Ellis-van Creveld syndrome

Ellis-van Creveld syndrome is an inherited disorder of bone growth that results in very short stature (dwarfism). People with this condition have particularly short forearms and lower legs and a narrow chest with short ribs. Ellis-van Creveld syndrome is also characterized by the presence of extra fingers and toes (polydactyly), malformed fingernails and toenails, and dental abnormalities. More than half of affected individuals are born with a heart defect, which can cause serious or life-threatening health problems.

The features of Ellis-van Creveld syndrome overlap with those of another, milder condition called Weyers acrofacial dysostosis. Like Ellis-van Creveld syndrome, Weyers acrofacial dysostosis involves tooth and nail abnormalities, although affected individuals have less pronounced short stature and typically do not have heart defects. The two conditions are caused by mutations in the same genes.

Frequency

In most parts of the world, Ellis-van Creveld syndrome occurs in 1 in 60,000 to 200,000 newborns. It is difficult to estimate the exact prevalence because the disorder is very rare in the general population. This condition is much more common in the Old Order Amish population of Lancaster County, Pennsylvania, and in the indigenous (native) population of Western Australia.

Causes

Ellis-van Creveld syndrome can be caused by mutations in the *EVC* or *EVC2* gene. Little is known about the function of these genes, although they appear to play important roles in cell-to-cell signaling during development. In particular, the proteins produced from the *EVC* and *EVC2* genes are thought to help regulate the Sonic Hedgehog signaling pathway. This pathway plays roles in cell growth, cell specialization, and the normal shaping (patterning) of many parts of the body.

The mutations that cause Ellis-van Creveld syndrome result in the production of an abnormally small, nonfunctional version of the EVC or EVC2 protein. It is unclear how the defective proteins lead to the specific signs and symptoms of this condition. Studies suggest that they prevent normal Sonic Hedgehog signaling in the developing embryo, disrupting the formation and growth of the bones, teeth, and other parts of the body.

Together, mutations in the *EVC* and *EVC2* genes account for more than half of all cases of Ellis-van Creveld syndrome. The cause of the remaining cases is unknown.

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

- chondroectodermal dysplasia
- Ellis-van Creveld dysplasia

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Chondroectodermal dysplasia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0013903/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Ellis-van+Creveld+syndrome%22

Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Congenital Heart Disease
  https://medlineplus.gov/ency/article/001114.htm
- MedlinePlus Encyclopedia: Ellis-van Creveld Syndrome
  https://medlineplus.gov/ency/article/001667.htm
- MedlinePlus Encyclopedia: Polydactyly
  https://medlineplus.gov/ency/article/003176.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Congenital Heart Disease
  https://medlineplus.gov/ency/article/001114.htm
- Encyclopedia: Ellis-van Creveld Syndrome
  https://medlineplus.gov/ency/article/001667.htm
- Encyclopedia: Polydactyly
  https://medlineplus.gov/ency/article/003176.htm
- Health Topic: Dwarfism
  https://medlineplus.gov/dwarfism.html

Genetic and Rare Diseases Information Center

- Ellis-Van Creveld syndrome
  https://rarediseases.info.nih.gov/diseases/1301/ellis-van-creveld-syndrome

Educational Resources

- MalaCards: ellis-van creveld syndrome
  https://www.malacards.org/card/ellis_van_creveld_syndrome
- Nemours Children's Health System
  https://www.nemours.org/services/skeletal-dysplasia/ellisvancreveld.html?tab=about
- Orphanet: Ellis Van Creveld syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=289

Patient Support and Advocacy Resources

- American Heart Association
  https://www.heart.org/en/health-topics/congenital-heart-defects
- Human Growth Foundation
  https://www.hgfound.org/
- International Skeletal Dysplasia Registry, UCLA
  https://www.uclahealth.org/ortho/isdr
- Little People of America
  https://www.lpaonline.org/
- Little People UK
  https://littlepeopleuk.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/ellis-van-creveld-syndrome/
- Resource list from the University of Kansas Medical Center: Dwarfism / Short Stature
  http://www.kumc.edu/gec/support/skeldysp.html

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Ellis-Van+Creveld+Syndrome%5BMAJR%5D%29+AND+%28Ellis-van+Creveld+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ELLIS-VAN CREVELD SYNDROME
  http://omim.org/entry/225500

Sources for This Summary

- Baujat G, Le Merrer M. Ellis-van Creveld syndrome. Orphanet J Rare Dis. 2007 Jun 4;2:27. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17547743
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1891277/
- Galdzicka M, Patnala S, Hirshman MG, Cai JF, Nitowsky H, Egeland JA, Ginns EI. A new gene, EVC2, is mutated in Ellis-van Creveld syndrome. Mol Genet Metab. 2002 Dec;77(4):291-5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12468274
- Hills CB, Kochilas L, Schimmenti LA, Moller JH. Ellis-van Creveld syndrome and congenital heart defects: presentation of an additional 32 cases. Pediatr Cardiol. 2011 Oct;32(7):977-82. doi: 10.1007/s00246-011-0006-9. Epub 2011 May 1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21533779
- McKusick VA. Ellis-van Creveld syndrome and the Amish. Nat Genet. 2000 Mar;24(3):203-4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10700162
- O'Connor MJ, Collins RT 2nd. Ellis-van Creveld syndrome and congenital heart defects: presentation of an additional 32 cases. Pediatr Cardiol. 2012 Apr;33(4):491; discussion 491-2. doi: 10.1007/s00246-012-0155-5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22286269
- Ruiz-Perez VL, Goodship JA. Ellis-van Creveld syndrome and Weyers acrodental dysostosis are caused by cilia-mediated diminished response to hedgehog ligands. Am J Med Genet C Semin Med Genet. 2009 Nov 15;151C(4):341-51. doi: 10.1002/ajmg.c.30226. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19876929
- Ruiz-Perez VL, Ide SE, Strom TM, Lorenz B, Wilson D, Woods K, King L, Francomano C, Freisinger P, Spranger S, Marino B, Dallapiccola B, Wright M, Meitinger T, Polymeropoulos MH, Goodship J. Mutations in a new gene in Ellis-van Creveld syndrome and Weyers acrodental dysostosis. Nat Genet. 2000 Mar;24(3):283-6. Erratum in: Nat Genet 2000 May;25(1):125.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10700184
- Ruiz-Perez VL, Tompson SW, Blair HJ, Espinoza-Valdez C, Lapunzina P, Silva EO, Hamel B, Gibbs JL, Young ID, Wright MJ, Goodship JA. Mutations in two nonhomologous genes in a head-to-head configuration cause Ellis-van Creveld syndrome. Am J Hum Genet. 2003 Mar;72(3):728-32. Epub 2003 Feb 4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12571802
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180248/
- Tompson SW, Ruiz-Perez VL, Blair HJ, Barton S, Navarro V, Robson JL, Wright MJ, Goodship JA. Sequencing EVC and EVC2 identifies mutations in two-thirds of Ellis-van Creveld syndrome patients. Hum Genet. 2007 Jan;120(5):663-70. Epub 2006 Sep 21.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17024374
- Valencia M, Lapunzina P, Lim D, Zannolli R, Bartholdi D, Wollnik B, Al-Ajlouni O, Eid SS, Cox H, Buoni S, Hayek J, Martinez-Frias ML, Antonio PA, Temtamy S, Aglan M, Goodship JA, Ruiz-Perez VL. Widening the mutation spectrum of EVC and EVC2: ectopic expression of Weyer variants in NIH 3T3 fibroblasts disrupts Hedgehog signaling. Hum Mutat. 2009 Dec;30(12):1667-75. doi: 10.1002/humu.21117.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19810119

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