Hand-foot-genital syndrome

Description

Hand-foot-genital syndrome is a rare condition that affects the development of the hands and feet, the urinary tract, and the reproductive system. People with this condition have abnormally short thumbs and first (big) toes, small fifth fingers that curve inward (clinodactyly), and short feet. The bones in the wrists and ankles may be fused in people with this condition, or hardening of these bones may be delayed. The other bones in the arms and legs are normal.

Abnormalities of the genitals and urinary tract can vary among affected individuals. Many people with hand-foot-genital syndrome have defects in the ureters, which are tubes that carry urine from each kidney to the bladder, or in the urethra, which carries urine from the bladder to the outside of the body. Recurrent urinary tract infections and an inability to control the flow of urine (urinary incontinence) have been reported. About half of males with this disorder have the urethra opening on the underside of the penis (hypospadias).

People with hand-foot-genital syndrome are usually able to have children (fertile). In some affected females, problems in the early development of the uterus can later increase the risk of pregnancy loss, premature labor, and stillbirth.

Frequency

Hand-foot-genital syndrome is very rare; only a few families with the condition have been reported worldwide.

Causes

Variants (also called mutations) in the *HOXA13* gene cause hand-foot-genital syndrome. The *HOXA13* gene provides instructions for producing a protein that plays an important role in development before birth. Specifically, this protein appears to be critical for the formation and development of the limbs (particularly the hands and feet), urinary tract, and reproductive system.

Variants in the *HOXA13* gene cause the characteristic features of hand-foot-genital syndrome by disrupting the early development of these structures. Some variants in the *HOXA13* gene cause nonfunctional versions of the HOXA13 protein to be produced. Other variants alter the protein's structure and interfere with its normal function within

cells. Variants that result in an altered but functional HOXA13 protein may cause more severe signs and symptoms of hand-foot-genital syndrome than variants that lead to a nonfunctional version of this protein.

Learn more about the gene associated with Hand-foot-genital syndrome

- HOXA13

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- Hand-foot-uterus syndrome
- HFG syndrome
- HFGS
- HFU syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hand-foot-genital syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1841679/)

Genetic and Rare Diseases Information Center

- Hand-foot-genital syndrome (https://rarediseases.info.nih.gov/diseases/2594/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- HAND-FOOT-GENITAL SYNDROME; HFG (https://omim.org/entry/140000)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=((hand-foot-genital+syndrome)+O

R+(hand-foot-uterus+syndrome))+AND+english%5Bla%5D+AND+%22last+6000+days%22%5Bdp%5D)

References

- Geng W, Li F, Zhang R, Cao L, Du X, Gu W, Xu M. Hand-foot-genital syndrome dueto a duplication variant in the GC-rich region of HOXA13. Eur J Med Genet. 2023Mar;66(3):104711. doi: 10.1016/j.ejmg.2023.104711. Epub 2023 Jan 24. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/36702441)
- Goodman FR, Bacchelli C, Brady AF, Brueton LA, Fryns JP, Mortlock DP, InnisJW, Holmes LB, Donnenfeld AE, Feingold M, Beemer FA, Hennekam RC, Scambler PJ. Novel HOXA13 mutations and the phenotypic spectrum of hand-foot-genital syndrome.Am J Hum Genet. 2000 Jul;67(1):197-202. doi: 10.1086/302961. Epub 2000 Jun 5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10839976) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1287077/)
- Goodman FR. Limb malformations and the human HOX genes. Am J Med Genet. 2002Oct 15;112(3):256-65. doi: 10.1002/ajmg.10776. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12357469)
- Innis JW, Mortlock D, Chen Z, Ludwig M, Williams ME, Williams TM, Doyle CD, Shao Z, Glynn M, Mikulic D, Lehmann K, Mundlos S, Utsch B. Polyalanine expansionin HOXA13: three new affected families and the molecular consequences in a mousemodel. Hum Mol Genet. 2004 Nov 15;13(22):2841-51. doi: 10.1093/hmg/ddh306. Epub2004 Sep 22. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15385446)
- Innis JW. Hand-Foot-Genital Syndrome. 2006 Jul 11 [updated 2019 Aug 8]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, AmemiyaA, editors. GeneReviews(R) [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1423/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301596)
- Mortlock DP, Innis JW. Mutation of HOXA13 in hand-foot-genital syndrome. NatGenet. 1997 Feb;15(2):179-80. doi: 10.1038/ng0297-179. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9020844)
- Quinonez SC, Innis JW. Human HOX gene disorders. Mol Genet Metab. 2014Jan; 111(1):4-15. doi: 10.1016/j.ymgme.2013.10.012. Epub 2013 Oct 29. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/24239177)
- Utsch B, McCabe CD, Galbraith K, Gonzalez R, Born M, Dotsch J, Ludwig M, Reutter H, Innis JW. Molecular characterization of HOXA13 polyalanine expansionproteins in hand-foot-genital syndrome. Am J Med Genet A. 2007 Dec15; 143A(24):3161-8. doi: 10.1002/ajmg.a.31967. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17935235)

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