Thanatophoric dysplasia

Thanatophoric dysplasia is a severe skeletal disorder characterized by extremely short limbs and folds of extra (redundant) skin on the arms and legs. Other features of this condition include a narrow chest, short ribs, underdeveloped lungs, and an enlarged head with a large forehead and prominent, wide-spaced eyes.

Researchers have described two major forms of thanatophoric dysplasia, type I and type II. Type I thanatophoric dysplasia is distinguished by the presence of curved thigh bones and flattened bones of the spine (platyspondyly). Type II thanatophoric dysplasia is characterized by straight thigh bones and a moderate to severe skull abnormality called a cloverleaf skull.

The term thanatophoric is Greek for "death bearing." Infants with thanatophoric dysplasia are usually stillborn or die shortly after birth from respiratory failure; however, a few affected individuals have survived into childhood with extensive medical help.

Frequency

This condition occurs in 1 in 20,000 to 50,000 newborns. Type I thanatophoric dysplasia is more common than type II.

Causes

Mutations in the FGFR3 gene cause thanatophoric dysplasia. Both types of this condition result from mutations in the FGFR3 gene. This gene provides instructions for making a protein that is involved in the development and maintenance of bone and brain tissue. Mutations in this gene cause the FGFR3 protein to be overly active, which leads to the severe disturbances in bone growth that are characteristic of thanatophoric dysplasia. It is not known how FGFR3 mutations cause the brain and skin abnormalities associated with this disorder.

Inheritance Pattern

Thanatophoric dysplasia is considered an autosomal dominant disorder because one mutated copy of the FGFR3 gene in each cell is sufficient to cause the condition. Virtually all cases of thanatophoric dysplasia are caused by new mutations in the FGFR3 gene and occur in people with no history of the disorder in their family. No affected individuals are known to have had children; therefore, the disorder has not been passed to the next generation.
Other Names for This Condition
• Dwarf, thanatophoric
• thanatophoric dwarfism
• thanatophoric short stature

Diagnosis & Management

Genetic Testing Information
• What is genetic testing? 
/ primer/testing/genetic testing
• Genetic Testing Registry: Thanatophoric dysplasia type 1 
• Genetic Testing Registry: Thanatophoric dysplasia, type 2 

Research Studies from ClinicalTrials.gov
• ClinicalTrials.gov 
https://clinicaltrials.gov/ct2/results?cond=%22thanatophoric+dysplasia%22

Other Diagnosis and Management Resources
• GeneReview: Thanatophoric Dysplasia 
https://www.ncbi.nlm.nih.gov/books/NBK1366

Additional Information & Resources

Health Information from MedlinePlus
• Health Topic: Craniofacial Abnormalities 
https://medlineplus.gov/craniofacialabnormalities.html
• Health Topic: Dwarfism 
https://medlineplus.gov/dwarfism.html
• Health Topic: Respiratory Failure 
https://medlineplus.gov/respiratoryfailure.html

Genetic and Rare Diseases Information Center
• Thanatophoric dysplasia 
Educational Resources

- MalaCards: thanatophoric dysplasia, type i
  https://www.malacards.org/card/thanatophoric_dysplasia_type_i

- MalaCards: thanatophoric dysplasia, type ii
  https://www.malacards.org/card/thanatophoric_dysplasia_type_ii

- Orphanet: Thanatophoric dysplasia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2655

Patient Support and Advocacy Resources

- International Skeletal Dysplasia Registry, UCLA
  https://www.uclahealth.org/ortho/isdr

- Little People of America, Inc.
  https://www.lpaonline.org/

- Little People UK
  https://littlepeopleuk.org/

- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/skeldysp.html

- The MAGIC Foundation
  https://www.magicfoundation.org/

Clinical Information from GeneReviews

- Thanatophoric Dysplasia
  https://www.ncbi.nlm.nih.gov/books/NBK1366

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Thanatophoric+Dysplasia%5BMAJR%5D%29+AND+%28thanatophoric+dysplasia%5BTA%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- THANATOPHORIC DYSPLASIA, TYPE I
  http://omim.org/entry/187600

- THANATOPHORIC DYSPLASIA, TYPE II
  http://omim.org/entry/187601
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12357475

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22045636
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3240715/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301540

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20034074

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19449430

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10696568

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18698630

Reprinted from Genetics Home Reference: 

Reviewed: October 2012
Published: August 20, 2019

Lister Hill National Center for Biomedical Communications
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