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My46 Trait Profile

5-alpha reductase deficiency

5-alpha reductase deficiency is a rare genetic condition that affects sexual development in genetically male individuals. It is caused by mutations in the SRD5A2 gene which makes the steroid 5-alpha reductase 2 enzyme.

Characteristics of 5-alpha reductase deficiency

5-alpha reductase deficiency is an inherited condition that affects sexual development. It is also known as a disorder of sex development. This condition affects individuals who are genetically male (i.e., those with one X chromosome and one Y chromosome), and results from a deficiency of the steroid 5-alpha reductase 2 enzyme. This enzyme is responsible for converting the male hormone testosterone to its more active form, dihidrotestosterone (DHT). DHT plays an important role in the development of external male sex development. If not enough DHT is produced, the external genitalia do not develop as expected. Thus, an individual with 5-alpha reductase deficiency may be born with external genitalia that appears female or with external genitalia that is not clearly male or female (i.e., ambiguous).

During puberty, individuals with 5-alpha reductase deficiency often develop some secondary male sex characteristics like increased muscle mass, deepening voice, and growth of male external genitalia, but most of these men are not able to have children. Most individuals born with 5-alpha reductase deficiency are assigned a female gender at birth. However, about 70% of them choose to live as males later in life when they develop secondary male sex characteristics.

Diagnosis/Testing

Diagnosis is often made in the newborn period when a baby is born with ambiguous genitalia, not appearing clearly male or female. 5-alpha reductase deficiency is caused by mutations in the SRD5A2 gene. This gene makes the 5-alpha reductase 2 enzyme that plays a role in the development of male external genitalia early in development. If a baby is suspected to have 5-alpha reductase deficiency, a genetic test can be done to confirm this diagnosis. Hormone tests measuring the amount of male hormones testosterone and DHT can also be conducted to diagnose this condition.

Management/Surveillance

The management of 5-alpha reductase deficiency depends on many factors including external genitalia appearance, potential surgical and hormone treatment outcomes, and family and cultural considerations. Different types of genital surgery can be performed depending on whether individuals are raised as males or females. Hormone therapy may also be used to help with the development of secondary sex characteristics.

Mode of inheritance

5-alpha reductase deficiency is inherited in an autosomal recessive pattern. This means that an individual has to inherit two SRD5A2 mutations (i.e., one from each parent) to be affected with 5-alpha reductase deficiency. If both parents are carriers of a SRD5A2 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with 5-alpha reductase deficiency. However, only those who are genetically male (i.e., those with one X chromosome and one Y chromosome), are affected. Genetic females (i.e., those with two X chromosomes) who inherit two SRD5A2 mutations will not be affected, but will pass on a mutation to their children.

Risk to family members

Parents of a child with 5-alpha reductase deficiency are carriers of 5-alpha reductase deficiency. If a sibling of a child with 5-alpha reductase deficiency is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of 5-alpha reductase deficiency.

Special considerations

None

Resources

Genetics Home Reference: 5-alpha reductase deficiency
http://ghr.nlm.nih.gov/condition/5-alpha-reductase-deficiency
Accord Alliance
http://www.accordalliance.org
AboutKidsHealth: 5ARD
http://www.aboutkidshealth.ca/En/HowTheBodyWorks/SexDevelopmentAnOverview/AISand5ARD/Pages/default.aspx
Syndromes of Abnormal Sex Differentiation: A guide for patients and their families
http://www.hopkinschildrens.org/intersex/index.html

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