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My46 Trait Profile

Congenital adrenal hyperplasia

Congenital adrenal hyperplasia is a group of genetic conditions that cause an excess of male sex hormones to be produced. Approximately 95% of individuals with CAH have mutations in the CYP21A2 gene, which is involved in the production of an enzyme called 21-hydroxylase.

Characteristics of Congenital adrenal hyperplasia

Congenital adrenal hyperplasia (CAH) is a rare inherited disorder that is present at birth (congenital) and causes the adrenal glands (glands on top of the kidneys that make many hormones important to the body) to produce too much of the male hormone called androgens. There are three types of CAH caused by 21-hydroxylase deficiency (21-OHD). Two of these types, salt-wasting CAH and simple virilizing CAH, are considered “classic” forms. The third type is called non-classic CAH.

The classic forms of CAH are more severe than the non-classic form, with salt-wasting being the more severe and common of the two classic forms. Classic CAH may affect males and females differently. The classic forms are characterized by an increase in male sex characteristics in both females and males. Females with classic forms of CAH have ambiguous (not clearly male or female) external genitalia, although internal genitalia is normal. Males with CAH have normal genitalia that may mature earlier. In salt-wasting CAH, individuals have very low levels of a hormone called aldosterone. When aldosterone is very low, salt levels in the body and the body’s hydration (water) level over all become very low, causing a potentially fatal adrenal crisis. Adrenal crises in individuals with CAH usually occur within the first few weeks of life. Symptoms of adrenal crisis may include poor feeding, vomiting, diarrhea, confusion, irritability, rapid heart rate, or coma. In simple virilizing CAH, individuals produce small amounts of aldosterone so they do not experience salt-wasting.

Non-classic CAH is the least severe, most common type of CAH. Non-classic CAH may cause milder symptoms and, unlike salt-wasting CAH, is not lethal. Both males and females may experience early onset (precocious) puberty, early growth spurts, short stature, acne, and infertility. Additionally, females with non-classic CAH may have menstrual irregularities, excessive hair growth (hirsutism), or symptoms of polycystic ovarian syndrome (PCOS).

Diagnosis/Testing

Most individuals with CAH have changes or mutations in the CYP21A2 gene. This gene is involved in making an enzyme called 21-hydroxylase that is responsible for helping to make certain hormones (cortisol and aldosterone) in the adrenal glands. Mutations in the CYP21A2 gene that cause the 21-hydroxylase enzyme to not be made or to not be made properly result in many of the health problems seen in individuals with CAH.

Many babies with congenital adrenal hyperplasia are diagnosed early in life through newborn screening (NBS). NBS tests a spot of blood from the baby’s heel, and looks to see if the 21-hydroxylase enzyme is working properly. NBS test results are confirmed with additional blood and urine chemical tests, and possibly genetic testing of the CYP21A2 gene.

Management/Surveillance

Individuals with CAH are typically managed by a team of specialty providers that can include: geneticists, genetic counselors, primary care doctors, endocrinologists, surgeons, and social workers. The goal of treatment is to get the

hormone levels as close to normal. Individuals with classic forms of CAH are often treated with daily hydrocortisone, a form of cortisol, daily. During times of stress (e.g., acute illness, injury, etc.), hydrocortisone dosage may need to be increased. Individuals with salt-wasting CAH may need to take an additional medication to help retain salt and prevent salt-wasting. Additionally, females who experience virilization (male appearing external genitalia) may require corrective surgery which may be done in early childhood or even later on into the teenage years. Hormones may also be used to regulate symptoms of precocious puberty. It is important to monitor CAH treatment closely, as too much or too little of these medications may cause other complications. Non-classic CAH may also be treated with hydrocortisone, but lifetime treatment may not be necessary.

CAH identified in babies before they are born may be treated prenatally with a medication called dexamethasone given to the mother. Dexamethasone may reduce virilization of female children, but will not eliminate the need for treatment.

Individuals with CAH may benefit from counseling to get help and support in understanding their condition and how their sexual development may be affected. It is also recommended that individuals with the classic forms of CAH wear a Medic-Alert bracelet.

Mode of inheritance

CAH due to 21-OHD is inherited in an autosomal recessive pattern. This means that an individual has to inherit two CYP21A2 mutations (i.e., one from each parent) to be affected with CAH. If both parents are carriers of a CYP21A2 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with CAH.

Risk to family members

Parents of a child with CAH due to 21-OHD are carriers of CAH. If a sibling of a child with CAH is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of CAH.

Special considerations

None

Resources

Cares Foundation
http://www.caresfoundation.org/productcart/pc/index.html
Genetics Home Reference: 21-hydroxylase deficiency
http://ghr.nlm.nih.gov/condition/21-hydroxylase-deficiency
Living with CAH
http://www.livingwithcah.com/
National Adrenal Diseases Foundation
http://www.nadf.us/adrenal-diseases/congenital-adrenal-hyperplasia-cah/
Star-G Newborn Screening: Congenital Adrenal Hyperplasia
http://www.newbornscreening.info/Parents/otherdisorders/CAH.html

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