Aarskog-Scott syndrome

Description

Aarskog-Scott syndrome is a genetic disorder that affects the development of many parts of the body, most commonly the head and face, the hands and feet, and the genitals and urinary system (genitourinary tract). This condition mainly affects males, although females may have mild features of the syndrome.

People with Aarskog-Scott syndrome often have distinctive facial features, such as widely spaced eyes (hypertelorism), a small nose, a long area between the nose and mouth (philtrum), and a widow's peak hairline. They frequently have mild to moderate short stature during childhood, but their growth usually catches up with that of their peers during puberty. Hand abnormalities are common in this syndrome and include short fingers (brachydactyly), curved pinky fingers (fifth finger clinodactyly), webbing of the skin between some fingers (cutaneous syndactyly), and a single crease across the palm. Affected individuals can also have wide, flat feet with broad, rounded toes. Other abnormalities in people with Aarskog-Scott syndrome include heart defects and a split in the upper lip (cleft lip) with or without an opening in the roof of the mouth (cleft palate).

Most males with Aarskog-Scott syndrome have a shawl scrotum, in which the scrotum surrounds the penis instead of hanging below. Less often, they have undescended testes (cryptorchidism) or a soft out-pouching around the belly-button (umbilical hernia) or in the lower abdomen (inguinal hernia).

The intellectual development of people with Aarskog-Scott syndrome varies widely. Most individuals with Aarskog-Scott syndrome have normal intelligence; however, some may have mild learning and behavior problems, and in rare cases, severe intellectual disability has been reported.

Frequency

Aarskog-Scott syndrome is believed to be a rare disorder; however, its prevalence is unknown because mildly affected people may not be diagnosed.

Causes

Variants (also known as mutations) in the *FGD1* gene are the only known genetic cause of Aarskog-Scott syndrome. The *FGD1* gene provides instructions for making a protein that turns on (activates) another protein called Cdc42, which transmits signals that are

important for various aspects of development before and after birth.

Variants in the *FGD1* gene lead to the production of an abnormally functioning protein. These variants disrupt Cdc42 signaling, leading to the wide variety of abnormalities that occur in people with Aarskog-Scott syndrome.

Only about 20 percent of people with this disorder have identifiable variants in the *FGD1* gene. The cause of Aarskog-Scott syndrome in other affected individuals is unknown.

Learn more about the gene associated with Aarskog-Scott syndrome

- FGD1

Inheritance

When caused by *FGD1* gene variants, Aarskog-Scott syndrome is inherited in an X-linked recessive pattern. The *FGD1* gene is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a variant would have to occur in both copies of the gene to cause Aarskog-Scott syndrome. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. Females who carry one altered copy of the *FGD1* gene may show mild signs of the condition, such as hypertelorism, short stature, or a widow's peak hairline. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Evidence suggests that Aarskog-Scott syndrome is inherited in an autosomal dominant or autosomal recessive pattern in some families, although the genetic cause of these cases is unknown. In autosomal dominant inheritance, one copy of the altered gene in each cell is sufficient to cause the disorder. In autosomal recessive inheritance, both copies of the gene in each cell have variants. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Aarskog syndrome
- AAS
- Facio-digito-genital dysplasia
- Faciodigitogenital syndrome
- Faciogenital dysplasia
- FGDY

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Aarskog syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0175701/)

Genetic and Rare Diseases Information Center

- Aarskog-Scott syndrome (https://rarediseases.info.nih.gov/diseases/4775/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- AARSKOG-SCOTT SYNDROME; AAS (https://omim.org/entry/305400)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28aarskog-scott+syndrome%5BTIAB%5D%29+OR+%28aarskog+syndrome%5BTIAB%5D%29+OR+%28faciogenital+dysplasia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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