Aromatase deficiency

Aromatase deficiency is a condition characterized by reduced levels of the female sex hormone estrogen and increased levels of the male sex hormone testosterone.

Females with aromatase deficiency have a typical female chromosome pattern (46,XX) but are born with external genitalia that do not appear clearly female or male (ambiguous genitalia). These individuals typically have normal internal reproductive organs, but develop ovarian cysts early in childhood, which impair the release of egg cells from the ovaries (ovulation). In adolescence, most affected females do not develop secondary sexual characteristics, such as breast growth and menstrual periods. They tend to develop acne and excessive body hair growth (hirsutism).

Men with this condition have a typical male chromosome pattern (46,XY) and are born with male external genitalia. Some men with this condition have decreased sex drive, abnormal sperm production, or testes that are small or undescended (cryptorchidism).

There are other features associated with aromatase deficiency that can affect both males and females. Affected individuals are abnormally tall because of excessive growth of long bones in the arms and legs. The abnormal bone growth results in slowed mineralization of bones (delayed bone age) and thinning of the bones (osteoporosis), which can lead to bone fractures with little trauma. Males and females with aromatase deficiency can have abnormally high blood sugar (hyperglycemia) because the body does not respond correctly to the hormone insulin. In addition, they can have excessive weight gain and a fatty liver.

Women who are pregnant with fetuses that have aromatase deficiency often experience mild symptoms of the disorder even though they themselves do not have the disorder. These women may develop hirsutism, acne, an enlarged clitoris (clitoromegaly), and a deep voice. These features can appear as early as 12 weeks of pregnancy and go away soon after delivery.

Frequency

The prevalence of aromatase deficiency is unknown; approximately 20 cases have been described in the medical literature.

Causes

Mutations in the *CYP19A1* gene cause aromatase deficiency. The *CYP19A1* gene provides instructions for making an enzyme called aromatase. This enzyme converts a class of hormones called androgens, which are involved in male sexual development, to different forms of estrogen. In females, estrogen guides female sexual development before birth and during puberty. In both males and females, estrogen plays a role in

regulating bone growth and blood sugar levels. During fetal development, aromatase converts androgens to estrogens in the placenta, which is the link between the mother's blood supply and the fetus. This conversion in the placenta prevents androgens from directing sexual development in female fetuses. After birth, the conversion of androgens to estrogens takes place in multiple tissues.

CYP19A1 gene mutations that cause aromatase deficiency decrease or eliminate aromatase activity. A shortage of functional aromatase results in an inability to convert androgens to estrogens before birth and throughout life. As a result, there is a decrease in estrogen production and an increase in the levels of androgens, including testosterone. In affected individuals, these abnormal hormone levels lead to impaired female sexual development, unusual bone growth, insulin resistance, and other signs and symptoms of aromatase deficiency. In women who are pregnant with an affected fetus, excess androgens in the placenta pass into the woman's bloodstream, which may cause her to have temporary signs and symptoms of aromatase deficiency.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the 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.

Other Names for This Condition

- 46,XX disorder of sex development (DSD) due to placental aromatase deficiency
- estrogen synthetase deficiency
- oestrogen synthetase deficiency
- placental aromatase deficiency

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Aromatase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1960539/

Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Ovarian Overproduction of Androgens
  https://medlineplus.gov/ency/article/001165.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Ambiguous Genitalia
  https://medlineplus.gov/ency/article/003269.htm
- Encyclopedia: Ovarian Overproduction of Androgens
  https://medlineplus.gov/ency/article/001165.htm
- Encyclopedia: Virilization
  https://medlineplus.gov/ency/article/002339.htm
- Health Topic: Endocrine Diseases
  https://medlineplus.gov/endocrinediseases.html

Genetic and Rare Diseases Information Center

- Aromatase deficiency
  https://rarediseases.info.nih.gov/diseases/365/aromatase-deficiency

Educational Resources

- Boston Children's Hospital: Ambiguous Genitalia in Children
  http://www.childrenshospital.org/conditions-and-treatments/conditions/a/ambiguous-genitalia
- MalaCards: aromatase deficiency
  https://www.malacards.org/card/aromatase_deficiency

Patient Support and Advocacy Resources

- Resource List from the University of Kansas Medical Center: Endocrine Genetic Conditions
  http://www.kumc.edu/gec/support/endocrin.html
- Resource List from the University of Kansas Medical Center: Sexuality and Sexual Differentiation Syndromes
  http://www.kumc.edu/gec/support/ambig.html
- The UK Intersex Association
  http://www.ukia.co.uk/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28aromatase+deficiency%5BTIAB%5D%29+OR+%28placental+aromatase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- AROMATASE DEFICIENCY
  http://omim.org/entry/613546

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