X-linked adrenal Hypoplasia Congenita

Subjects: Genetics
Submitted by: Bruce Ren
(This entry belongs to Entry Collection "MedlinePlus")

Definition

X-linked adrenal hypoplasia congenita is a disorder that mainly affects males. It involves many hormone-producing (endocrine) tissues in the body, particularly a pair of small glands on top of each kidney called the adrenal glands. These glands produce a variety of hormones that regulate many essential functions in the body.

1. Introduction

One of the main signs of this disorder is adrenal insufficiency, which occurs when the adrenal glands do not produce enough hormones. Adrenal insufficiency typically begins in infancy or childhood and can cause vomiting, difficulty with feeding, dehydration, extremely low blood sugar (hypoglycemia), and shock. If untreated, these complications are often life-threatening.

Affected males may also have a shortage of male sex hormones, which leads to underdeveloped reproductive tissues, undescended testicles (cryptorchidism), delayed puberty, and an inability to father children (infertility). Together, these characteristics are known as hypogonadotropic hypogonadism.

The onset and severity of these signs and symptoms can vary, even among affected members of the same family.

2. Frequency

X-linked adrenal hypoplasia congenita appears to be an uncommon condition. It has been reported to affect approximately 1 in 12,500 newborns, but this is likely an overestimate. The true prevalence of this condition is unknown.

3. Causes

Mutations in the *NR0B1* gene cause X-linked adrenal hypoplasia congenita. The *NR0B1* gene provides instructions to make a protein called DAX1. This protein plays an important role in the development and function of several hormone-producing (endocrine) tissues including the adrenal glands, two hormone-secreting glands in the brain (the hypothalamus and pituitary), and the gonads (ovaries in females and testes in males). The hormones produced by these glands control many important body functions.

Some *NR0B1* mutations result in the production of an inactive version of the DAX1 protein, while other mutations delete the entire gene. The resulting shortage of DAX1 disrupts the normal development and function of hormone-producing tissues in the body. The signs and symptoms of adrenal insufficiency and hypogonadotropic hypogonadism occur when endocrine glands do not produce the right amounts of certain hormones.

3.1 The gene associated with X-linked adrenal hypoplasia congenita

- NR0B1

4. Inheritance

This condition is inherited in an X-linked recessive pattern. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, 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 mutation must be present

in both copies of the gene to cause the disorder. Males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In X-linked recessive inheritance, a female with one mutated copy of the gene in each cell is called a carrier. She can pass on the altered gene, but usually does not experience signs and symptoms of the disorder. In rare cases, however, females who carry a *NR0B1* mutation may experience adrenal insufficiency or signs of hypogonadotropic hypogonadism such as underdeveloped reproductive tissues, delayed puberty, and an absence of menstruation.

5. Other Names for This Condition

- Adrenal hypoplasia congenita
- X-linked AHC

References

1. Achermann JC, Vilain EJ. NR0B1-Related Adrenal Hypoplasia Congenita. 2001 Nov 20 [updated 2018 Jan 25]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, BeanLJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA):University of Washington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1431/
2. Ahmad I, Paterson WF, Lin L, Adlard P, Duncan P, Tolmie J, Achermann JC,Donaldson MD. A novel missense mutation in DAX-1 with an unusual presentation of X-linked adrenal hypoplasia congenita. Horm Res. 2007;68(1):32-7.
3. Clipsham R, McCabe ER. DAX1 and its network partners: exploring complexity in development. Mol Genet Metab. 2003 Sep-Oct;80(1-2):81-120. Review.
4. Fujieda K, Okuhara K, Abe S, Tajima T, Mukai T, Nakae J. Molecularpathogenesis of lipoid adrenal hyperplasia and adrenal hypoplasia congenita. JSteroid Biochem Mol Biol. 2003 Jun;85(2-5):483-9. Review.
5. Fujieda K, Tajima T. Molecular basis of adrenal insufficiency. Pediatr Res.2005 May;57(5 Pt 2):62R-69R.
6. Hammer GD, Parker KL, Schimmer BP. Minireview: transcriptional regulation ofadrenocortical development. Endocrinology. 2005 Mar;146(3):1018-24.
7. Lalli E, Sassone-Corsi P. DAX-1, an unusual orphan receptor at the crossroads of steroidogenic function and sexual differentiation. Mol Endocrinol. 2003Aug;17(8):1445-53.
8. Ludbrook LM, Harley VR. Sex determination: a 'window' of DAX1 activity. TrendsEndocrinol Metab. 2004 Apr;15(3):116-21. Review.
9. Mantovani G, De Menis E, Borretta G, Radetti G, Bondioni S, Spada A, PersaniL, Beck-Peccoz P. DAX1 and X-linked adrenal hypoplasia congenita: clinical andmolecular analysis in five patients. Eur J Endocrinol. 2006 May;154(5):685-9.
10. Sehgal A, Stack J. Complex glycerol kinase deficiency: an X-linked disorderassociated with adrenal hypoplasia congenita. Indian J Pediatr. 2005Jan;72(1):67-9.
11. Tabarin A. Congenital adrenal hypoplasia and DAX-1 gene mutations. AnnEndocrinol (Paris). 2001 Apr;62(2):202-6. Review.

Keywords

genetic conditions