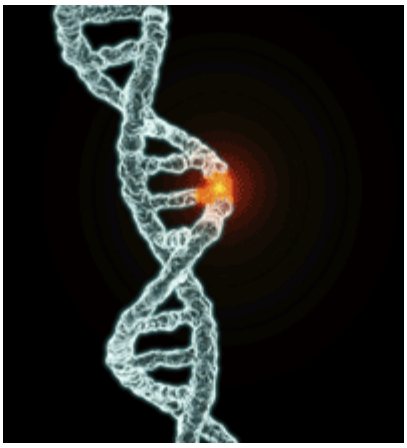
Genetics in Special Education Series

March 2011



Genetic disorders presented in this issue:

WAGR

What is WAGR Syndrome?

WAGR syndrome is a rare genetic condition that can affect both boys and girls. Babies born with WAGR syndrome often have eye problems, and are at high risk for developing certain types of cancer, and mental retardation. The term "WAGR" stands for the first letters of the physical and mental problems associated with the condition:

- (W)ilms' Tumor, the most common form of kidney cancer in children.
- (A)niridia, some or complete absence of the colored part of the eye, called the iris (singular), or irises/irides (plural).
- (G)enitourinary problems, such as testicles that are not descended or hypospadias (abnormal location of the opening for urination) in boys, or genital or urinary problems inside the body in girls.
- Mental (R)etardation.

Most people who have WAGR syndrome have two or more of these conditions. Also, people can have WAGR syndrome, but not have all of the above conditions.

Other names for WAGR syndrome that are used are:

- WAGR Complex
- Wilms' Tumor-Aniridia-Genitourinary Anomalies-Mental Retardation Syndrome
- Wilms' Tumor-Aniridia-Gonadoblastoma-Mental Retardation Syndrome
- Chromosome 11p deletion syndrome
- 11p deletion syndrome

The cause of WAGR syndrome is deletion of a group of genes located on chromosome number 11 (11p13 - the "p13" refers to the specific place on chromosome 11 that is affected). Chromosomes are packages of genetic characteristics. There are 22 pairs of chromosomes that are the same in males and females. The 23rd pair determines a person's sex with males having an X and Y chromosome and females having two X chromosomes.

What are the symptoms of WAGR syndrome?

WAGR is called a genetic syndrome. The symptoms of WAGR syndrome are usually seen after the baby is born. The mother's pregnancy and the baby's birth history are not unusual. Enlargement of the baby's kidneys may be seen on a prenatal ultrasound. The eye problems (aniridia) are usually noticed in the newborn period, and for infant boys, the problems with the genitals and urinary systems are also usually obvious in the newborn period.

Individuals born with WAGR syndrome are at higher risk for developing other problems during infancy, childhood, and adulthood. These problems can affect the kidneys, eyes, testes or ovaries. The specific symptoms that happen in a person who has WAGR syndrome depend on the combination of disorders that are present.

Wilms' tumor: About one half of individuals who have WAGR syndrome develop a type of kidney cancer called Wilms' tumor. In the early stages of Wilms' tumor there are usually no symptoms. The first signs of this cancer may be blood in the urine, a low-grade fever, loss of appetite, weight loss, lack of energy or swelling of the abdomen.

Aniridia: In infants who are born with aniridia that is associated with WAGR syndrome, the irises of the eyes fail to develop normally before birth. This causes partial or complete absence of the round colored part of the eye (iris). Aniridia is almost always present in babies born with WAGR syndrome. Other eye problems are often present or can develop as the child grows older. These include: clouding of the lens of the eye (cataract); rapid, involuntary movements of the eye (nystagmus); and all or partial loss of vision due to high pressure of the fluid in the eye (glaucoma).

Genital and urinary (GU) problems: A range of GU problems may be present in a baby born with WAGR syndrome. For boys, these may involve the urinary tract opening somewhere along the shaft of the penis rather than at the tip (hypospadias) or undescended testes (cryptorchidism). In girls, these problems may include underdeveloped (streak) ovaries, and malformations of the uterus, fallopian tubes or vagina. In some people with WAGR syndrome, problems with the development of the genitals may make their sexual assignment at birth (male or female) uncertain. Individuals with WAGR syndrome may have a higher risk for a type of cancer called gonadoblastoma, a cancer of the cells that form the testes in males and the ovaries in females.

Mental retardation: Mental retardation and developmental delay are common in children with WAGR syndrome. The severity of mental retardation varies from person to person, ranging from severe to mild mental retardation. Some children who have WAGR syndrome may have normal intelligence.

Other symptoms of WAGR syndrome may also include:

- Developmental, behavioral, and/or psychiatric disorders including autism, attention deficit disorder, obsessive compulsive disorder, anxiety disorders, and depression.
- Early-onset overweight (obesity) and high blood cholesterol levels.
- Excessive food intake (polyphagia/hyperphagia).
- Chronic kidney failure, most often after age 12 years.
- Breathing problems, asthma and pneumonia and breathing problems during sleep (sleep apnea).
- Frequent infections of the ears, nose, and throat, especially during infancy and early childhood.
- Teeth problems - crowded or uneven teeth.
- Problems with muscle tone and strength, especially during infancy and childhood.
- Seizure disorder (epilepsy).
- Inflammation of the pancreas (pancreatitis).

How is WAGR syndrome diagnosed?

Symptoms that suggest WAGR syndrome, like aniridia, are usually noted shortly after birth, and genetic testing for the 11p13 deletion is done. A genetic test called a chromosome analysis or karyotype is done to look for the deleted area (11p13) on chromosome number 11. A more specific genetic test called FISH (fluorescent in situ hybridization) is sometimes done to look for the deletion of specific genes on chromosome number 11.

How is WAGR syndrome treated?

Treatment of WAGR syndrome is aimed at the specific symptoms present in the individual. Monitoring to look for problems is also important to catch problems early so that treatment can be given as soon as possible.

Wilms' tumor: Wilms' tumor happens in about half of children with WAGR syndrome. The tumor usually develops between the ages of 1 and 3 years. Most cases of Wilms' tumor have been detected by age 8 years, but in rare cases may occur later. Babies who are suspected to have WAGR syndrome should have ultrasounds of their abdomen at birth. They then need to have abdominal ultrasounds every 3 months until they reach age 8 years. Feeling the abdomen for signs of swelling and masses can be done by both the baby's doctor and the parents, when they are taught how to do this. After age 8 years, watching for signs of Wilms tumor may be done by ultrasound and/or by watching for symptoms such as a low-grade fever, loss of appetite, weight loss, lack of energy or swelling of the abdomen.

Wilms' tumor can often be treated successfully. The overall survival rate of patients with Wilms tumor is excellent and is related to the features of the tumor, and the stage of the disease. Treatment may include surgery to remove the kidney, radiation therapy and chemotherapy.

Aniridia: The treatment of aniridia is aimed at keeping the person's vision. Drugs or surgery may help when there is glaucoma or cataracts. Contact lenses can harm the cornea and should be avoided.

Genital and urinary problems: Children with WAGR syndrome should have regular evaluations to detect abnormal development of their ovaries or testes. Surgery may be needed to remove abnormal gonads or to prevent cancer of the gonads (gonadoblastoma). When both gonads are removed, the individual is given hormone replacement treatment. Surgery may also be done when a boy with WAGR syndrome has undescended testes. When girls with WAGR syndrome have abnormal ovaries, they have routine pelvic ultrasounds or MRI's (magnetic resonance imaging) to watch for the development of gonadoblastoma.

Mental Retardation/developmental delays: Individuals with WAGR syndrome may have mental retardation ranging from severe to mild. Some individuals with WAGR syndrome have normal intelligence.

Children with WAGR syndrome should be referred for Early Intervention Services soon after they are born, or when the diagnosis is made. Treatments include: vision therapy, physical, occupational and speech therapies. Special Education services are also used to help children with WAGR syndrome develop to their fullest ability.

Kidney (renal) failure: The renal failure that can happen in WAGR syndrome often causes the person to have high blood pressure, high cholesterol, and leakage of protein from the blood into the urine (called proteinuria). All individuals with WAGR syndrome should be routinely screened for high blood pressure and urinary protein. These problems are treated with medications called "ACE inhibitors" or "ARBs." Some people with WAGR syndrome and renal failure are treated with dialysis or kidney transplant.

Is WAGR syndrome inherited?

WAGR syndrome is called a "contiguous gene deletion syndrome." This means that it is caused by the loss of a section of genes on chromosome 11 (11p13). Most of the time the changes on chromosome 11p13 happen by chance when the egg or sperm are being formed or during the very early stages of the baby's development in the womb. More rarely, the gene changes are inherited because one of the parents carries a rearrangement (called a translocation) between two chromosomes that can cause the loss of some genes when he or she has a baby. A baby can also have a mixture of normal cells and cells that have the 11p13 changes in his or her body. This is called mosaic WAGR syndrome.

Genetic counseling is helpful for determining whether there may be an increased risk of having another child with WAGR syndrome.

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Poland Anomaly

What is Poland anomaly?

Named after Sir Alfred Poland, Poland anomaly (PA) is described as an underdevelopment or absence of the chest muscle (pectoralis) on one side of the body and webbing of the fingers (cutaneous syndactyly) of the hand on the same side (ipsilateral hand). Sometimes referred to as "Poland syndrome," it is an uncommon condition present at birth (congenital). For people born with PA, the breastbone portion (sternal) of the pectoralis is also missing.

Since the severity of Poland anomaly differs from person to person, it is not often diagnosed or reported. Sometimes, a person does not realize they have the condition until puberty, when lopsided (asymmetrical) growth makes it more obvious. The incidence, therefore, is difficult to determine. Current estimates are between one in 10,000 to one in 100,000 births. Poland anomaly is more common in boys than girls, and the right side is affected twice as often as the left. The reasons for these differences are unknown.

What are the associated features of Poland anomaly?

People born with Poland anomaly have several physical and cosmetic disabilities, which can be treated if correctly diagnosed. Although severity and associated features vary from patient to patient, there are some common characteristics of this condition:

- Absence (aplasia) of some of the chest (pectoralis) muscles.
- The end of the main chest muscle, where it attaches to the breastbone, is usually missing.
- The nipple, including the darkened area around it (areola) is underdeveloped or missing. And in females, this may extend to the breast and underlying tissues.
- Abnormally short, webbed fingers (syndactyly).
- Often, the armpit (axillary) hair is missing.
- The skin in the area is underdeveloped (hypoplastic) with a thinned subcutaneous fat layer.
- The upper rib cage can be underdeveloped or missing. Sometimes, such abnormal development extends to the shoulder blade or the bones of the arm.
- Rarely, spine or kidney problems may also be present.

All these symptoms occur on one side of the body (unilateral). Also, it is important to note that Poland anomaly does not typically affect intelligence.

What causes Poland anomaly?

The cause of Poland anomaly is unknown. Most evidence supports the idea that something happens during the sixth week of fetal development (gestation). This event most likely involves the vascular (blood and lymph) system. Speculations include:

- An interruption of the embryonic blood supply of the arteries that lie under the collarbone (subclavian arteries). This could be caused by the forward growth of the ribs reducing the flow of blood.

- A malformation of the subclavian arteries causes a reduced amount of blood delivered to the developing tissues on one side of the body.

How is Poland anomaly diagnosed and treated?

Poland anomaly can be detected as early as birth and as late as adolescence, depending on how severe it is. PA can be detected through thorough clinical evaluation and from a variety of specialized tests. Tests may include advanced magnetic resonance imaging (MRI) techniques, computerized tomography (CT) scans and X-Rays. CT scans help determine the extent to which the muscles may be affected, by showing cross-sectional images of particular structures within the body. X-Rays can help identify and characterize any specific abnormality in the hand, forearm, ribs and/or shoulder blades.

Under mild circumstances, a person may not know he or she has PA until puberty. Puberty makes the difference between the two sides of the body more obvious. This is especially true for girls, who may notice a difference in the development of the breasts. When the anomaly is more severe, hand and arm abnormalities make the disorder more apparent early in life.

The most viable treatment for PA is reconstructive surgery. Existing chest muscles are used to rebuild the chest. Muscle can be taken from other parts of the body, for instances where there is not enough chest muscle for rebuilding. For males with PA, reconstructive surgery can be done as early as age 13. For females, surgery may have to be postponed until breast development is complete. Reconstructive surgery can be helpful for the psychological development of teenagers, who are especially aware of physical differences.

However, if surgery is performed too early, while the individual is growing, asymmetry can result or be made greater than before. For females, reconstructive surgery may be performed to correct the different sizes of the two breasts. Differences in the nipple and areola can be treated by therapeutic tattooing. This treatment is intended to give the breast the appearance of a nipple and areola.

What do we know about heredity and Poland anomaly?

Poland anomaly is rarely inherited and generally sporadic. Though instances of patients with PA are isolated within the family, familial occurrence has been observed. The exact mode of transmission has not yet been confirmed. Familial occurrences include: transmission from parent to offspring; in siblings born to unaffected parents; and with the presence of PA in distant family members such as cousins. Some researchers suggest that familial PA may stem from inherited susceptibility to events such as interruption of blood flow that may predispose a person to the anomaly.

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