46,XX Testicular Disorder

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46,XX testicular disorder of sex development is a condition in which individuals with two X chromosomes in each cell, the pattern normally found in females, have a male appearance. People with this disorder have male external genitalia. They generally have small testes and may also have abnormalities such as undescended testes (cryptorchidism) or the urethra opening on the underside of the penis (hypospadias). A small number of affected people have external genitalia that do not look clearly male or clearly female (ambiguous genitalia). Affected children are typically raised as males and have a male gender identity.

Keywords: genetic conditions

1. Introduction

At puberty, most affected individuals require treatment with the male sex hormone testosterone to induce development of male secondary sex characteristics such as facial hair and deepening of the voice (masculinization). Hormone treatment can also help prevent breast enlargement (gynecomastia). Adults with this disorder are usually shorter than average for males and are unable to have children (infertile).

2. Frequency

Approximately 1 in 20,000 individuals with a male appearance have 46,XX testicular disorder.

3. Causes

People normally have 46 chromosomes in each cell. Two of the 46 chromosomes, known as X and Y, are called sex chromosomes because they help determine whether a person will develop male or female sex characteristics. Females typically have two X chromosomes (46,XX), and males usually have one X chromosome and one Y chromosome (46,XY).

The *SRY* gene, normally located on the Y chromosome, provides instructions for making the sex-determining region Y protein. The sex-determining region Y protein causes a fetus to develop as a male.

In about 80 percent of individuals with 46,XX testicular disorder of sex development, the condition results from an abnormal exchange of genetic material between chromosomes (translocation). This exchange occurs as a random event during the formation of sperm cells in the affected person's father. The translocation causes the *SRY* gene to be misplaced, almost always onto an X chromosome. If a fetus is conceived from a sperm cell with an X chromosome bearing the *SRY* gene, it will develop as a male despite not having a Y chromosome. This form of the condition is called *SRY*-positive 46,XX testicular disorder of sex development.

About 20 percent of people with 46,XX testicular disorder of sex development do not have the *SRY* gene. This form of the condition is called *SRY*-negative 46,XX testicular disorder of sex development. The cause of the disorder in these individuals is often unknown, although changes affecting other genes have been identified. Individuals with *SRY*-negative 46,XX testicular disorder of sex development are more likely to have ambiguous genitalia than are people with the *SRY*-positive form.

3.1. The genes and chromosomes associated with 46,XX testicular disorder of sex development

- SOX9
- SRY
- x chromosome
- y chromosome

4. Inheritance

SRY-positive 46,XX testicular disorder of sex development is almost never inherited. This condition results from the translocation of a Y chromosome segment containing the *SRY* gene during the formation of sperm (spermatogenesis). Affected people typically have no history of the disorder in their family and cannot pass on the disorder because they are infertile.

In rare cases, the *SRY* gene may be misplaced onto a chromosome other than the X chromosome. This translocation may be carried by an unaffected father and passed on to a child with two X chromosomes, resulting in 46,XX testicular disorder of sex development. In another very rare situation, a man may carry the *SRY* gene on both the X and Y chromosome; a child who inherits his X chromosome will develop male sex characteristics despite having no Y chromosome.

The inheritance pattern of SRY-negative 46,XX testicular disorder of sex development is unknown. A few families with unaffected parents have had more than one child with the condition, suggesting the possibility of autosomal recessive inheritance. Autosomal recessive means both copies of a gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- 46,XX sex reversal
- XX male syndrome
- XX sex reversal

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