Townes-Brocks Syndrome

Townes-Brocks syndrome is a genetic condition that affects several parts of the body. The most common features of this condition are a malformation of the anal opening (imperforate anus), abnormally shaped ears, and hand malformations that most often affect the thumbs. People with this condition often have at least two of these three major features.

Other signs and symptoms of Townes-Brocks syndrome can include kidney abnormalities, mild to profound hearing loss, eye abnormalities, heart defects, foot abnormalities, and genital malformations. These features vary among affected individuals, even within the same family. Mild intellectual disability or learning problems have been reported in about 10 percent of people with Townes-Brocks syndrome.

Frequency

The prevalence of this condition is unknown. It is difficult to determine how frequently Townes-Brocks syndrome occurs because the varied signs and symptoms of this disorder overlap with those of other genetic syndromes.

Causes

Mutations in the SALL1 gene cause Townes-Brocks Syndrome. This gene provides instructions for making a protein that is involved in development before birth. The SALL1 protein acts as a transcription factor, which means it attaches (binds) to specific regions of DNA and helps control the activity of particular genes that direct the formation of many different tissues and organs before birth.

It is uncertain how SALL1 gene mutations result in the features of Townes-Brocks syndrome. Most mutations lead to the production of an abnormally short version of the SALL1 protein that malfunctions within the cell. The malfunctioning protein is thought to interfere with normal copies of the SALL1 protein, which are produced from the other copy of the SALL1 gene that does not have a mutation. This interference prevents the normal proteins from regulating gene activity. In addition, the malfunctioning protein may interact with other proteins, disrupting their function. For example, some research indicates that the abnormally short SALL1 protein interferes with proteins that control the formation of cellular structures called cilia. Cilia are important for the structure and function of many types of cells and the normal development of several tissues. Abnormalities in cilia can disrupt development and may contribute to the features of Townes-Brocks syndrome.

Some rare mutations prevent the gene from making any protein; this reduces by half the amount of SALL1 protein produced in cells. A shortage of functioning SALL1 protein, due to either type of mutation, likely impairs the regulation of genes that direct
the development of many different organs and tissues before birth. Interference by the malfunctioning SALL1 protein, if present, may disrupt other developmental processes and contribute to the birth defects associated with Townes-Brocks syndrome.

Inheritance Pattern

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

- anal-ear-renal-radial malformation syndrome
- deafness-imperforate anus-hypoplastic thumbs syndrome
- imperforate anus-hand and foot anomalies syndrome
- renal-ear-anal-radial syndrome (REAR)
- sensorineural deafness-imperforate anus-hypoplastic thumbs syndrome
- Townes syndrome

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  https://primer/testing/genetictesting
- Genetic Testing Registry: Townes-Brocks syndrome 1

Other Diagnosis and Management Resources

- GeneReview: Townes-Brocks Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1445
- MedlinePlus Encyclopedia: Ear Disorders (image)
  https://medlineplus.gov/ency/imagepages/17281.htm
- MedlinePlus Encyclopedia: Imperforate Anus
  https://medlineplus.gov/ency/article/001147.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Ear Disorders (image)
  https://medlineplus.gov/ency/imagepages/17281.htm
- Encyclopedia: Imperforate Anus
  https://medlineplus.gov/ency/article/001147.htm
• Health Topic: Hand Injuries and Disorders
  https://medlineplus.gov/handinjuriesanddisorders.html
• Health Topic: Hearing Disorders and Deafness
  https://medlineplus.gov/hearingdisordersanddeafness.html
• Health Topic: Kidney Diseases
  https://medlineplus.gov/kidneydiseases.html

Genetic and Rare Diseases Information Center
• Townes-Brocks syndrome

Educational Resources
• Cincinnati Children’s Hospital Medical Center: Anorectal Malformations
  https://www.cincinnatichildrens.org/health/a/anorectal-malformations
• MalaCards: townes-brocks syndrome
  https://www.malacards.org/card/townes_brocks_syndrome
• Orphanet: Townes-Brocks syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=857

Patient Support and Advocacy Resources
• National Association of the Deaf
  https://www.nad.org/
• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/townes-brocks-syndrome/
• Resource List from the University of Kansas Medical Center: Deafness and Hard of Hearing
  http://www.kumc.edu/gec/support/hearing.html

Clinical Information from GeneReviews
• Townes-Brocks Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1445

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28townes-brocks+syndrome%5BTIAB%5D%29+OR+%28townes+syndrome%5BTIAB%5D%29%29+AND+english%5Blan%5D+AND+humain%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D
Catalog of Genes and Diseases from OMIM

- TOWNES-BROCKS SYNDROME 1
  http://omim.org/entry/107480
- TOWNES-BROCKS SYNDROME 2
  http://omim.org/entry/617466

Medical Genetics Database from MedGen

- Townes-Brocks syndrome 1

Sources for This Summary

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10051003
Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1734298/

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19247946

Reprinted from Genetics Home Reference: 

Reviewed: June 2020
Published: August 17, 2020

Lister Hill National Center for Biomedical Communications
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